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Visual Dysfunction in Patients with Traumatic Brain Injury: A Systematic Review

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PREFACE

Quality Enhancement Research Initiative's (QUERI) Evidence-based Synthesis Program (ESP) was established to provide timely and accurate syntheses of targeted healthcare topics of particular importance to Veterans Affairs (VA) clinicians, managers and policymakers as they work to improve the health and healthcare of Veterans. The ESP disseminates these reports throughout the VA, and some evidence syntheses inform the clinical guidelines of large professional organizations.

QUERI provides funding for four ESP Centers and each Center has an active university affiliation. The ESP Centers generate evidence syntheses on important clinical practice topics, and these reports help:

- develop clinical policies informed by evidence;
- guide the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- set the direction for future research to address gaps in clinical knowledge.

In 2009, the ESP Coordinating Center was created to expand the capacity of HSR&D Central Office and the four ESP sites by developing and maintaining program processes. In addition, the Center established a Steering Committee comprised of QUERI field-based investigators, VA Patient Care Services, Office of Quality and Performance, and Veterans Integrated Service Networks (VISN) Clinical Management Officers. The Steering Committee provides program oversight, guides strategic planning, coordinates dissemination activities, and develops collaborations with VA leadership to identify new ESP topics of importance to Veterans and the VA healthcare system.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP Coordinating Center Program Manager, at Nicole.Floyd@va.gov.

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EXECUTIVE SUMMARY

INTRODUCTION

In 2009, approximately 3.5 million people sought treatment related to a traumatic brain injury (TBI) in the United States (U.S.), just over 1% of the U.S. population. Researchers estimate that approximately 15% of Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn (OEF/OIF/OND) U.S. Service Members have incurred TBI during deployment. This equates to 390,000 of the 2.6 million Service Members who have deployed as of 2014. Given that intact visual functioning depends on portions of the brain interacting in complex ways, there are multiple potential mechanisms through which TBI can result in visual dysfunction. To provide relevant data for policymakers, optometrists, ophthalmologists, rehabilitation specialists, and others who provide services for Veterans with TBI history, we conducted a systematic review of the prevalence and types of visual dysfunction in individuals with a history of TBI.

Key Questions are:

Key Question 1: What is the prevalence or incidence of visual dysfunction in a general population of individuals who have been diagnosed with a TBI?

Key Question 2: What are the types of visual dysfunction reported by individuals who have been diagnosed with a TBI and are presenting to eye care clinics?

METHODS

We used a previous systematic review on visual problems in traumatic brain injury to identify studies published prior to 2009. We searched Medline (OVID), PsychINFO (OVID), the Cochrane Register of Controlled Trials (OVID), SPORTDiscus, Rehabilitation & Sports Medicine Source (EBSCO), and Rehabdata (National Rehabilitation Information Center) for studies published between January 1st, 2009 and March 27th, 2014. We included studies reporting visual dysfunctions likely to be treated in eye care clinics in patients over 5 years of age with a history of TBI diagnosis of any severity; studies included for Key Question 1 were based on unselected populations (*ie*, participants not selected for inclusion in the study based on visual dysfunction). Data abstraction and quality assessment were dual reviewed by investigators. Standard quality criteria were applied as relevant for each Key Question. We provide both qualitative synthesis of results and evidence tables for each type of visual dysfunction identified.

RESULTS

We examined 1299 titles and abstracts, selecting 118 articles for full-text review. We report the results of 12 primary studies meeting inclusion criteria for Key Question 1, and 4 primary studies that provide data for Key Question 2. Study results were grouped and synthesized according to common sample characteristics. Evidence from a large retrospective cohort study of U.S. Service Members who were diagnosed with visual dysfunction and treated in military healthcare settings suggests that visual dysfunction is infrequently diagnosed in unscreened populations

of U.S. Service Members with TBI history, occurring in less than 1% of the population in most cases. Disorders of accommodation and refraction are slightly more common, with a frequency of 7.3% in this population. Other studies included in this review focused on Veterans seen at the Department of Veterans Affairs (VA) Polytrauma Rehabilitation Centers (PRCs) and Polytrauma Network Sites (PNSs). Visual dysfunction was much more frequent in these populations, with estimates of over 50% for many conditions such as accommodation and refraction disorders, convergence insufficiency or dysfunction, dry eye syndrome, photosensitivity, pursuit or saccadic dysfunction, and self-reported visual impairments. Table 1 summarizes results across studies.

CONCLUSIONS

Studies included in this review report a wide range in the frequency of visual dysfunction in people with TBI history. The range of estimates is likely due to differences in setting and patient population across studies. While some studies reported results from individuals regardless of current symptoms, many of the included studies were conducted in VA PRCs and PNSs, clinics that only serve Veterans who have current symptoms as well as other, often serious, comorbidities. Overall, visual dysfunction diagnosed in U.S. Service Members treated in military healthcare settings is uncommon, occurring in less than 1% of individuals for most disorders. However, studies of Veterans with TBI history and current symptoms who are treated in TBI rehabilitation clinics report much higher frequencies, often over 50% for many types of visual dysfunction.

Table 1. Summary of Findings: Ranges of Visual Dysfunction Frequencies Across Studies

	Studies including patients with TBI history regardless of current symptoms		**Studies including patients with TBI history who all have current symptoms**
Outcome	**Unscreened**	**Screened**	**Screened**
Accommodation Dysfunction and Refractive Errors	7.3% (1 study)	3.0% (1 study)	19.0 - 66.7% (6 studies)
Convergence Insufficiency or Dysfunction	No studies	No studies	11.0 - 62.5% (6 studies)
Diplopia	No studies	No studies	3.0 - 40.0% (4 studies)
Dry Eye	0.1% (1 study)	2.0% (1 study)	93.0% with one or more positive tests (1 study)
Nystagmus or Fixation Dysfunction	No studies	No studies	0.0 - 23.4% (5 studies)
Photosensitivity, Photophobia, or Light Sensitivity	No studies	5.0 – 54.0% (1 study, diagnosed vs self-report)	51.0 - 59.0% (3 studies, all self-report)
Pursuit or Saccadic Dysfunction	No studies	No studies	2.0 - 70.8% (5 studies)
Strabismus and Cranial Nerve Palsy	0.6% (1 study)		0.0 - 37.5% (4 studies)
Visual Field Defect	0.1% (1 study)	2.0% (1 study)	0.0% - 38.8% (3 studies)
Visual Impairment or Dysfunction, Diagnosed	0.4% (1 study)	22.0% (1 study)	8.5% (1 study)
Visual Impairment or Dysfunction, Self-Reported	No studies	8.8 - 47.0% (3 studies)	32.2 - 77.4% (6 studies)

EVIDENCE REPORT

INTRODUCTION

There is a high prevalence of traumatic brain injury (TBI) in both military and non-military populations. The Centers for Disease Control and Prevention reported that, in 2009, approximately 3.5 million people (just over 1% of the population) received healthcare treatment related to a TBI in the United States (U.S.).[1,2] Researchers estimate that approximately 15% of Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn (OEF/OIF/OND) Service Members have incurred TBI during deployment, equating to 390,000 of the 2.6 million who have deployed through 2014.[3,4] The risk that patients with a history of TBI will experience symptoms over the long-term depends in part on the severity of injury. However, many patients with even mild TBI (mTBI) present with long-term symptoms, though it is unclear whether these symptoms are directly attributable to the brain injury.[5,6]

Vision-related symptoms are increasingly recognized as one possible long-term sequelae of TBI. Given that intact vision depends on portions of the brain interacting in complex ways, there are multiple potential mechanisms through which trauma can result in visual deficits. In brief, the visual pathways are organized in afferent and efferent arcs. The afferent arc receives and processes visual stimuli while the efferent arc moves the eyes in the direction of the object of visual regard. In the midst of this complex milieu, there exist anticipatory and interpretive systems which add neurocognitive input to the visual imagery.[7] TBI can cause a wide variety of injuries to the visual system including anterior and posterior visual pathway damage affecting visual acuity, color vision, and resultant visual fields defects. Cranial nerve injuries can manifest as diplopia and nystagmus due to oculomotor dysfunction.[8] Patients with TBI history may experience photosensitivity or difficulty reading, or may exhibit abnormal fixation and accommodative dysfunction.[9]

Although vision is an important sensory modality for critical activities of daily living (ADLs), the diagnosis and treatment of functional vision deficits has been inconsistent.[10] In 2008, the VA issued a policy statement requiring all TBI patients seen at Polytrauma Rehabilitation Centers (PRCs) be seen by an optometrist or ophthalmologist for a visual health examination, but the vision screening and treatment of other Veterans and U.S. Service members treated outside of PRCs varies.[11] Additionally, there are ongoing efforts in the VA and Department of Defense (DoD) to determine relationships among visual symptoms and TBI history, including efforts to examine oculomotor tracking as a way to detect mTBI.[12] To help inform VA policymakers and clinicians responsible for TBI program planning and service delivery, we conducted a systematic review of the literature examining the prevalence and type of visual dysfunction in military and non-military populations with a history of TBI.

METHODS

TOPIC DEVELOPMENT

This topic was submitted to the ESP Coordinating Center for development by Mary G. Lawrence, MD, MPH, Interim Director, VA/DoD Vision Center of Excellence (VCE), in collaboration with other key stakeholders Felix Barker, Associate Director, Research, Rehabilitation and Reintegration, Vision Center of Excellence, Salisbury VAMC; Christopher Moore, PhD, VA Scientific Program Manager for Sensory Systems and Communication Disorders Program; and Stuart W. Hoffman, PhD, Scientific Program Manager for Brain Injury, Rehabilitation Research and Development Service, TBI Point of Contact and Subject Matter Expert, Office of Research and Development. We also received input from a technical expert panel (see Appendix A).

The goal of this evidence report is to summarize current evidence examining the prevalence and types of visual dysfunction and impairment among patients diagnosed with TBI. Understanding the scope of visual disorders among these populations will aid the VHA in determining appropriate screening strategies for visual dysfunction and impairment among returning Veterans diagnosed with TBI. Better understanding of the specific visual dysfunctions that may be associated with TBI will also enable appropriate intervention within the vision care system. A secondary goal is to develop a strategy for the monitoring of outcomes from the assessment and management of TBI-related visual disorders, thus potentially producing improved outcomes in the overall rehabilitation and reintegration of affected Veterans.

The Key Questions, which were developed in concert with the stakeholders, are as follows:

Key Question 1: What is the prevalence or incidence of visual dysfunction in a general population of individuals who have been diagnosed with a TBI?

Key Question 2: What are the types of visual dysfunction reported by individuals who have been diagnosed with a TBI and are presenting to eye care clinics?

SEARCH STRATEGY

We identified an existing systematic review of visual dysfunction in patients with TBI published in 2009 by Adams and colleagues.[13] Because of overlapping Key Questions and inclusion criteria in that review and our current report, we based our search prior to 2009 on the studies included in the Adams 2009 review.[13] We also searched Medline (OVID), PsychINFO (OVID), and the Cochrane Register of Controlled Trials (OVID), SPORTDiscus, Rehabilitation & Sports Medicine Source (EBSCO), and Rehabdata (National Rehabilitation Information Center) for studies published between January 1st, 2009 and March 27th, 2014. The search strategy is reported in Appendix B. We obtained additional articles from systematic reviews, reference lists of pertinent studies, reviews, editorials, and by consulting clinical and research experts. All citations were imported into an electronic database (EndNote X4).

STUDY SELECTION

We included studies reporting outcomes in patients with a history of TBI diagnosis of any severity. We included studies using a definition of TBI consistent with that used in the Adams 2009 review, which is inclusive of cases meeting both American Congress of Rehabilitation Medicine (ACRM) and VA/DoD criteria: "This report will include clinical research of TBI caused by detonation or other mechanisms of diffuse closed head injury such as diffuse axonal injury from motor vehicle accidents, falls and sport/recreational activities that are likely to resemble the types of exposure experienced by our newest Veteran population; it will exclude causes of focal brain injury such as stroke, infection, and tumors."[13] Studies reporting only data on patients with ocular injuries were excluded, though studies that included a portion of patients with ocular injuries were included. Patients under 5 years of age were excluded. For Key Question 1, but not Key Question 2, we excluded studies reporting a population selected for the study based even in part on visual dysfunction.

We included visual dysfunction and outcomes that would likely be diagnosed or treated in an eye care clinic (*eg*, oculomotor disorders, visual acuity loss, strabismus, convergence insufficiency, diplopia, hemianopsia, other homonymous visual field defects, photosensitivity, nystagmus). We excluded physical injuries to the eye such as open globe injuries or retinal hemorrhage; shaken baby syndrome; visually administered cognitive assessments that do not assess a primarily visual outcome (*eg*, visual agnosia, spatial neglect, visuospatial abilities, visual scanning, visually administered tests primarily assessing memory, executive functioning including Stroop tests, academic achievement, reading, writing, math, language abilities, reaction time, attention, or concentration); vision-related outcomes that are primarily neurocognitive in nature and would not be diagnosed or treated in an eye care clinic; brain imaging results not reporting associated visual dysfunctions; and self-reported global vision difficulties reported on general screening tools (*eg*, single items on screening questionnaires assessing vision problems, blurred vision, double vision, trouble seeing, or light sensitivity). Research conducted at any length of time since injury was included.

For Key Question 1, included settings were primary care settings, school or athletic programs, or any settings serving a general population that is not being examined for suspected TBI-related vision symptoms. Studies of prevalence or incidence were included if they were cohort, case-control, controlled trials, or studies with a control or comparison group including self as control. Studies with fewer than 50 participants with a history of TBI were excluded.

For Key Question 2, included settings were eye care clinics. All study designs were considered. Consistent with the inclusion criteria for the Adams review, studies reporting type of visual dysfunction in eye care clinic populations were excluded if they reported fewer than 10 cases with visual dysfunction.

We published our key questions and abstract online so that they were available for public review.

DATA ABSTRACTION

We abstracted data from each included study on study design; sample size; TBI definition; participant selection and characteristics; key moderators and potential confounders including

mechanism of injury, time since injury, and ocular injuries; outcome measures; and results. These data are reported in Tables 3 to 12. Data was abstracted by one investigator and reviewed for accuracy by at least one additional investigator.

QUALITY ASSESSMENT

We assessed the quality of included studies pertaining to both Key Questions. Because the focus of this review is on estimating prevalence, we examined study quality using the Quality in Prognostic Studies (QUIPS) study appraisal tool[14] and highlight factors such as sample selection and outcome assessment which have the potential to impact prevalence estimates. Study data relevant to risk of bias was extracted by one investigator and reviewed for accuracy by at least one additional investigator. Specific study quality factors are summarized as relevant for each Key Question.

DATA SYNTHESIS

We constructed evidence tables showing the study characteristics and results for all included studies organized by outcome. We critically analyzed studies to compare their characteristics, methods, and findings. We compiled a summary of findings for each outcome category and key question, and drew conclusions based on qualitative synthesis of the findings. We did not combine the studies in a quantitative manner via meta-analysis because of the heterogeneity of study characteristics, particularly because studies did not report proportions of patients with different levels of TBI severity and those with ocular injuries, both of which likely influence the outcomes of interest. The synthesis was conducted by the principal investigator, though all results were reviewed with the team of investigators to review and obtain consensus on the reported findings.

RATING THE BODY OF EVIDENCE

Key questions focus on prevalence estimates and common types of visual dysfunctions treated in clinical settings; therefore, we did not formally rate the strength of the body of evidence as most rating schemes are applicable to strength of evidence for interventions or diagnostic tests (*eg*, Grading of Recommendations Assessment, Development, and Evaluation (GRADE) criteria).[15]

PEER REVIEW

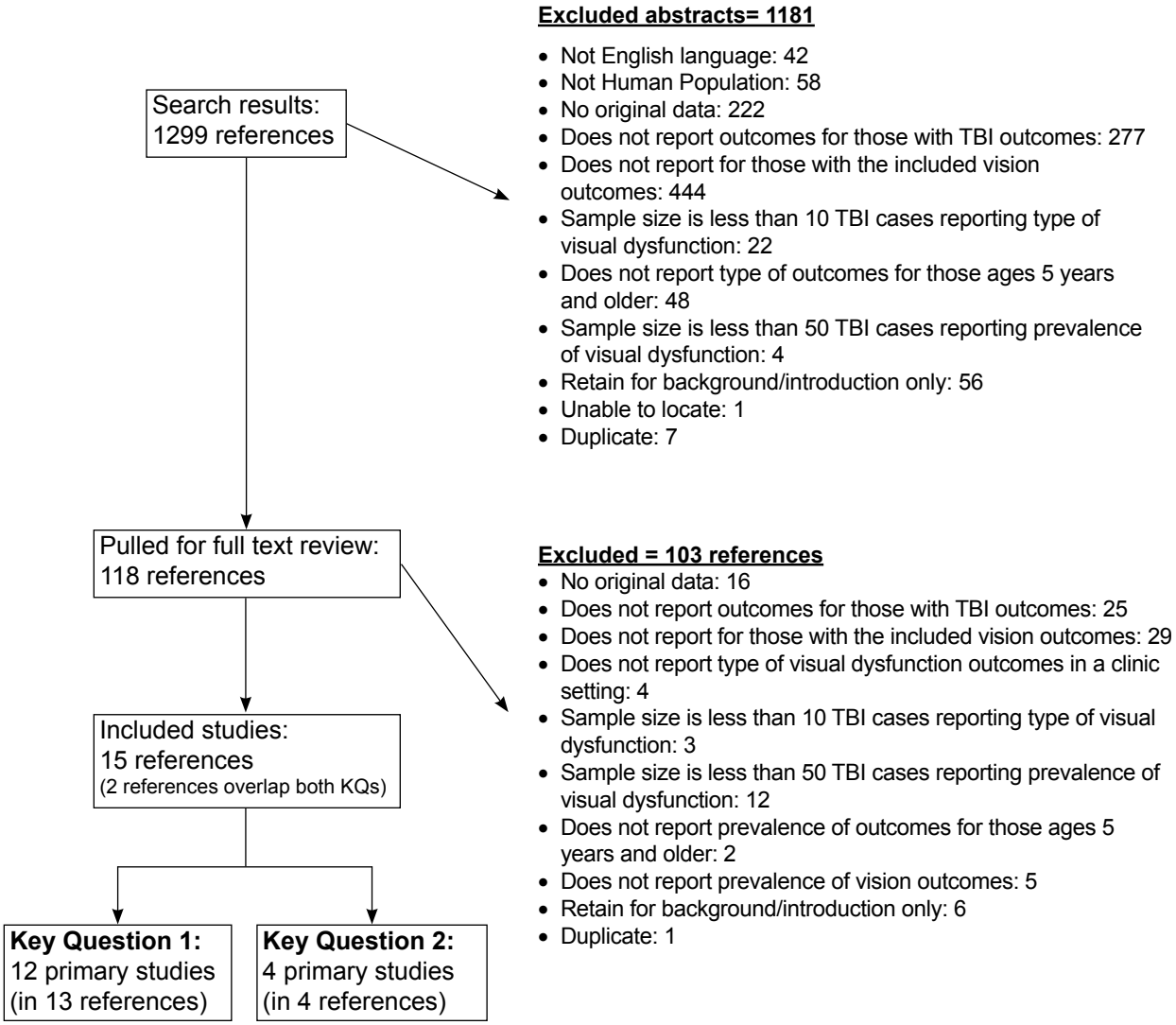
A draft version of this report was reviewed by 8 technical experts and clinical leaders. Their comments and the authors' responses are presented in Appendix C.

RESULTS

LITERATURE FLOW

We reviewed 1299 titles and abstracts from the electronic search. After applying inclusion/exclusion criteria at the abstract level, 118 full-text articles were reviewed, as shown in Figure 1. Of the full-text articles, we excluded 103 that did not meet inclusion criteria. We grouped the studies by outcome and Key Question. Figure 1 details the exclusion criteria and the number of references related to each of the Key Questions. We identified 12 primary studies (13 references) that addressed Key Question 1, and 4 primary studies that addressed Key Question 2; 2 studies provided information addressing both Key Questions for a total of 13 included primary studies published in 15 papers.[8,9,16-27] Two studies reported results for U.S. or Canadian civilians[16,22]; the rest reported results for U.S. Veterans or active-duty Service Members of the U.S. military. Table 2 shows the characteristics of the primary studies, and the following sections detail findings according to Key Questions, outcomes, and moderators.

Figure 1: Literature Flow Chart



KEY QUESTION 1: What is the prevalence or incidence of visual dysfunction in a general population of individuals who have been diagnosed with a TBI?

Twelve studies (published in 13 papers) of patients with TBI history met inclusion criteria for Key Question 1. The prevalence of visual dysfunction ranged widely according to the patient population examined, study setting, and whether or not patients underwent examination to screen for visual dysfunction. We excluded studies only providing data on patients who were referred or self-referred to the study based on visual complaints because these studies do not provide accurate data on the prevalence of visual dysfunction in unselected populations (*ie*, participants not selected for inclusion in the study based on visual dysfunction) with history of TBI. Sample selection criteria for each study are documented in Table 2. None of the studies meeting inclusion criteria stratified results based on TBI severity. There were 2 main types of study settings: settings that treat patients *regardless* of current, suspected TBI-related symptoms, and settings that treat *only* patients with current, suspected TBI-related symptoms.

Summary of findings from studies of patients in settings that treat patients regardless of current symptoms

Four studies included general populations of patients with TBI history *regardless* of current symptoms. In these studies, participants were all patients with TBI history (1) seen at a post-deployment clinic for a general medical appointment and screened for vision-related symptoms,[18] (2) with military record diagnostic data on visual dysfunctions,[19] (3) presenting to a Canadian emergency department related to a motor vehicle crash and screened for post-concussive symptoms including vision-related symptoms,[22] and (4) who had TBI evaluations performed at the VA and were screened for neurobehavioral symptoms including vision-related symptoms.[26]

One study by Dougherty and colleagues of an unscreened group of U.S. Service Members used a large administrative database to identify those with clinically diagnosed visual dysfunction.[19] This study reported data on clinical diagnosis in an unscreened group of U.S. Service Members, and excluded individuals with ocular injury and diagnosis of ocular or vision disorders prior to the TBI. This study found low rates of individual types of visual problems or dysfunction (0.1% to 7.3%, see Table 1), and reported that, overall, 11% of patients were diagnosed with one or more types of visual dysfunction. Unlike studies in which all participants are screened, this study provides an assessment of clinically significant impairment because patients experienced visual dysfunction to a degree that resulted in clinical presentation and diagnosis.

The other 3 studies used self-report measures to screen participants[18,22,26] and found higher rates of visual dysfunction (8.8% to 54%, see Table 1) than the data from Dougherty and colleagues that reported on unscreened patients with diagnosed visual dysfunction. One of these screening studies[18] also referred patients who self-reported visual problems for eye examinations, and the resulting visual diagnoses were less frequent upon examination compared to self-report (2% to 22%, see Table 1).

Summary of findings from studies of only patients with current symptoms

The second main type of study population examined in this review came from studies conducted

in Polytrauma Rehabilitation Centers (PRCs) and Polytrauma Network Sites (PNSs) within the VA.[8,9,17,20,21,23-25,27] Both types of treatment facilities provide interdisciplinary, rehabilitation care to Veterans who experienced TBI or polytrauma, but serve populations with different care needs. The 5 PRCs provide acute, inpatient care to those with more complex and severe TBI or polytrauma. The 23 PNSs provide care to those who are discharged from PRCs and need continued rehabilitation services, as well as to Veterans who require less intensive care for their TBI or polytrauma. In 2008, the VA began requiring all PRC patients with a history of TBI to "have a TBI-specific ocular health and visual functioning examination performed by an optometrist or ophthalmologist."[11] While Veterans treated at PRCs and PNSs differ in symptom severity and complexity, their results are grouped in this report because data from PRCs and PNSs were commonly aggregated in the included studies. However, results tables for each type of visual dysfunction stratify findings according to inpatient versus outpatient status, when these data were available in the original studies.

Because PRC and PNS patients receive care based on current symptoms, some of which may be vision-related, and because the patients undergo eye exams designed to screen for many types of visual problems, it is not surprising that the rates of visual dysfunction in these patient populations were generally much higher (0 to 93%, see Table 1) than in general VA populations.

A summary of the range of frequencies for each type of visual dysfunction included in this report is illustrated in Table 1, with results separated to reflect different study populations.

Table 1. Summary of Findings: Ranges of Visual Dysfunction Frequencies Across Studies

	Studies including patients with TBI history regardless of current symptoms		**Studies including patients with TBI history who all have current symptoms**
Outcome	Unscreened	Screened	Screened
Accommodation Dysfunction and Refractive Errors	7.3% (1 study[19])	3.0% (1 study[18])	19.0 - 66.7% (6 studies[9,17,20,21,24,27,28])
Convergence Insufficiency or Dysfunction	No studies	No studies	11.0 - 62.5% (6 studies[9,17,20,21,24,27,28])
Diplopia	No studies	No studies	3.0 - 40.0% (4 studies[9,20,21,27,28])
Dry Eye	0.1% (1 study[19])	2.0% (1 study[18])	93.0% with one or more positive tests (1 study[8])
Nystagmus or Fixation Dysfunction	No studies	No studies	0.0 - 23.4% (5 studies[9,17,20,21,24,27])
Photosensitivity, Photophobia, or Light Sensitivity	No studies	5.0 – 54.0% (1 study, diagnosed vs self-report[18])	51.0 - 59.0% (3 studies, all self-report[9,21,24,28])
Pursuit or Saccadic Dysfunction	No studies	No studies	2.0 - 70.8% (5 studies[9,17,21,24,27])
Strabismus and Cranial Nerve Palsy	0.6% (1 study[19])		0.0 - 37.5% (4 studies[9,17,21,24,27])
Visual Field Defect	0.1% (1 study[19])	2.0% (1 study[18])	0.0% - 38.8% (3 studies[17,20,27])
Visual Impairment or Dysfunction, Diagnosed	0.4% (1 study[19])	22.0% (1 study[18])	8.5% (1 study[17])
Visual Impairment or Dysfunction, Self-Reported	No studies	8.8 - 47.0% (3 studies[18,22,26])	32.2 - 77.4% (6 studies[9,17,21,23,25,27,28])

Methodological considerations

In addition to participant populations and selection factors, another factor that can influence prevalence estimates relates to outcome assessment.[14] The included studies used a variety of assessment methods to evaluate different types of visual dysfunction. These outcomes and assessment methods are reported in the results tables for each type of visual dysfunction. Studies based on administrative databases likely underestimate prevalence of outcomes as populations are not screened and diagnostic outcome data may be inconsistently entered.[19,22,26] In contrast, studies using clinic-based outcome assessments may be biased if providers or patients are aware of study hypotheses, particularly if outcomes require subjective assessment (*ie*, there is the potential for outcome ascertainment bias). None of the studies that employed clinic-based outcome assessment methods described outcome validation methods such as dual or blinded assessment, and therefore the potential for biased results from these studies is unclear.[8,9,17,18,20,21,23-25,27]

Key Questions in this systematic review do not focus on assessing causality or determining if visual dysfunction is more common in individuals with TBI history compared to those without. Though some included studies report data on control groups without TBI history, we did not assess study quality related to causal associations between TBI history and visual dysfunction.

Table 2. Sample and Study Characteristics

Citation and KQ	Study design; TBI Comparison group	TBI, control sample size	TBI severity; definition	Mechanism of injury; time since injury	Ocular injuries	Age in years, M (SD)	Gender; Race/ Ethnicity	Sample characteristics and selection
Alvarez, 2012[16] KQ2	Case series; None	557	NR	MVCs (70.9%), falls (14.7%), a strike or blow to the head (9.2%), sports injury (2.5%), other (2.7%; gunshot, assaults, or unspecified) Time NR	NR	40.3 (SD 17.4, range 5-89)	338/557 (61%) male	Inpatients with vision symptoms referred from Kesser Institute of Rehabilitation, John F. Kennedy Medical Center, and Robert Wood Johnson University Hospital in New Jersey. Outpatients: New Jersey private practice. January 1989 to February 2003; Sample is approximately one half of all neurologically impaired patients referred by neurologists.
Brahm, 2009[17] KQ1	Cross-sectional; None	192	Mild, moderate, and severe. Inpatients: No definition; Outpatients: Mild TBI screening using expanded version of 3-item DVBIC tool	57/68 (84%) blast, 11/68 (16%) non-blast in the PRC- group. Time NR	26/68 (38.2%) had "ocular injuries"	28.6 (median = 26.0) for PRC inpatients.	65/68 (96%) male	Palo Alto PRC inpatients: 68 consecutive patients; December 2004 to April 2008 Palo Alto PNS outpatients: 124 consecutive patients; August 2006 to December 2007
Bulson, 2012[18] KQ1 & KQ2	Case series and cross-sectional data; None	100 (KQ 1) 33 (KQ 2)	NR; TBI diagnosis given at initial post-deployment evaluation by a medical doctor.	Multiple blast injuries (69%), blasts associated with MVCs (13%), single blasts (10%), falls (7%), isolated MVCs (1%) Time NR	NR	29.9 (range 21-55)	99% male	Portland VA Medical Center Post-deployment Clinic: 185 OEF/OIF Veterans; January 2009 to 2012
Cockerham, 2013[8] KQ1	Case control; Recruited 18 men similar age range, ethnicity, but without TBI	53, 18	32% = mild, 49% = moderate, 19% = severe; definition NR	44/53 (83%) blast, 6/53 (11%) MVC, 3/53 (6%) fall Time ranged from 1-60 months (median = 6 months).	Eyes with open-globe injury and those using topical ocular medications were excluded	26 (range 19-46)	100% male 34/53 (65%) White, 19/53 (35%) non-White.	VA Palo Alto PRC inpatients; began testing tear production in 2006 in inpatients and former inpatients returning for eye examinations. No report of consecutive patient selection.

Citation and KQ	Study design; TBI Comparison group	TBI, control sample size	TBI severity; definition	Mechanism of injury; time since injury	Ocular injuries	Age in years, M (SD)	Gender; Race/ Ethnicity	Sample characteristics and selection
Dougherty, 2011[19] KQ1	Retrospect-ive cohort; same patient group with non-TBI blast injury	837, 1417	NR; rating system used was 0 = no TBI, 1 = minor, 2 = moderate, 3-5 = serious to critical according to ICD-9-CM (Thurman et al 1995) and AIS (Gennarelli et al 2005)	All TBI and control participants were injured by blast exposure Time NR, based on data collected during deployment in the combat zone	"Those who sustained eye injury were excluded from this analysis"	TBI: Median = 22 (range 18-59) Control: Median = 23 (range 18-59)	99.4% male Control = 98.7% male	Expeditionary Medical Encounter Database; March, 2004 to February, 2007: Medical records completed "in the combat zone, nearest to the point of injury" merged with DOD records. All had blast exposure. "US Service members who met the following criteria were included" suggesting all eligible participants included. Inclusion criteria stated "having only one recorded injury event and having not received a diagnosis of ocular or visual disorder prior to the injury event."
Goodrich, 2013[9] Goodrich, 2013[21] KQ1	Cross-sectional; None	100	27/98 Mild; 71/98 Moderate-Severe; Severity obtained from a DVBIC evaluation record, physician entry, and ACRM criteria applied to chart review	50/100 blast, all in Afghanistan or Iraq. 50/100 non-blast: MVC (58%); fall (16%); assault (12%); pedestrian struck by vehicle, gunshot, bicycle injury (4% each); snowboard injury (2%). Most occurred in the U.S. M = 8 months (range 2-56 wks) PTSD: M = 15.3 months No PTSD: M = 2.9 months Blast: M = 1.01 yrs (SD = 1.18) No Blast: M = .32 yrs (SD = .52)	29/98 "eye/ orbit trauma" Non-blast: 29% Blast: 31%	PTSD: M = 32.8 (range 19-59) No PTSD: M = 26.37 (range 19-63) No Blast: 29 (range, 19 to 63); Blast: 29 (range, 19 to 55)	95% Male Non-blast: 48/50 (96%) male. Blast: 47/50 (94%) male.	Palo Alto PRC inpatients with documented eye examinations with optometry. 16/50 blast TBI patients exposed to more than one blast; 4/50 non-blast TBI patients had past head injuries. No report of consecutive patient selection.

Citation and KQ	Study design; TBI Comparison group	TBI, control sample size	TBI severity; definition	Mechanism of injury; time since injury	Ocular injuries	Age in years, M (SD)	Gender; Race/ Ethnicity	Sample characteristics and selection
Goodrich, 2007[20] KQ1	Cross-sectional; None	50	NR	Blast = 50%; MVCs = 26%; Assault = 8%; Falls = 8%; Gunshot and/or shrapnel wounds = 4%; Anoxia = 4%. Combat = 59%. Time NR	17 (34.0%) "eye or orbit damage"	M = 28.1 (median 26, range 19-56)	45/50 (90%) male	Palo Alto PRC: Comprehensive vision examinations of OEF/OIF inpatients injured during combat or deployment from December 2004 to November 2006. "A specific eye complaint was unnecessary for referral, and the clinic attempted to see all Veterans and active-duty personnel admitted to the PRC."
Hartvigsen, 2014[22] KQ1	Cross-sectional; None	1716	100% Mild; endorsed one or more: amnesia or loss of memory; LOC, confusion or disorientation; excluded those with LOC > 30 mins.	All MVCs Included those who made an insurance claim within 42 days of injury, followed up at 6 weeks and 3, 6, 9, and 12 months following the insurance claim	NR	M = 37.7 (16.1)	812/1716 (47.3%) male	December, 1997 to November, 1999. All traffic injuries in persons 18 years or older who made an insurance claim in Saskatchewan, Canada.
Lemke, 2013[23] KQ1	Case control; Healthy controls (age M = 59, gender = 39% male); comparison data from a different study	60	Mild 37%, Moderate or Severe 38%, Penetrating 25%; Severity based on duration of LOC, PTA, GCS, history of penetrating head injury, imaging	Blast exposure 8.7 months (range 2-82 months) to initial testing	No open globe injury	Mean = 27	95% male	VHA hospital rehabilitation center; December, 2006 to January, 2012. TBI from combat blast exposure. Consecutive patients.
Lew, 2011[26] KQ1	Retrospect-ive cohort; Deployed non-TBI patients	12,521 9,196	Mild 85.4%; definition NR	Deployment-related TBI, including blast; blast exposure in 83.3% of cases, 70.4% of controls. Time NR	NR	31.3 (8.6)	93.9% male	Retrospective record review of 36,919 TBI evaluations performed in VHA between Oct 2007 and June 2009. 12,521 with deployment-related TBI and 9106 without TBI. Excluded patients with non-deployment TBI. Sample selection not specified, implies inclusion of all records.

Citation and KQ	Study design; TBI Comparison group	TBI, control sample size	TBI severity; definition	Mechanism of injury; time since injury	Ocular injuries	Age in years, M (SD)	Gender; Race/ Ethnicity	Sample characteristics and selection
Lew, 2009[25] KQ1	Cross-sectional; None	62	Mild, n=25 (40.3%) Moderate, n=12 (19.4%) Severe, n=25 (40.3%) Definition NR	Blast exposure M = 238.5 days	NR	27.3 (7.0)	93.5% male 74.2% Caucasian	Palo Alto PRC patients admitted Dec 2004 to March 2008 not previously admitted to the PRC for TBI treatment. Patients with blast-related TBI who completed both hearing and vision evaluations. "Retrospective chart review on all new admissions." 79 patients with blast-related TBI had hearing and vision evaluations ordered, but only 62 completed evaluations and were included.
Lew, 2007[24] KQ1	Cross-sectional; None	62	NR; 50% reported LOC; 31% reported only alteration of consciousness	79% blast, 8% MVC, 8% blunt trauma, 3% penetrating head injuries Time NR	NR	NR	NR	Palo Alto PNS; July 2006 to February 2007; 89% OEF/OIF Veterans, 5% Veterans from prior wars, 6% did not have combat related injuries (the latter 2 groups were retained to accurately represent the population flagged by the screening process). 71% PTSD, 55% Cognitive Disorder, 42% Both, 16% Neither. Consecutive participants.
Magone, 2014[28]	Case series	31	Mild; LOC for up to 30 min or an alteration in mental state and/ or memory loss for less than 24 hours	Blast-induced M = 50.5, SD = 19.8 months since injury, range 16-91 months	None	30.5(8.3)	94% male	All Washington DC VAMC eye clinic patients with blast induced mTBI; January 2009-December 2011.
Stelmack, 2009[27] KQ1 & KQ2	Case series and cross-sectional data; None	88	NR	NR	6% = orbit/ eye trauma	M = 31	92% male	Hines PNS; October 2005 to March 2008. "The majority (88%) were injured in OEF or OIF. Most (95%) presented with nonpenetrating injuries." No report of consecutive patient selection: "A list of patients was provided by a social work care manager and the Rehabilitation Service Line Coordinator."

Note. M = Mean; ED = Emergency Department; TBI = Traumatic Brain Injury; KQ = Key Question; NR = Not Reported; PRC = Polytrauma Rehabilitation Center; PNS = Polytrauma Network Site; MVC = Motor Vehicle Crash; DVBIC = Defense and Veterans Brain Injury Center; Abbreviated Injury Scale = AIS; DOD = Department of Defense; ACRM = American Congress of Rehabilitation Medicine; GCS = Glasgow Coma Scale; LOC = Loss of Consciousness, PTA = Posttraumatic Amnesia.

Summary of Findings

The following sections describe the findings from studies addressing Key Question 1 in this review. The sections are presented alphabetically according to visual dysfunction outcome, and include prevalence estimates from included studies as well as comparison data, when available.

Accommodation Dysfunction and Refractive Errors Findings

Seven studies described in 8 publications reported data on accommodation and refraction dysfunction in individuals with a history of TBI. These results are summarized in Table 3. Frequency of accommodation dysfunction and refractive errors varied greatly across the 6 studies reporting estimates not stratified by potentially confounding factors, ranging from under 10 percent in 2 studies,[18,19] around 20 percent in 3 studies,[20,24,27] to 66.7% in one study.[9,21] Only one study included a control group: Dougherty and colleagues report a 7.3% frequency of disorders of accommodation and refraction for those with TBI history compared to 5.8% for a similar population of control participants who were also deployed and blast-exposed, but who did not experience a TBI.[19]

Three studies reported frequency of accommodation dysfunction and refractive errors in those with TBI history stratified by subgroups. Brahm and colleagues reported a frequency of 39.6% for inpatients compared to 47.5% of outpatients.[17] The authors report higher frequencies for blast-exposed inpatients than non-blast exposed inpatients, but lower frequencies for blast-exposed outpatients compared to non-blast exposed outpatients. Goodrich and colleagues report similar rates of accommodation dysfunction and refractive errors for blast- and non-blast exposed inpatients (69.2% and 63.9%, respectively).[9] In a later paper on the same sample of inpatient Veterans treated in a PRC, Goodrich and colleagues report identical rates of accommodation dysfunction and refractive errors for both Veterans with TBI history with and without comorbid PTSD (66.7% in both groups).[21]

Table 3. Accommodation Dysfunction and Refractive Errors in Individuals with TBI History

Citation	Outcome measure	Prevalence estimates (stratified if available)	P value
Brahm, 2009[17]	Pull-away method used for patients under age 40	Inpatient: 21/53 (39.6%) Outpatient: 47/99 (47.5%) Blast, inpatient: 19/45 (42.2%) No Blast, inpatient: 2/8 (25.0%) Blast, outpatient: 42/92 (45.7%) No Blast, outpatient: 5/7 (71.4%)	NR
Bulson, 2012[18]	Diagnosed accommodative dysfunction during eye clinic evaluation	3/100 (3%)	NR
Dougherty, 2011[19]	ICD-9-CM code 367 “Disorders of accommodation and refraction”	61/837 (7.3%) No TBI Control: 82/1417 (5.8%)	NR
Goodrich, 2013[9] Goodrich, 2013[21]	Accommodative amplitude tested monocularly on patients 40 years of age and younger with pull-away technique, rated as normal or deficient using age-established norms.	50/75 (66.7%) PTSD: 18/27 (66.7%) No PTSD: 32/48 (66.7%) Blast: 27/39 (69.2%) No Blast: 23/36 (63.9%)	PTSD vs no PTSD: p = “non-significant” Blast vs No Blast: p = “non-significant”
Goodrich, 2007[20]	Push-up/pull-away technique	10/46 (21.7%) Blast: 5/21 (23.8%) No Blast: 5/25 (20.0%)	NR

Citation	Outcome measure	Prevalence estimates (stratified if available)	P value
Lew, 2007[24]	NR; assessed at comprehensive eye exam.	13/62 (21%)	NR
Stelmack, 2009[27]	NR	17/88 (19%)	NR

Note. TBI = Traumatic Brain Injury; NR = Not Reported; PTSD = Post-traumatic Stress Disorder. No effect sizes were reported.

Convergence Insufficiency or Dysfunction Findings

Data on convergence insufficiency or dysfunction in individuals with a history of TBI were reported in 5 studies (described in 6 publications). These results are summarized in Table 4. Frequency of convergence insufficiency or dysfunction varied greatly across the 4 studies reporting estimates not stratified by potentially confounding factors, ranging from 11% in one study[27] to 62.5% in another.[9,21] The other 2 studies reported frequencies of 30.4% and 46%.[20,24] No studies with control groups reported data on convergence insufficiency or dysfunction.

Three studies report frequency of convergence insufficiency or dysfunction in those with TBI history stratified by subgroups. Brahm and colleagues report similar frequencies for inpatients and outpatients (42.6% and 48.4%, respectively).[17] The authors also report similar frequencies for blast- and non-blast exposed Veterans with the exception of a slightly higher rate for the outpatient, non-blast exposed subgroup (63.6%). Goodrich and colleagues report rates of convergence insufficiency or dysfunction for blast- and non-blast exposed Veterans of 78.3% and 48.0%, respectively, in a sample of PRC inpatients;[20] however, in a different sample of PRC inpatients, they report rates of 23.8% and 36.0% for blast- and non-blast exposed Veterans.[9,21] Goodrich and colleagues also report rates for those with and without comorbid PTSD (70.8% and 54.2%, respectively).[9,21]

Table 4. Convergence Insufficiency or Dysfunction in Individuals with TBI History

Citation	Outcome measure	Prevalence estimates (stratified if available)	P value
Brahm, 2009[17]	Near Point of Convergence, > 7 cm	Inpatient: 26/61 (42.6%) Outpatient: 59/122 (48.4%) Blast, inpatient: 22/52 (42.3%) No Blast, inpatient: 4/9 (44.9%) Blast, outpatient: 52/111 (46.8%) No Blast, outpatient: 7/11 (63.6%)	NR
Goodrich, 2013[9] Goodrich, 2013[21]	Near Point of Convergence measured by the patient fixating on a single 20/50 letter, > 8 cm	30/48 (62.5%) PTSD: 17/24 (70.8%) No PTSD: 13/24 (54.2%) Blast: 18/23 (78.3%) No Blast: 12/25 (48.0%)	PTSD vs no PTSD: p = "non-significant" Blast vs No Blast: p = .062
Goodrich, 2007[20]	Near point of convergence was measured with a confrontation near target.	14/46 (30.4%) Blast: 5/21 (23.8%) No Blast: 9/25 (36.0%)	NR
Lew, 2007[24]	NR; assessed at comprehensive eye exam.	28/62 (46%)	NR
Stelmack, 2009[27]	NR	10/88 (11%)	NR

Note. TBI = Traumatic Brain Injury; NR = Not Reported; PTSD = Post-traumatic Stress Disorder. No effect sizes were reported.

Diplopia

Diplopia in individuals with a history of TBI was reported in 3 studies (described in 4 publications). These results are summarized in Table 5. Diplopia was infrequent in 2 studies (3% and 6.5%),[20,27] though significantly more common in another (40%).[9,21] No studies with control groups reported diplopia outcomes.

Two studies report frequency of diplopia in those with TBI history stratified by subgroups. One study reports rates of diplopia for blast- and non-blast exposed inpatients of 37.2% and 42.6% in a sample of PRC inpatients,[9] while another study reports rates of 0% and 12.0% for blast- and non-blast exposed Veterans.[20] One study reports rates for those with and without comorbid PTSD (44.7% and 36.5%, respectively).[21]

Table 5. Diplopia in Individuals with TBI History

Citation	Outcome measure	Prevalence estimates (stratified if available)	P value
Goodrich, 2013[9] Goodrich, 2013[21]	NR	36/90 (40%) PTSD: 17/38 (44.7%) No PTSD: 19/52 (36.5%) Blast: 16/43 (37.2%) No Blast: 20/47 (42.6%)	Blast vs No Blast: p = .670
Goodrich, 2007[20]	Binocular vision function was assessed with cover tests in primary gaze at distance and near.	Total: 3/46 (6.5%) Blast: 0/21 (0.0%) No Blast: 3/25 (12.0%)	NR
Stelmack, 2009[27]	NR	3/88 (3%)	NR

Note. TBI = Traumatic Brain Injury; NR = Not Reported; PTSD = Post-traumatic Stress Disorder. No effect sizes were reported.

Dry Eye

Three studies reported data on dry eye in individuals with a history of TBI. These results are summarized in Table 6. Frequency of dry eye varied greatly across the 3 studies reporting estimates not stratified by potentially confounding factors, ranging from .1% to 2% in 2 studies[18,19] to 93% of Veterans obtaining at least one positive measure of dry eye in one study.[8] The study by Cockerham and colleagues reported significant differences between those with TBI history compared to a control group in terms of more than one positive test of dry eye or ocular strain, but non-significant differences for basal tear production, tear film break-up time, and tear osmolarity; however, the control group was potentially very different from cases in terms of factors other than TBI history.[8] Another study by Dougherty and colleagues reported a 0.1% frequency of dry eye for those with TBI history compared to 0.3% for a similar population of control participants who were deployed and blast-exposed, but did not experience a TBI.[19]

One study reported frequency of dry eye in those with TBI history stratified by blast and no blast mechanism of injury subgroups.[8] Different studies of dry eye yielded mixed findings among blast-exposed subgroups depending on the measures, and statistical significance of these differences was not reported in this study.

One study reported Ocular Surface Disease Index subscale scores for visual complaints, functional limitations, and sensitivity to conditions related to dry eye.[8] This study reported significantly higher scores indicating greater symptoms by those with TBI compared to controls; however, as noted above, control participants were likely different from cases in regards to more than just TBI status.

Table 6. Dry Eye in Individuals with TBI History

Citation	Outcome measure	Prevalence estimates or Mean (SD) (stratified if available)	Prevalence estimates or Mean (SD) for control group (if available)	P value	Effect size (95% CI)
Bulson, 2012[18]	Diagnosed dry eye syndrome during eye clinic evaluation	2/100 (2%)	NR	NR	NR
Cockerham, 2013[8]	Basal tear production (BTP) < 4mm; tear film break-up time (TFBUT) < 10 sec.; tear osmolarity > 314 milliosmoles; ocular staining present (flourescein and lissamine green staining pattern scored on Oxford scale)	Total TBI, at least 1 positive test: 49/53 (93%) Total TBI, BTP: 19/53 (36%) Blast, BTP: 17/44 (39%) No Blast, BTP: 2/9 (22%) Total TBI, TFBUT: 14/53 (28%) Blast, TFBUT: 14/44 (33%) No Blast, TFBUT: 0/9 (0%) Total TBI, Tear Osmolarity: 19/53 (58%) Blast, Tear Osmolarity: 13/44 (54%) No Blast, Tear Osmolarity: 6/9 (67%) Total TBI, Ocular Stain: 42/53 (28%) Blast, Ocular Stain: 35/44 (80%) No Blast, Ocular Stain: 7/9 (78%)	At least 1 positive test: 8/18 (44%) BTP: 3/18 (17%) TFBUT: 1/18 (6%) Tear Osmolarity: 4/18 (33%) Ocular Stain: 5/18 (28%)	At least 1 positive test: p < .001 BTP: p = .13 TFBUT: p = .06 Tear Osmolarity: p = .15 Ocular Stain: p < .001	At least 1 positive test: chi-square = 19.56 BTP: chi-square = 2.3 TFBUT: chi-square = 3.57 Tear Osmolarity: chi-square = 2.07 Ocular Stain: chi-square = 15.91 No significant differences in results accounting for those on antidepressant medications considered risk factors for dry eye syndrome.
	3 Ocular Surface Disease Index (OSDI) categories: Visual complaints; Functional limitations; Sensitivity to conditions. Each of 12 questions scored 1 (mild) to 4 (severe) with total score tallied. Results reported as mean (SD) OSDI scores.	Total TBI, visual complaints: 23 (SD = 10) Blast, visual complaints: 24 (SD = 10) No Blast, visual complaints: 16 (SD = 10) Total TBI, functional limitations: 19 (SD = 28) Blast, functional limitations: 18 (SD = 28) No Blast, functional limitations: 24 (SD = 29) Total TBI, sensitivity: 17 (SD = 29) Blast, sensitivity: 19 (SD = 31) No Blast, sensitivity: 7 (SD = 17)	visual complaints: 2 (4) functional limitations: 0 (0) sensitivity: 1 (4)	visual complaints: p < .001 functional limitations: p < .001 sensitivity: p = .03	visual complaints: Z = 3.5 functional limitations: Z = 3.6 sensitivity: Z = 2.2
Dougherty, 2011[19]	ICD-9-CM code 375 “Disorders of lacrimal system”	1/837 (0.1%)	4/1417 (0.3%)	NR	NR

Note. TBI = Traumatic Brain Injury; NR = Not Reported; PTSD = Post-traumatic Stress Disorder.

Nystagmus or Fixation Dysfunction

Data on nystagmus or fixation dysfunction in individuals with a history of TBI were reported in 5 studies (described in 6 publications). These results are summarized in Table 7. Frequency of nystagmus or fixation dysfunction ranged from 0%[27] to 23.4%[9,21] in 4 studies reporting results not stratified by potentially confounding factors. The other 2 studies reported frequencies of 2.2% and 5%.[20,24] No studies with control groups reported outcome data on nystagmus or fixation dysfunction.

Three studies report frequency of nystagmus or fixation dysfunction in those with TBI history stratified by subgroups. Brahm and colleagues report similar frequencies for inpatients and outpatients (9.5% and 6.5%, respectively).[17] The authors report similar frequencies for blast- and non-blast exposed Veterans with the exception of similarly exposed outpatient Veterans (7.1% vs 0.0%, respectively). Goodrich and colleagues report rates of nystagmus or fixation dysfunction for blast- and non-blast exposed Veterans of 0% and 4.0%, respectively, in a sample of PRC inpatients.[20] In a different sample of PRC inpatients, they report rates of 17.4% and 29.2% for blast- and non-blast exposed Veterans and report rates for those with and without comorbid PTSD as 23.6% and 23.2%, respectively.[9,21]

Table 7. Nystagmus or Fixation Dysfunction in Individuals with TBI History

Citation	Outcome measure	Prevalence estimates (stratified if available)	P value
Brahm, 2009[17]	Various targets depending on patient abilities and acuity limits including penlights, colored targets, and single letters down to 1.25 M letter size.	Inpatient: 6/63 (9.5%) Outpatient: 8/124 (6.5%) Blast, inpatient: 5/54 (9.3%) Non-blast, inpatient: 1/9 (11.1%) Blast, outpatient: 8/112 (7.1%) Non-blast, outpatient: 0/12 (0.0%)	NR
Goodrich, 2013[9] Goodrich, 2013[21]	Fixation was assessed by having the patient fixate on a 20/50 near target and noting any unsteadiness or nystagmus	22/94 (23.4%) PTSD: 9/38 (23.6%) No PTSD: 13/56 (23.2%) Blast: 8/46 (17.4%) No Blast: 14/48 (29.2%)	PTSD vs no PTSD: p = "non-significant" Blast vs No Blast: p = "non-significant"
Goodrich, 2007[20]	Fixation stability on a near target was assessed for steadiness, and any nystagmus noted	Total: 1/46 (2.2%) Blast: 0/21 (0.0%) Nonblast: 1/25 (4.0%)	NR
Lew, 2007[24]	NR; assessed at comprehensive eye exam.	3/62 (5%)	NR
Stelmack, 2009[27]	NR	0/88 (0%)	

Note. TBI = Traumatic Brain Injury; NR = Not Reported; PTSD = Post-traumatic Stress Disorder; M = M-unit, 1 M-unit is the ability to recognize a standard letter at a distance of 1 meter. No effect sizes were reported.

Photosensitivity, Photophobia, or Light Sensitivity

Three studies published in 4 papers reported data on photosensitivity, photophobia, or light sensitivity in individuals with a history of TBI. These results are summarized in Table 8. Frequency of photosensitivity, photophobia, or light sensitivity when assessed by patient self-report in 3 studies ranged from 51% to 59%.[9,18,21,24] The study by Bulson and colleagues also reported photosensitivity diagnosed during an eye clinic exam; in this study, only 5% of patients with TBI history received such a diagnosis.[18]

One study reported frequency of photosensitivity, photophobia, or light sensitivity as 67.4% and 77.5% in those with TBI history stratified by blast versus no blast mechanism of injury subgroups respectively, a difference that was statistically significant.[9,21] This same study reported rates of 86.1% for those with PTSD compared to only 27.1% for those without. This comparison was statistically significant ($p < .001$) and remained so after adjustment for age, medication, TBI severity, and mechanism of injury ($p = .002$).

Table 8. Photosensitivity, Photophobia, or Light Sensitivity in Individuals with TBI History

Citation	Outcome measure	Prevalence estimates (stratified if available)	P value	Effect size (95% CI)
Bulson, 2012[18]	22-item Neurobehavioral Symptom Inventory (NSI-22), self-report measure item assessing "light sensitivity" with score of 2 or greater	54/100 (54%)	NR	NR
	Diagnosed photosensitivity during eye clinic evaluation	5/100 (5%)	NR	NR
Goodrich, 2013[9] Goodrich, 2013[21]	Self-reported photosensitivity	44/86 (51%) PTSD: 31/36 (86.1%) No PTSD: 13/48 (27.1%) Blast: 31/46 (67.4%) No Blast: 13/40 (77.5%)	PTSD vs no PTSD: p < .001 PTSD vs no PTSD adjusted for age, medication, TBI severity, and mechanism of injury: p = .002 Blast vs No Blast: p = .002	PTSD vs no PTSD: chi-square = 23.08 PTSD vs no PTSD adjusted for age, medication, TBI severity, and mechanism of injury: Adjusted OR = 8.22 (95% CI 2.20-30.70)
Lew, 2007[24]	Self-reported photosensitivity during evaluation	36/62 (59%)	NR	NR

Note. TBI = Traumatic Brain Injury; NR = Not Reported; PTSD = Post-traumatic Stress Disorder.

Pursuit or Saccadic Dysfunction

Data on pursuit or saccadic dysfunction in individuals with a history of TBI were reported in 5 studies (described in 6 publications). These results are summarized in Table 9. Frequency of pursuit or saccadic dysfunction ranged from 2%[27] to 70.8% (saccadic dysfunction) and 37.4% (pursuit dysfunction)[9,21] in 4 studies reporting results not stratified by potentially confounding factors. The other 2 studies reported saccadic and/or pursuit dysfunction frequencies of 19.6% and 25%.[20,24] No studies with control groups reported outcome data on pursuit or saccadic dysfunction.

Three studies report frequency of pursuit or saccadic dysfunction in those with TBI history stratified by subgroups. Brahm and colleagues report similar frequencies for inpatients and outpatients (30.2% and 23.4%, respectively).[17] When analyzed by blast versus non-blast exposure mechanism of injury, the authors report higher frequencies for those exposed to blast for both inpatients and outpatients. Goodrich and colleagues report rates of pursuit or saccadic dysfunction in the opposite direction for blast- and non-blast exposed Veterans (4.8% and 32.0%, respectively) in a sample of PRC inpatients.[20]

Table 9. Pursuit or Saccadic Dysfunction in Individuals with TBI History

Citation	Outcome measure	Prevalence estimates (stratified if available)	P value
Brahm, 2009[17]	Various targets depending on patient abilities and acuity limits including penlights, colored targets, and single letters down to 1.25 M letter size.	Inpatient: 19/63 (30.2%) Outpatient: 29/124 (23.4%) Blast, inpatient: 18/54 (33.3%) Non-blast, inpatient: 1/9 (11.1%) Blast, outpatient: 27/112 (24.1%) Non-blast, outpatient: 2/12 (16.7%)	NR
Goodrich, 2013[9] Goodrich, 2013[21]	Saccades assessed by having a patient switch fixation between 2 targets located approximately 10 cm apart and 40 cm in front of midline; rated as normal or deficient following Northeastern State University College of Optometry oculomotor test criteria. Pursuits evaluated by having the patient follow a target that was moved into the cardinal positions of gaze.	Saccadic dysfunction: 68/96 (70.8%) Pursuit abnormalities: 37/99 (37.4%) PTSD, Saccadic dysfunction: 26/39 (66.7%) No PTSD, Saccadic dysfunction: 42/57 (73.6%) PTSD, Pursuit abnormalities: 14/41 (34.1%) No PTSD, Pursuit abnormalities: 23/58 (39.6%) Blast, Saccadic dysfunction: 29/50 (58.0%) No Blast, Saccadic dysfunction: 39/46 (84.8) Blast, Pursuit abnormalities: 15/50 (30.0%) No Blast, Pursuit abnormalities: 22/49 (44.9%)	PTSD vs no PTSD: p = "non-significant" Saccadic dysfunction, Blast vs No Blast: p = .006 Pursuit abnormalities: p = "non-significant"
Goodrich, 2007[20]	Saccadic eye movements were assessed for accuracy and speed of eye movements between the targets. Pursuit eye movements were assessed for accuracy and smoothness.	Total: 9/46 (19.6%) Blast: 1/21 (4.8%) No Blast: 8/25 (32.0%)	NR
Lew, 2007[24]	NR; assessed at comprehensive eye exam.	15/62 (25%)	NR
Stelmack, 2009[27]	NR	2/88 (2%)	NR

Note. TBI = Traumatic Brain Injury; NR = Not Reported; PTSD = Post-traumatic Stress Disorder. No effect sizes were reported.

Strabismus and Cranial Nerve Palsy

Strabismus and cranial nerve palsy in individuals with a history of TBI was reported in 5 studies (described in 6 publications). These results are summarized in Table 10. Frequency of strabismus and cranial nerve palsy was rare in most studies, ranging from 0% to 11% in 3 studies[19,24,27] though one study reported that 37.5% of Veterans with TBI history had strabismus diagnosed during an ocular exam. [9,21] One study reported similar rates of strabismus and other disorders of binocular eye movement in Veterans with TBI history compared to similar controls (0.6% vs 0.4%, respectively).[19]

Two studies report frequencies of strabismus and cranial nerve palsy in those with TBI history stratified by patient status. Brahm and colleagues report higher frequencies for inpatients (25.0%) than outpatients (7.3%), though they do not report statistical significance. Their results were similar after subanalysis by mechanism of injury.[17] Goodrich and colleagues report non-significantly different rates of strabismus and cranial nerve palsy stratified by mechanism of injury and PTSD diagnosis in a sample of PRC inpatients.[9,21]

Table 10. Strabismus and Cranial Nerve Palsy in Individuals with TBI History

Citation	Outcome measure	Prevalence estimates (stratified if available)	P value	Effect size (95% CI)
Brahm, 2009[17]	NR	Inpatient: 17/68 (25.0%) Outpatient: 9/124 (7.3%) Blast, inpatient: 14/57 (24.6%) Non-blast, inpatient: 3/11 (27.3%) Blast, outpatient: 8/112 (7.1%) Non-blast, outpatient: 1/12 (8.3%)	NR	NR
Dougherty, 2011[19]	ICD-9-CM code 378 "Strabismus and other disorders of binocular eye movements"	5/837 (0.6%) No TBI Control: 5/1417 (0.4%)	NR	NR
Goodrich, 2013[9] Goodrich, 2013[21]	Ocular exam categorized by type of tropia (abnormal binocular eye position)	33/88 (37.5%) PTSD: 10/38 (26.3%) No PTSD: 23/50 (46.0%) Blast: 12/42 (28.6%) No Blast: 21/46 (45.7%)	PTSD vs no PTSD: p = .10 Blast vs No Blast: p = .125	PTSD vs no PTSD: chi-square = 2.78
Lew, 2007[24]	NR; strabismus assessed at comprehensive eye exam	7/62 (11%)	NR	NR
Stelmack, 2009[27]	NR; strabismus	3/103 (3%)	NR	NR
	Cranial Nerve Palsy or Disorder diagnosed by oculomotor function examination	0/88 (0%)	NR	NR

Note. TBI = Traumatic Brain Injury; NR = Not Reported; PTSD = Post-traumatic Stress Disorder.

Visual Field Defect

Visual field defects were assessed in a variety of ways in 5 included studies.[17-20,27] All reported low frequency of visual field defects in Veterans with TBI history (6% or less) with the exception of one study by Brahm and colleagues which reported rates of 3.2% and 38.8% for outpatient and inpatient groups, respectively.[17] Dougherty and colleagues reported similar rates for TBI and control groups.[19] Results are reported in Table 11.

Table 11. Visual Field Defect in Individuals with TBI History

Citation	Outcome measure	Prevalence estimates (stratified if available)
Brahm, 2009[17]	Confrontation or Goldmann	38.8% inpatient, 3.2% outpatient
Bulson, 2012[18]	Diagnosed visual field defect during eye clinic evaluation	2/100 (2%)
Dougherty, 2011[19]	ICD-9-CM code 377 "Disorders of optic nerve and visual pathways"	1/837 (0.1%) No TBI Control: 4/1417 (0.3%)

Goodrich, 2007[20]	Paracentral Scotoma assessed by confrontation or Goldmann visual field testing	Right eye: 0/50 (0.0%) Left eye: 2/50 (4.0%)
	Visual field defect assessed by confrontation or Goldmann visual field testing	Right eye: 3/50 (6.0%) Left eye: 3/50 (6.0%)
	Hemianopsia, Left, with Macular Sparing assessed by confrontation or Goldmann visual field testing	Right eye: 3/50 (6.0%) Left eye: 4/50 (8.0%)
	Hemianopsia, Left, with Macular Splitting assessed by confrontation or Goldmann visual field testing	Right eye: 0/50 (0.0%) Left eye: 1/50 (2.0%)
	Hemianopsia, Right, with Macular Sparing assessed by confrontation or Goldmann visual field testing	Right eye: 0/50 (0.0%) Left eye: 1/50 (2.0%)
	Quadrantopsia, Left Inferior assessed by confrontation or Goldmann visual field testing	Right eye: 1/50 (2.0%) Left eye: 0/50 (0.0%)
	Quadrantopsia, Left Superior assessed by confrontation or Goldmann visual field testing	Right eye: 1/50 (2.0%) Left eye: 0/50 (0.0%)
Stelmack, 2009[27]	Visual field defect assessed by confrontation or Goldmann visual field testing	5/88 (6%)
	Optic Nerve and Visual Pathways Disorders assessed by confrontation or Goldmann visual field testing	2/88 (2%)

Note. TBI = Traumatic Brain Injury; NR = Not Reported. No p values or effect sizes were reported.

Visual Impairment or Dysfunction

Various aspects of visual impairment or dysfunction not previously categorized in this report were reported in the body of included literature. Three studies reported visual impairment diagnoses[17-19] while 8 studies (described in 9 papers) described self-reported visual impairment.[9,17,18,21-23,25-27] The variety of visual impairment/dysfunction and assessment tools precludes concise synthesis of data from this group of studies, though individual study results are reported in Table 12. One study described changes in self-reported visual impairment over time in a population of Canadian civilian adults who had sustained a TBI in a motor vehicle crash.[22] This study documents a decline in self-reported visual symptoms from 6 weeks to 12 months following injury.

One study reported that IDC-9-CM diagnosis of visual disturbances was significantly more common in those with TBI history compared to a control group without a TBI history that had similar characteristics (1.9% vs 0.6%, $p = .003$).[19] Another study compared visual impairment assessed using the 25-item National Eye Institute Visual Functioning Questionnaire (VFQ-25) self-report measure in Veterans with data from healthy controls obtained from another published paper. The authors note that Veterans with TBI history reported significantly worse functioning on this measure compared with controls ($p = .001$), though the control group was likely very different from cases in ways other than just TBI history.[23] Lew and colleagues compared self-reported visual symptoms in previously deployed Veterans with and without TBI history. After adjustment for demographic characteristics and hearing impairment, the authors reported that TBI and blast accounted for 0.69% and 0.14% of the variance in self-reported vision impairment.[26]

Table 12. Visual Impairment or Dysfunction in Individuals with TBI History

Citation	Outcome measure	Prevalence estimates or Mean (SD) (stratified if available)	Prevalence estimates or Mean (SD) for control group (if available)	P value	Effect size (95% CI)
Visual Impairment or Dysfunction, Diagnosed					
Brahm, 2009[17]	Visual acuity assessed by Feinbloom chart at 10 feet, Snellen worse than 20/60	Inpatient: 14/63 (23.2%) Outpatient: 2/124 (1.6%) Blast, inpatient: 11/54 (20.4%) Non-blast, inpatient: 3/9 (33.3%) Blast, outpatient: 2/112 (1.8%) Non-blast, outpatient: 0/12 (0.0%)	NR	NR	NR
Bulson, 2012[18]	Diagnosed uncorrected refractive error during eye clinic evaluation	22/100 (22%)	NR	NR	NR
Dougherty, 2011[19]	ICD-9-CM code 369 "Blindness and low vision"	3/837 (0.4%)	2/1417 (0.1%)	NR	NR
	ICD-9-CM code 378 "Other disorders of eye"	5/837 (0.6%)	5/1417 (0.4%)	NR	NR
	ICD-9-CM code 368 "Visual Disturbances"	16/837 (1.9%)	8/1417 (0.6%)	0.003	chi-square = 9.063
Visual Impairment or Dysfunction, Self-Reported					
Brahm, 2009[17]	Self-reported visual impairment	Inpatient: 46/61 (75.4%) Outpatient: 94/124 (75.8%) Blast, inpatient: 41/53 (77.4%) Non-blast, inpatient: 5/8 (62.5%) Blast, outpatient: 85/112 (75.9%) Non-blast, outpatient: 9/12 (75.0%)	NR	NR	NR
Bulson, 2012[18]	NSI-22, self-report measure item assessing "blur/trouble seeing" with score of 2 or greater	47/100 (47%)	NR	NR	NR
Goodrich, 2013[9] Goodrich, 2013[21]	Self-reported blurred vision, hazy vision, or other general visual symptoms	67/100 (67.0%) PTSD: 31/41 (75.6%) No PTSD: 36/59 (61.0%) No Blast: 34/49 (69.4%) Blast: 33/50 (66.0%)	NR	PTSD vs no PTSD: p = .19 Blast vs No Blast: p = "non-significant"	PTSD vs no PTSD: chi-square = 1.72

Citation	Outcome measure	Prevalence estimates or Mean (SD) (stratified if available)	Prevalence estimates or Mean (SD) for control group (if available)	P value	Effect size (95% CI)
Hartvigsen,2014[22]	Self-reported "vision problems"	6 weeks: 276/1716 (19.3) 3 months: 232/1716 (16.9) 6 months: 208/1716 (16.4) 9 months: 178/1716 (15.9) 12 months: 156/1716 (14.4)	NR	NR	NR
Lemke, 2013[23]	25-item National Eye Institute Visual Functioning Questionnaire (VFQ-25) self-report measure	General vision mean: 69 Ocular pain mean: 81 Near activities mean: 72 Distance activities mean: 77 Social functioning mean: 85 Mental health mean: 69 Role difficulties mean: 69 Dependency mean: 75 Driving mean: 73 Color vision mean: 89 Peripheral vision mean: 71 Composite score mean: 75	General vision mean: 83 Ocular pain mean: 90 Near activities mean: 92 Distance activities mean: 93 Social functioning mean: 99 Mental health mean: 92 Role difficulties mean: 93 Dependency mean: 92 Driving mean: 99 Color vision mean: 87 Peripheral vision mean: 98 Composite score mean: 97	Healthy control composite score: $p < .001$ Comparisons to patients with diabetes mellitus, glaucoma, and macular degeneration: $p < .001$ Comparisons to patients with dry eye: $p < .05$ Comparisons to patients with macular telangiectasia and cataract: p = "non-significant"	NR
Lew, 2011[26]	NSI-22, self-report measure item assessing "vision problems, blurring, trouble seeing."	44.5% Vision only: 9.9% Vision and hearing: 34.6% Blast: 44.2% Blast, vision only: 8.8% Blast, vision and hearing: 35.4% No blast: 46.0% No blast, vision only: 15.7% No blast, vision and hearing: 30.3%	Blast: 33.1% Blast, vision only: 8.5% Blast, vision and hearing: 24.6% No blast: 35.9% No blast, vision only: 13.2% No blast, vision and hearing: 22.7%	Regression predicting visual impairment from demographics, hearing, TBI, and blast: $p < .0001$	TBI accounted for .69% and blast for .14% of variance in vision impairment adjusting for demographics and hearing impairment.
Lew, 2009[25]	Combination of vision status self-report before/after injury; distance and near visual acuity measurements; visual field status; binocular vision status; and other vision measures, including reading speed and comprehension assessments.	41/62 (66%) Vision only: 21 (33.9%) Vision and hearing: 20 (32.3%)	NR	NR	NR
Stelmack, 2009[27]	NSI-22, self-report measure item assessing "vision problems, blurring, trouble seeing."	55/88 (63%)	NR	NR	NR

Note. TBI = Traumatic Brain Injury; NR = Not Reported; PTSD = Post-traumatic Stress Disorder.

KEY QUESTION 2: What are the types of visual dysfunction reported by individuals who have been diagnosed with a TBI and are presenting to Eye Care clinics?

Summary of Findings

Four studies met inclusion criteria for Key Question 2. All 4 provided case series data. Study and sample characteristics are reported in Table 2. Results are presented by outcome in Table 13, which includes presentation of results stratified by or adjusted for key modifiers such as mechanism of injury and inpatient versus outpatient status, when available. One study reports data from civilians[16] though 3 others report data from Veterans treated within the VA.[18,27,28] Two of the VA studies also provided data relevant to Key Question 1, describing frequency of visual dysfunction in populations of Veterans with TBI history, while also reporting data solely from those who were seen in eye care clinics.[15,24] As expected, the rates of visual dysfunction for Veterans seen in eye care clinics are higher than rates for unselected samples (*ie*, samples not selected studies based on visual dysfunction). Studies meeting inclusion criteria for Key Question 2 reported similar types of visual dysfunction as studies included for Key Question 1.

Given that Key Question 2 relates to types of visual dysfunction seen in eye care clinics, quality considerations are primarily related to generalizability of population and setting as summarized in Key Question 1. One included study reports on TBI in civilian populations[16]; the other 3 studies providing data relevant to Key Question 2 report data from Veterans presenting to eye clinics in conjunction with VA care including PNS and post-deployment clinics and referrals.[18,27,28]

Table 13. Visual Dysfunction in Individuals with TBI Presenting to an Eye Care Clinic

Citation	Outcome measure	Frequencies (stratified if available)	P value	Effect size (95% CI)
Accommodation Dysfunction and Refractive Errors				
Bulson, 2012[18]	Diagnosed accommodative dysfunction during eye clinic evaluation	3/23 (13%)	NR	NR
Magone, 2014[28]	Diagnosed when the lower limit of the expected value for the patient's age was abnormal according to Hofstetter's formula	7/31 (23%)	NR	NR
Stelmack, 2009[27]	NR	17/36 (47%)	NR	NR
Convergence Insufficiency or Dysfunction				
Alvarez, 2012[16]	Near point of convergence was measured with an approaching near target.	130/557 (23.3%) MVC: 90/395 (22.7%) Fall: 17/82 (20.7%) Strike/blow: 15/51 (29.4%) Sports: 2/14 (14.3%) Other: 6/15 (40.0%) Inpatient: 63/270 (23.3%) Outpatient: 67/287 (23.3%)	p = 0.36 (mechanism of injury)	chi-square = 4.4 (mechanism of injury)
Magone, 2014[28]	Diagnosed when there was exophoria greater at near compared with distance, an abnormal near point of convergence (NPC), and positive fusional vergence. NPC measures the ability to maintain binocularly with increased accommodative and vergence demand. NPC was measured with the red lens method. A red lens was placed in front of patient's right eye and the muscle light was moved close to the patient until the break (2 lights) was reported or a break in fusion was observed by the examiner. A remote NPC with a break of greater than 8 cm and recovery greater than 12 cm was considered abnormal.	8/31 (25%)	NR	NR
Stelmack, 2009[27]	NR	10/36 (28%)	NR	NR
Diplopia				
Magone, 2014[28]	NR	4/31 (13%)	NR	NR
Stelmack, 2009[27]	NR	3/36 (8%)	NR	NR

Citation	Outcome measure	Frequencies (stratified if available)	P value	Effect size (95% CI)
Dry Eye Syndrome				
Alvarez, 2012[16]	Slit-lamp evaluation of the corneal tear layer; portable blue filter with fluorescent staining was used for some inpatients.	58/557 (10.4%) Inpatient: 32 (11.9%) Outpatient: 26 (9.1%)	NR	NR
Bulson, 2012[18]	Diagnosed dry eye syndrome during eye clinic evaluation	2/23 (9%)	NR	NR
Nystagmus or Fixation Dysfunction				
Alvarez, 2012[16]	Findings outside the normal range on oculomotor examination	22/557 (3.9%) Inpatient: 10 (3.7%) Outpatient: 12 (4.2%)	NR	NR
Stelmack, 2009[27]	NR	0/36 (0%)	NR	NR
Photosensitivity, Photophobia, or Light Sensitivity				
Alvarez, 2012[16]	Patient sensitivity to direct light stimulation during pupil examination	56/557 (10.1%) Inpatient: 19 (7.0%) Outpatient: 35 (12.2%)	p = .04 (inpatient; non-significant after Bonferroni adjustment)	z = 2.06 (inpatient)
Bulson, 2012[18]	Diagnosed photosensitivity during eye clinic evaluation	5/23 (22%)	NR	NR
Magone, 2014[28]	Self-reported by patient	17/31 (55%)	NR	NR
Pursuit or Saccadic Dysfunction				
Alvarez, 2012[16]	Patients asked to track a transilluminator or other visual target. Pursuit and saccadic movements were noted to be smooth and accurate, or had fixation losses, or abnormal saccades, respectively (or were unable to perform the test)	42/557 (7.5%) Inpatient: 23 (8.5%) Outpatient: (19 (6.6%)	NR	NR
Stelmack, 2009[27]	NR	2/36 (6%)	NR	NR

Citation	Outcome measure	Frequencies (stratified if available)	P value	Effect size (95% CI)
Strabismus and Cranial Nerve Palsy				
Alvarez, 2012[16]	Cranial Nerve Palsy or Disorder diagnosed by oculomotor function examination	Third cranial nerve: 33 (5.9%) Inpatient, third: 19 (7.0%) Outpatient, third: 14 (4.9%) Fourth cranial nerve: 56 (10.1%) Inpatient, fourth: 28 (10.4%) Outpatient, fourth: 28 (9.8%) Sixth cranial nerve: 24 (4.3%) Inpatient, sixth: 19 (7.0%) Outpatient, sixth: 35 (12.2%)	p = .002 (inpatient, sixth cranial nerve palsy)	z = 3.08 (inpatient, sixth cranial nerve palsy)
Stelmack, 2009[27]	NR; strabismus	3/36 (8%)	NR	NR
	Cranial Nerve Palsy or Disorder diagnosed by oculomotor function examination	0/36 (0%)	NR	NR
Visual Field Defect				
Alvarez, 2012[16]	Homonymous Hemianopsia assessed by confrontation or Humphrey Field Test, depending on patient functionality	Right: 21/557 (3.8%) Left: 24/557 (4.3%)	NR	NR
	Quadrantopsia assessed by confrontation or Humphrey Field Test, depending on patient functionality	28 (15.7%)	NR	NR
Bulson, 2012[18]	Diagnosed visual field defect during eye clinic evaluation	2/23 (9%)	NR	NR
Stelmack, 2009[27]	Visual field defect assessed by confrontation or Goldmann visual field testing	5/36 (14%)	NR	NR
	Optic Nerve and Visual Pathways Disorders assessed by confrontation or Goldmann visual field testing	2/36 (6%)	NR	NR
Visual Impairment or Dysfunction				
Alvarez, 2012[16]	Visual acuity assessed by Snellen (eye chart) with targets appropriate to patient's cognitive functioning	>/= 20/60 = 473/557 (84.9%) 20/70-20/100 = 16/557 (2.9%) <20/100 = 27/557 (4.8%) No light perception = 4 (.07%) Patient unable to respond = 37 (6.6%)	NR	NR
Bulson, 2012[18]	Diagnosed uncorrected refractive error during eye clinic evaluation	22/23 (96%)	NR	NR
Magone, 2014[28]	Distance visual acuity was measured using the projected Snellen eye chart	21/31 (68%)	NR	NR

Note. TBI = Traumatic Brain Injury; NR = Not Reported; Hofstetter's formula: 18.5 - (0.30 * patient age in years)

SUMMARY AND DISCUSSION

SUMMARY OF EVIDENCE BY KEY QUESTION

Key Question 1

Twelve studies meeting inclusion criteria provided data relevant to Key Question 1.[8,9,17-27] These studies addressed a variety of objectively assessed and self-reported visual dysfunctions including accommodation dysfunction and refractive errors; convergence insufficiency or dysfunction; diplopia; dry eye; nystagmus or fixation dysfunction; photosensitivity, photophobia, or light sensitivity; pursuit or saccadic dysfunction; strabismus and cranial nerve palsy; visual field defect; and other types of visual impairment or dysfunction.

Evidence from a large study by Dougherty and colleagues[19] suggests that visual dysfunction is not commonly diagnosed in U.S. Service Members who experienced a TBI but who do not have an ocular injury or prior history of visual or ocular dysfunction. However, prevalence estimates of visual dysfunction varied greatly across the studies included in this review. The differences in frequencies reported across studies are likely due to differences in study populations and settings. Specifically, studies included different proportions of participants with mild versus moderate/severe TBI history, inpatient and outpatient settings, and settings treating only patients with current symptoms.

The study by Dougherty and colleagues[19] provides strong evidence about the prevalence of visual dysfunction diagnosed in Veterans who have TBI documented in their VA medical records. However, there are likely many other Veterans who may have experienced one or more TBIs or blast exposures but do not have this coded in their medical record for a variety of reasons (*eg*, not reporting TBIs or blast exposure while in combat, not being aware that blast exposure or hit to the head is severe enough to warrant a TBI diagnosis, *etc*). While large administrative datasets can provide valuable information about entire populations of Veterans served by the VA, these data need to be interpreted with caution because of the lack of granularity and manner in which the data is collected and compiled. For example, in the Dougherty study, it is unclear what type of provider diagnosed visual dysfunction, and what types of assessments were conducted. This study relied on ICD-9 data likely gathered from routine eye care appointments; data gathered in non-screening contexts are expected to provide lower prevalence estimates than data gathered during comprehensive screening assessments for a broad range of visual dysfunction.

Many of the included studies were conducted at PRCs or PNSs, in particular, at Palo Alto VA clinics. We contacted some of the authors in an attempt to ensure that data on the same patients were not reported in more than one study, though it is possible that there may be some overlap in study populations across some of the included studies. Because of the productivity of the researchers at these facilities, it is likely that this review provides a relatively thorough summary of data for these specific clinical populations, and additional research in other settings is likely needed to provide a more general, comprehensive picture of visual dysfunction in U.S. Service Members and Veterans across clinical settings.

Though this review was not designed to determine whether visual dysfunction is more common in individuals with TBI history compared to those without, similar inconsistency in results across

settings was found in studies comparing visual dysfunction frequency in individuals with TBI history versus control participants without TBI history. Overall, while visual dysfunction may be commonly reported by or diagnosed in some groups with TBI history (*eg*, PRC inpatients screened using comprehensive visual examination, many with comorbid ocular injuries[9,21]), visual dysfunction is infrequently diagnosed in other groups with TBI history (*eg*, unscreened samples of U.S. Service members without ocular injuries or prior history of visual dysfunction[19]).

Key Question 2

Only 4 studies meeting inclusion criteria provided evidence for Key Question 2.[16,18,27,28] These studies reported outcomes similar to those found for Key Question 1. In aggregate, all studies included in this review can provide policymakers and clinicians with a rough estimate of the types of visual dysfunctions that some individuals with TBI history may present with in eye care clinic settings, though the findings are limited by the small body of included literature.

Study Characteristics and Quality

Study quality was assessed pertaining to the Key Questions for all included studies. Though we excluded studies selecting patients based on visual dysfunction for Key Question 1, some methods such as outcome assessment were unclearly reported in some studies (see Tables 3-13), resulting in the potential for biased results. Additionally, none of the included studies stratified results by TBI severity. The best estimates of frequency of clinically significant, diagnosed visual dysfunction come from a study by Dougherty and colleagues which excluded patients with ocular injuries or visual disorders prior to the TBI.[19] This study did not screen patients to determine prevalence, instead reporting U.S. Service Member diagnostic results from a large-scale administrative military healthcare database. Eight studies reporting prevalence estimates included only those patients with TBI history who had current symptoms and were being treated at VA PRCs and PNSs; not surprisingly, frequencies of visual dysfunction were significantly higher in these studies.

Publication Bias

Given that the body of evidence relevant to this review was based on observational studies, and none of the studies reported registered protocols or *a priori* established primary aims or analyses, we were not able to formally assess publication bias.

Heterogeneity

Included studies addressed a variety of visual outcomes assessed by different methods in unique populations. Therefore, we were unable to combine studies quantitatively. Instead we provided a summary of findings for each key question and group of outcomes, with tabular presentations of study-level results. We provided a synthesis of the data for certain outcomes assessed across multiple studies, though results were often inconsistent across these studies, likely due to heterogeneity of study populations and assessment methods.

Applicability of Findings to the VA Population

The findings from this body of evidence are very applicable to the VA population, as the majority of the included studies were conducted in VA or U.S. military healthcare settings. Prevalence

estimates of a broad group of unscreened U.S. Service Members suggest that clinically significant, diagnosed visual dysfunction is uncommon in this general population,[19] though this study by Dougherty and colleagues relied on data from 2004 through 2007; it is likely that as the OEF/OIF/OND conflicts progressed, clinicians and Veterans became more aware of both TBI and potential associations with visual dysfunctions. Therefore, an examination of more recent data on these populations and outcomes is likely warranted to ensure comprehensiveness and generalizability of the results. Results from studies of patients screened for visual problems at VA PNSs or PRCs suggest that visual dysfunction is quite common for this group of Veterans who often have histories of severe injuries and multiple comorbid conditions.

FUTURE RESEARCH NEEDS

Well-designed, large-scale, prospective cohort studies on populations of interest provide the most accurate prevalence estimates and information about the relative frequency of symptoms. Ideally, longitudinal data on a large group of U.S. Service Members could be collected prior to TBI exposure. Screening the entire group for visual dysfunction after a portion had experienced a TBI could provide precise estimates of relative risk and prevalence when TBI history, ocular injuries, and time since injury are accounted for. Additionally, potential moderating variables such as comorbid PTSD or blast versus other mechanism of injury should be examined since studies included in this review provide preliminary evidence of associations among these variables and some types of visual dysfunction. Longitudinal studies could also better answer remaining questions related to prognosis over time than many of the cross-sectional studies included in this report. Research on effective treatments for visual problems experienced by individuals with TBI history was outside the scope of this review, though this information could help guide VA treatment options for affected Veterans, and additional research may be needed to establish referral guidelines for visual symptom complaints for Veterans with TBI history.

CONCLUSIONS

Studies included in this systematic review report a range of frequencies of visual dysfunction in people with TBI history. The wide ranges of frequencies for visual dysfunction outcomes reported in the included studies are likely due to population and setting heterogeneity across studies. While some studies reported results from individuals regardless of current symptoms, many of the included studies were conducted in VA PRCs and PNSs, clinics that only serve Veterans with current symptoms associated with TBI history as well as other, often serious, comorbidities. Overall, findings suggest that visual dysfunction in a general population of U.S. Service Members with TBI history who are treated in military healthcare systems is diagnosed with a frequency of 7.3% for disorders of accommodation and refractive errors and a frequency of less than 1% for other visual dysfunctions. Conversely, other studies of Veterans with TBI history and current symptoms being treated in inpatient and outpatient TBI rehabilitation clinics report higher frequencies, often over 50% for some types of visual dysfunction such as accommodation and refraction disorders, convergence insufficiency or dysfunction, dry eye syndrome, photosensitivity, pursuit or saccadic dysfunction, and self-reported visual impairments.

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APPENDIX A. TECHNICAL EXPERT PANEL

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APPENDIX B. SEARCH STRATEGIES

Concept	Mesh terms	Free language terms		
TBI 77364	"Brain Injuries"[Mesh] OR "Head Injuries, Closed"[Mesh] OR "Blast Injuries"[Mesh]	("head injury" OR "head injuries" OR concussion OR concusses OR concussive OR "brain trauma" OR "head trauma" OR "traumatic Brain injury" OR "traumatic brain injuries" OR "traumatic-brain-injury" OR tbi OR mtbi OR stbi OR "blast injury" OR "blast injuries" OR blast-injury)[Title/Abstract]		
Vision 73480	"Eye Movement Measurements"[Mesh] OR "Ocular Motility Disorders"[Mesh] OR "Ocular Physiological Processes"[Mesh] OR "Visual Perception"[Mesh] OR "Visual Acuity"[Mesh] OR "Eye"[Mesh] OR "Vision Disorders"[Mesh] OR "Vision, Ocular"[Mesh]	(amblyopia OR binocular vision dysfunction OR binocular vision dysfunctions OR binocular visual dysfunction OR binocular visual dysfunctions OR blind* OR blindness OR convergence insufficiency OR cranial nerve evaluation OR cranial nerve evaluations OR dark adapt* OR diplopia OR facial recognition OR fixation defect OR fixation defects OR hemianopsia OR light sensitiv* OR nystagmus OR ocular disease surface index OR ocular examination OR ocular examinations OR ocular health OR ocular migraine OR ocular migraines OR ocular pain OR ocular surface stain* OR ocular trauma OR oculo-motor disorder	OR photosensitivities OR photosensitivity OR pursuit abnormalit* OR quadrantonopsia OR spatial neglect OR strabismus OR tear film break-up time OR tear osmolarity OR tear production OR TFBUT OR vertical heterophoria OR vision accommodation OR vision acuity OR vision acuity loss OR vision agnosia OR vision deficit OR vision deficits OR Vision disorder OR Vision disorders OR vision disturbance OR vision disturbances OR vision field defect OR vision field defect OR vision field defects OR vision field defects OR vision function OR vision motor OR vision perception OR Vision problem OR Vision problems OR vision process OR vision processes OR vision processing OR vision reflex OR vision reflexes	OR vision scanning OR vision sequelae OR vision system OR vision system dysfunction OR vision system dysfunctions OR visiospatial ability OR visual accommodation OR visual acuity OR visual acuity loss OR visual agnosia OR visual deficit OR visual deficits OR Visual disorder OR Visual disorders OR visual disturbance OR visual disturbances OR visual field defect OR visual field defects OR visual function OR visual motor OR visual perception OR Visual problem OR Visual problems OR visual process OR visual processes OR visual processing OR visual reflex OR visual reflexes OR visual scanning OR visual sequelae OR visual system OR visual system dysfunction

		OR oculo-motor disorders OR oculo motor disorders OR oculo motor disorder OR ODSI OR ophthalmolog* OR optometr* OR photic stimulation		OR visual system dysfunctions OR visuospatial abilities OR visuo-spatial abilities)[Title/Abstract]
Above Combined with AND N= 3991				
Limited to 2009 and beyond N=932				

Medline (PubMed) Searched March 27, 2014 from January 1st, 2009 on
Saved as "TBI EYE" final in PubMed porvaesp myNCBI account
N=932

Additional Databases
Cochrane Central Register of Controlled Trials (OVID)

1. exp Visual Perception/
2. exp Visual Acuity/
3. exp Eye/
4. exp Vision Disorders/
5. exp Vision, Ocular/
6. 1 or 2 or 3 or 4 or 5
7. (amblyopia or binocular visionsysfunction or binocular vision dysfunctions).mp.
8. (binocular visual dysfunction or binocular visual dysfunctions or blind*).mp.
9. (blindness or convergence insufficiency or cranial nerve evaluation or cranial nerve evaluations).mp.
10. (dark adapt* or diplopia or facial recognition or fixation defect or fixation defects).mp.
11. (hemianopsia or light sensitiv* or nystagmus or ocular disease surface index).mp.
12. (ocular examination or ocular examinations or ocular health or ocular migraine or ocular migraines).mp.
13. (ocular pain or ocular surface stain* or ocular trauma or oculo-motor disorder).mp.
14. (oculo-motor disorders or ODSI or ophtahlmolog* or optometr* or photic stimulation).mp.
15. (photosensitivities or photosensitivity or pursuit abmormalit* or quadrantonopsia).mp.
16. (spacial neglect or strabismus or tear film break-up time or tear osmolarity or tear production or tfbut).mp.
17. (vertical heterophoria or vision accomidation or vision acuity or vision acuity loss).mp.
18. (vision agnosia or vision deficit or vision deficits or vision disorder or vision disorders).mp.
19. (vision disturbance or vision disturbances or vision field defect or vision field defects or vision function or vision motor).mp.
20. (vision perception or vision problem or vision problems or vision process or vision proccesses).mp.
21. (vision proccessing or vision reflex or vision reflexes or vision scanning or vision sequelae or vision system).mp.
22. (vision system dysfunction or vision system dysfunctions or visiospacial ability or visual accomidation or visual acuity).mp.

23. (visual acuity loss or visual agnosia or visual deficit or visual deficits or visual disorder or visual disorders).mp.
24. (visual disturbance or visual disturbances or visual field defect or visual field defects or visual function).mp.
25. (visual motor or visual perception or visual problem or visual problems).mp.
26. (visual process or visual proccesses or visual processing or visual reflex).mp.
27. (visual reflexes or visual scanning or visual sequelae or visual system or visual system dysfunction or visual systems dysfunctions or visuospacial abilities or visuo-spacial abilities).mp.
28. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27
29. exp Brain Injuries/
30. exp Head Injuries, Closed/
31. exp Blast Injuries/
32. (traumatic brain injury or traumatic brain injuries or traumatic-brain-injury or tbi or mtbi or stbi or blast injury or blast injuries or blast-injury).mp.
33. 29 or 30 or 31 or 32
34. 28 and 33
35. limit 34 to yr="2009"

Searched March 27, 2014 from January 1st, 2009 on
(Saved in OVID as "TBI EYE _2009")
N=123(before deduplication with Medline Search)
N=89 (after deduplication with Medline Search)

PsycINFO (OVID)

1. exp Visual Perception/
2. exp Visual Acuity/
3. exp Vision Disorders/
4. (amblyopia or binocular visionsysfunction or binocular vision dysfunctions).mp
5. (binocular visual dysfunction or binocular visual dysfunctions or blind*).mp
6. (blindness or convergence insufficiency or cranial nerve evaluation or cranial nerve evaluations).mp
7. (dark adapt* or diplopia or facial recognition or fixation defect or fixation defects).mp
8. (hemianopsia or light sensitiv* or nystagmus or ocular disease surface index).mp
9. (ocular examination or ocular examinations or ocular health or ocular migraine or ocular migraines).mp
10. (ocular pain or ocular surface stain* or ocular trauma or oculo-motor disorder).mp
11. (oculo-motor disorders or ODSI or ophtahlmolog* or optometr* or photic stimulation).mp
12. (photosensitivities or photosensitivity or pursuit abmormalit* or quadrantonopsia).mp
13. (spacial neglect or strabismus or tear film break-up time or tear osmolarity or tear production or tfbut).mp
14. (vertical heterophoria or vision accomidation or vision acuity or vision acuity loss).mp
15. (vision agnosia or vision deficit or vision deficits or vision disorder or vision disorders).mp
16. (vision disturbance or vision disturbances or vision field defect or vision field defects or

vision function or vision motor).mp
17. (vision perception or vision problem or vision problems or vision process or vision proccesses).mp
18. (vision proccessing or vision reflex or vision reflexes or vision scanning or vision sequelae or vision system).mp
19. (vision system dysfunction or vision system dysfunctions or visiospacial ability or visual accomidation or visual acuity).mp
20. (visual acuity loss or visual agnosia or visual deficit or visual deficits or visual disorder or visual disorders).mp
21. (visual disturbance or visual disturbances or visual field defect or visual field defects or visual function).mp
22. (visual motor or visual perception or visual problem or visual problems).mp
23. (visual process or visual proccesses or visual processing or visual reflex).mp
24. (visual reflexes or visual scanning or visual sequelae or visual system or visual system dysfunction or visual systems dysfunctions or visuospacial abilities or visuo-spacial abilities).mp
25. (traumatic brain injury or traumatic brain injuries or traumatic-brain-injury or tbi or mtbi or stbi or blast injury or blast injuries or blast-injury).mp
26. exp "Eye (Anatomy)"/
27. exp Vision/
28. exp Traumatic Brain Injury/
29. exp Head Injuries/
30. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 26 or 27
31. 25 or 28 or 29
32. 30 and 31
33. limit 32 to yr="2009 -Current"

Searched March 27, 2014 from January 1st, 2009 on
(Saved in OVID as "TBI EYE _2009 PsycINFO")
N=240 (before deduplication with Medline & Cochrane Searches)
N=130 (after deduplication with Medline & Cochrane Searches)

SPORTDiscus with Full Text, Rehabilitation & Sports Medicine Source (EBSCO)

Rehabilitation & Sports Medicine Source & SportDiscus with Full Text (searched together) (EBSCO)

S14 Limiters - Publication Date: 20090101-20141231
S13 S6 AND S12
S12 S7 OR S8 OR S9 OR S10 OR S11
S11 TI blast OR AB blast
S10 TI tbi OR AB tbi OR TI mtbi OR AB mtbi OR TI stbi OR AB stbi
S9 TI traumatic brain injury OR AB traumatic brain injury OR TI traumatic brain injuries OR AB traumatic brain injuries OR TI traumatic-brain-injury OR AB traumatic-brain-injury
S8 DE "HEAD injuries" OR DE "HEAD injuries -- Complications" OR DE "HEAD injuries -- Prevention"

S7 DE “BRAIN -- Wounds & injuries” OR DE “BRAIN -- Concussion” OR DE “BRAIN damage” OR DE “CHRONIC traumatic encephalopathy”
S6 S1 OR S2 OR S3 OR S4 OR S5
S5 TI visual OR AB visual
S4 TI vision OR AB vision
S3 (eye) OR (DE “EYE” OR DE “INTRAOCULAR pressure”)
S2 DE “VISION disorders” OR DE “BLINDNESS” OR DE “EYE -- Refractive errors” OR DE “HYPERMETROPIA”
S1 DE “VISION” OR DE “MOTION perception (Vision)” OR DE “VISUAL acuity” OR DE “VISUAL discrimination” OR DE “VISUAL evoked response” OR DE “VISUAL fields” OR DE “VISUAL perception” OR DE “VISUALIZATION”

Searched March 14, 2014 from January 1st, 2009 on
(Saved in EBSCO as “TBI EYE >2009 ”)
N= 130 (before deduplication with Medline & Cochrane Searches & PsycINFO)
N= 125 (after deduplication with Medline & Cochrane Searches & PsycINFO)

Rehabdata (National Rehabilitation Information Center http://www.naric.com/?q=en/REHABDATA)

Search Strategy: Visual Impairment (descriptor) AND Brain Injuries (descriptor) 2009 to present

Searched March 14, 2014
N=22 (after deduplication with all above searches)

APPENDIX C. PEER REVIEW COMMENTS AND RESPONSES

	Reviewer	Comment	Response
	Question 1: Are the objectives, scope, and methods for this review clearly described?		
1.	1	Yes	Noted.
2.	2	Yes	Noted.
3.	3	Yes	Noted.
4.	4	Yes	Noted.
5.	5	Yes	Noted.
6.	6	Yes	Noted.
7.	7	Yes	Noted.
8.	8	Yes. Clearly described	Noted.
	2. Is there any indication of bias in our synthesis of the evidence?		
9.	1	No	Noted.
10.	2	No	Noted.
11.	3	No	Noted.
12.	4	No	Noted.
13.	5	No. There may be a potential bias in the report due to the small total number of accepted publications with a significant percentage from the same location. Of 13 accepted articles, at least 5 (38%) include the Palo Alto Polytrauma Rehab Center patient population (Brahm 2009, Cockerham 2013, Goodrich in press, Lew 2009, and Lemke 2013- all author affiliations listed as Palo Alto and Stanford). It is not completely clear but there is some overlap in the time frame for patient recruitment from various studies raising the possibility of some patients being accounted for more than once in this limited body of literature. In addition the 2007 Lew study includes Veterans seen at the Palo Alto PNS which may include discharged PRC patients that remained in the area. This in no way diminishes the importance of the published work, it merely illustrates the productivity of a few capable researchers in this area. In addition there is potential bias in the report of dry eye following TBI in the Cockerham 2013 study. I am not certain if OEF/OIF/OND deployment is a risk factor for dry eye disease but it would seem that environmental exposure may be a factor, I do not see that analysis in the article other than blast vs non-blast tbi.	Noted. We have updated the discussion to reflect this point.

	Reviewer	Comment	Response
14.	6	Yes. There are a number of inherent problems from my perspective based on trying to research the literature myself and also from my experience on interviewing patients seen in our VA Eye Clinic. First, the denominator of the studies (number of people with TBI) is very difficult to assess. This is because the criteria for TBI (mild, moderate and severe) varies across medical systems in the US and the world, but even more importantly, IT REQURES THAT PATIENT ARE CODED IN THE ELECTRONIC DATABASE/MEDICAL RECORD AS HAVING TBI. This is a big problem, as it depends on the care giver coding this as one of the diagnoses. In addition, is speaking to many of the veterans with visual complaints, they deny having had "TBI" because in their minds, based on their criteria, they didn't lose consciousness or for only a brief time. Many of them have had multiple concussions or have been exposed to many blast injuries but do not "count" that as a TBI, so the diagnosis	Thank you for this comment. We have augmented information on visual tests and criteria in the tables when available from the original papers; however, often this information was not
		of whether they had TBI or concussion does not rest on firm ground. The net effect is that many veterans have had exposure to blast and/or concussion but are not part of the denominator. It would be helpful to explain this in the report in order to put some of the numbers into context. The other main problem with assessing visual disturbances is the definition. Many patients with vague visual symptoms are not tested with visual function and structure tests (visual fields, optical cohence tomography of the retinal nerve fiber layer and retinal ganglion cell layer, contrast sensitivity, low contrast visual acuity, accommodative and convergence amplitudes and ability to sustain them. In addition, you have excluded all patients with neurocognitive testing indicating visual processing problems from your analysis. Much of this explains the large range of prevalence and proportion of specific visual problems that were found in your analysis and this should be discussed to give a proper perspective. Also in your literature review of the prevalence of certain visual abnormalities, you have not specifically stated in many of the cases what were the criteria for being labeled abnormal. For example, in Table 10 listing Visual Field Defects, all of the defects cited were by confrontation or by Goldmann kinetic perimetry; there is no automated perimetry results and it is hard to ascertain how large and dense the defects needed to be in order to meet criteria for a defect. Similar problems with the other tables with respect to criteria used by each study cited which were used to classify the parameter being measured as abnormal.	reported. Additionally, we have included information on TBI diagnosis and selection factors which may impact prevalence estimates and updated our discussion to reflect these points.
15.	7	No	Noted.
16.	8	No. Report appears to be unbiased	Noted.
	3. Are there any <u>published</u> or <u>unpublished</u> studies that we may have overlooked?		
17.	1	No. Good literature review. A recent addition to the literature is: Magone, M.T., E. Kwon, and S.Y. Shin, *Chronic visual dysfunction after blast-induced mild traumatic brain injury.* JRRD, 2014. **51**(1): p. 71-80. In particular the study notes that binocular/oculomotor dysfunctions may not be detected in routine eye clinic appointments and that additional testing is needed to adequately screen this population. In addition, they not that almost half of their population did not report their TBI history during eye examinations.	Thank you for this suggestion. This study meets inclusion criteria for Key Question 2 and is now included in the final report.
18.	2	Yes. You may want to consider: Pogoda TK, Hendricks AM, Iverson KM, Stolzmann KL, Krengel MH, Baker E, Meterko M, Lew HL. Multisensory impairment reported by veterans with and without mild traumatic brain injury history. J Rehabil Res Dev. 2012;49(7):971-84.	We reviewed this study and because the results only reported MSI in aggregate without separating visual dysfunction, it did not meet inclusion criteria.
19.	3	No	Noted.

	Reviewer	Comment	Response
20.	4	No	Noted.
21.	5	No	Noted.
22.	6	Yes. See DOD report on eye movements and pupil abnormalities that I am attaching and the email from the VA regarding number of patients with visual disorders coded that had also a coded dx of TBI that was solicited by VA Blinded Veterans Association. There were not any references on pupil abnormalities found in TBI (see DOD report attached).	We examined the studies described in this report and did not identify additional studies meeting our inclusion criteria. However, we have referenced this report and included the citation for readers who would like additional information on research related to oculomotor tracking as a way of detecting mild TBI.
23.	7	No	Noted.
24.	8	No. Please ask additional stakeholders listed below. The studies of which I was aware have been included.	Noted.
	4. Please write additional suggestions or comments below. If applicable, please indicate the page and line numbers from the draft report.		
25.	1	1. Page 1 lines 3 – 11. In the executive summary the estimated number of U.S. TBIs is reported, however it goes on to state 15% of OEF/OIF/OND services members incurred TBI. Essentially the reader is asked to compare apples (number) to oranges (percent). It is possible to provide the estimated number of OEF/OIF/OND TBIs and this should be done. Ideally both the estimate number and percentage would be provided for both the civilian and OEF/OIF/OND population. Currently the report does not accurately reflect the rate at which TBIs occurred in OEF/OIF/OND which is significantly higher than in the civilian population. (Comment relevant to the Introduction on page 3 lines 3 – 11)	Thank you for this suggestion. We have added numbers and proportions reflecting both general population and OEF/OIF/OND TBI incidence.
26.	1	2. Page 5, lines 11 – 13. It is stated that the study included "visual dysfunction outcomes that would likely be diagnosed or treated in a vision clinic". I would question the accuracy of this statement in two respects. First, visual acuity loss and visual field loss are not dysfunctions, although they would likely be diagnosed in a "vision clinic". Second, whether the visual dysfunctions (accommodation, pursuits, strabismus, convergence insufficiency, etc.) would be detected in a "vision clinic" examination depends upon how you define "vision clinic". Most military and VA clinics (and indeed civilian clinics) are not designed to detect visual dysfunctions without the patient reporting specific symptoms and then only if a binocular/ oculomotor examination (or screen) were performed. Hence these dysfunctions would likely go undiagnosed in most "vision clinics". This is why virtually all papers cited in the report conclude that patients with a TBI history should be screened based upon the TBI diagnosis.	Thank you for this comment. We have clarified the examples of visual problems that are included to make this more explicit and hopefully better understood by readers.
27.	1	3. Page 9, lines 28 & 29. The sentence states that 0.1% - 7.3% rates of visual dysfunction were found in the Dougherty, et al (2011) study. This is accurate for individual dysfunctions, but somewhat misleading in that over-all the study reported 11% were diagnosed with a visual dysfunction within 12 months of combat injury (Dougherty, page 10).	We have added this data to this section.

	Reviewer	Comment	Response
28.	1	4. Page 9, lines 29 – 31. The sentence states "Unlike studies in which all participants are screened, this study may provide more accurate assessments of clinically significant impairment because patients experienced visual dysfunction to a degree that resulted in clinical presentation and diagnosis." Whether the Dougherty study is "more accurate" is subject to debate on several points. First, The authors do not report specifics of who conducted the vision exam (optometrist, ophthalmologist, or ??). Second, the specifics of the exam are not reported. This is particularly important since, as noted previously, "routine" eye exams are not likely to uncover many binocular/oculomotor dysfunctions. Obviously, some binocular/oculomotor problems were documented, however it is not possible to determine how many were missed simply because the vision exam was not sufficiently comprehensive. Third, the study was published in 2011, however the study relied on medical record data for the time period 1 March 2004 to 28 February 2007. This fact is important for two reasons. One reason is that this time period was prior to any professional awareness (published literature) of the relationship between TBI and visual dysfunctions in this population. Thus the examining clinician would likely not be "on the lookout" for these conditions and might only detect the most obvious cases and overlook others. A second reason is that the military culture of the time discouraged reporting of any symptoms. The DoD has acknowledge this and taken active steps to encourage reporting of symptoms. The patient history is an essential part of accurate diagnosis for any medical examination. In a culture where symptom reporting is "frowned upon" symptoms aren't reported and the examination is impaired. Related to this is that even TBI patients with visual symptoms often do not associate the symptoms with their visual status (their vision remains 20/20 or better "so what could be wrong?") and therefore do not equate a vision examination with a step in correcting their symptom. In short, while the Dougherty et al study is commendable, it does not rise to the level of a "gold standard" simply because it has a large N, and perhaps the review should include a discussion of potential limitations and hence generalizability to all "US Service Members".	We have altered this section slightly to better emphasize that we are referring to accurate assessment of *clinically significant impairment,* and not accuracy in general. We have also updated the discussion to reflect these points.
29.	1	5. Page 27. I wonder if the Lew, et al (2007) and portions of the Brahm (2009) should be included in the discussion of Key Question 2. The vision data in the Lew paper was based upon patients seen in a VA PNS clinic. The Brahm (2009) paper presented data on both PRC and PNS patients and data was reported separately.	We considered reporting these data for KQ2 as well, but determined that they best fit with KQ1 and are included in that section.
30.	1	6. Essentially all of the papers cited (including Dougherty, et al) include a statement recommending that a comprehensive visual examination of patients experiencing a TBI should be provided a comprehensive vision examination. As the manuscript represents a synthesis of these papers would a similar statement be appropriate? Perhaps on page 32 lines 15 – 22 "Applicability of Findings to the VA Population"	Though we try not to make clinical recommendations in our reports, we are hoping to collaborate on dissemination efforts such as cyber-seminars with TEP members and stakeholders who are better able to make clinical recommendations.
31.	1	7. Page 34 References. There are some formatting issues; see lines 26 – 34	Thank you, this has been addressed

	Reviewer	Comment	Response
32.	1	8. Page 23 "Future Research Needs". 9.1. I believe it would be worth considering a recommendation of a longitudinal study of patients with visual dysfunctions be undertaken to determine if, over time, these conditions recover or whether they are "permanent" and the effect they have on employment, quality of life, education, utilization of VA services, etc.. The literature indicates visual dysfunctions are associated with reduced quality of life, impair reading and near tasks (hence employment and vocations), negatively impact social function, self-esteem, driving, etc. and so may impact the ability of those affected over their entire lifetimes. Given the relatively young age of OEF/OIF/OND Service Members these conditions may present substantial challenges to the VA over the next half century and beyond thus a longitudinal study would be relevant to VA. 9.2. I believe the question of how prevalent binocular/oculomotor dysfunctions are following blast or non-blast TBI remains an important question to be answered. 9.3. Given that a) mTBI post-2001 veterans have presented to the VA with high rates of binocular/oculomotor dysfunctions and b) the literature indicates that conditions can be treated, studies should be undertaken to determine the most effective treatments VA can provide to address these dysfunctions to maximize the veteran's return to normal visual functioning.	Thank you. We have added these suggestions to the FRN section of the report.
33.	2	1. Page 1, line 17, instead of "2009 systematic review," what about, "a systematic review conducted in 2009"	Thank you for the suggestion. This has been addressed.
34.	2	2. Page 1, line 37, can you indicate "Department of Veterans Affairs (VA)" before mentioning the PRCs?	Thank you for the suggestion. This has been addressed.
35.	2	3. Page 1, line 39, consider using "Conditions" instead of "outcomes"	Thank you for the suggestion. This has been addressed.
36.	2	4. Page 1, line 7, "ongoing post-concussive symptoms" – please see next comment.	Noted and addressed.
37.	2	5. Page 2, lines 7-9, I think we have to be careful about using the term "ongoing post-concussive symptoms" especially when referring to patients seen in the PNSs. Without longitudinal data, it's difficult to determine whether symptoms being experienced months to years after a TBI are related to the TBI event or to other conditions. If the articles that you cite specify that these are postconcussive symptoms (with the implication that they're related to the TBI), then the terminology is fine. If the linkage can't be established, then I wouldn't use this phrase. In addition, these clinics can serve Veterans who haven't experienced TBI. Frequently TBI occurs in polytrauma, but it doesn't have to: http://www.polytrauma.va.gov/system-of-care/ You might want to consider rephrasing, "clinics that primarily serve Veterans who have incurred serious injury and experience current symptoms that may be related to TBI, other comorbid conditions, or both."	Noted and addressed.
38.	2	6. Page 2, line 12, "current symptoms" instead of "ongoing post-concussive"	Thank you for the suggestion. The document has been edited to reflect this throughout.
39.	2	7. Table 1, column headings: the term "ongoing post-concussive symptoms" is used. Maybe consider "current symptoms" instead?	Thank you for the suggestion. The document has been edited to reflect this throughout.

	Reviewer	Comment	Response
40.	2	8. Page 3, line 3, you can place (TBI) after this first mention of traumatic brain injury, and then in line 5, you only need to use "TBI since it will have been defined in line 3.	Thank you for the suggestion. This has been addressed.
41.	2	9. Page 3, line 9, consider putting (mTBI) after "mild TBI" since it's used as a search term later?	Thank you for the suggestion. This has been addressed.
42.	2	10. For Figure 1, in the Exclusion boxes, what does "Background" refer to?	We have clarified this diagram.
43.	2	11. Page 9, lines 13-14: consider using a phrase other than "ongoing post-concussive symptoms." Another phrase might be "suspected TBI-related symptoms"	Thank you for the suggestion. The document has been edited to reflect this throughout.
44.	2	12. Page 9, line 15, I think there should be a 1:1 match with this section title and what's described in line 13. The title should match what's described in line 12. So, something like: Studies of patients in settings that treat patients regardless of suspected TBI-related symptoms"	We have made this change
45.	2	13. Page 9, lines 17-18, Can you explain what "over a set time period" means?	We agree that this was confusing and removed it as it was irrelevant.
46.	2	14. Page 9, lines 22: With regard to the comprehensive TBI evaluation, one of the biggest criticisms has been that it's unclear whether the symptoms that patients are asked to self-report on the 22-item Neurobehavioral Symptom Inventory are related to TBI or to other conditions, because patients can have this evaluation months to years after a suspected TBI event. Because of this lack of specificity, clinicians can't, with confidence, link these symptoms with a TBI. I would be more literal and state something like, "…were screened for neurobehavioral symptoms, including vision-related symptoms." The VA/DoD clinical guidelines (p. 21) state: Most symptoms and signs that occur in the acute period following a single concussion resolve quickly (within hours or days) after the injury. There is debate about the incidence of developing persistent symptoms after concussion, largely due to the lack of an accepted case definition for persistent symptoms and the fact that none of the symptoms are specific to concussion. There is no consensus on a case definition for persistent symptoms attributed to concussion/mTBI and no consensus on the time course when acute symptoms should be considered persistent. As a result, the important focus should be on treating the symptoms rather than on determining the etiology of the symptoms.	We agree and have made this change.
47.	2	15. Page 9, line 24, these two references should be after "studies," rather than after "which." "Which" should be deleted from this sentence.	Thank you for the suggestion. This has been addressed.
48.	2	16. Page 9, line 26-31: Here you talk about a clinical diagnosis in an unscreened (line 26) group. This refers to being unscreened for visual dysfunction? The paragraph then continues that this study may "provide more accurate assessments of clinically significant impairment." Do you mean that it might provide a more accurate prevalence estimate, or that the visual examinations were a more accurate assessment? Could you clarify what the comparison is – why this study may be "more accurate"?	We have edited this section for clarity.

	Reviewer	Comment	Response
49.	2	17. Page 9, line 34: the "on unscreened patients" makes it unclear whether the unscreened patients are part of the three studies cited or Dougherty's study. I think I would reword: The other three studies used self-report measures to screen participants[15,19,23] and found higher rates of visual dysfunction (8.8% – 54%, see Table 1) than the data from Dougherty and colleagues THAT REPORTED ON unscreened patients with diagnosed visual dysfunction."	Thank you for the suggestion. This has been addressed.
50.	2	18. Page 10, lines 1-2: Similar to my statement about PCS, I would stick with language consistent with the PsoC directive: http://www.va.gov/optometry/docs/VHA_Handbook_1172_01_Polytrauma_System_of_Care.pdf Suggested rewording: "…designed to serve Veterans with polytrauma and TBI, they serve…"	We agree and have made this change, as below.
51.	2	19. Page 10, lines 1-5: suggested rewording: Both types of treatment facilities provide interdisciplinary, rehabilitation care to Veterans who experienced TBI or polytrauma, but serve populations with different care needs. The five PRCs provide acute, inpatient care to those with more complex and severe TBI or polytrauma. The 23 PNSs provide care to those who are discharged from PRCs and need continued rehabilitation services, as well as to Veterans who require less intensive care for their TBI or polytrauma.	Thank you for this suggestion. We have made this change.
52.	2	20. Page 10, line 8: instead of "differ greatly," what about "differ in symptom severity and complexity,"	Thank you for the suggestion. This has been addressed.
53.	2	21. Page 10, line 12: Because we don't know (especially for the PNSs) if they're post-concussive, I might say something like based on "current" or "ongoing" symptoms	Thank you for the suggestion. The document has been edited to reflect this throughout.
54.	2	22. Page 10, line 13: What do you mean by "screening eye exams?" I'm not sure about the extent of screening for visual problems at PNSs (or PRCs), but if this phrase is referring to the NSI, I wouldn't call this an "eye exam." Rather, I would say something like, "because the patients are only screened for vision symptoms, rather than given a comprehensive eye examination,"	We have clarified the meaning of this phrase.
55.	2	23. Page 10, line 15: "generally much higher" than… "general patient populations?" or patient populations seen in a general primary care clinic? What comparison is being made?	We have clarified this sentence.
56.	2	24. Page 10, line 17 "included" is included twice in the same sentence. For the second one, say "illustrated" or "shown" or "displayed" in Table 1"	Thank you for the suggestion. This has been addressed.
57.	2	25. Page 10, Table 1 title: Maybe expand to say: Summary of Findings: Ranges of Visual Dysfunction Frequencies Across Studies…""…for patients who were screened or not screened clinically for visual dysfunction."	Noted. We retained the original title for space reasons, but the subheadings reflect screening.
58.	2	Please see previous comments about "ongoing post-concussive symptoms:.	Thank you for the suggestion. The document has been edited to reflect this throughout.
59.	2	26. Page 11, line 4 – because assessment is used a few words earlier, what about use "evaluate different" rather than "assess different"	Thank you for the suggestion. This has been addressed.
60.	2	27. Page 11, line 4 – what do you mean by visual dysfunction "outcome"? Would it be appropriate to say "evaluate different types of visual dysfunction"	Thank you, we have made this change.
61.	2	28. Table 2, first row – since this column extends beyond one page, can you repeat the header row on each page?	Thank you for the suggestion. This has been addressed.

	Reviewer	Comment	Response
62.	2	29. Page 17, line 18 – should this be optical "strain?"	Thank you for the suggestion. This has been addressed.
63.	2	30. Page 17, line 24, just a thought, but instead of saying "were more and less commonly," what about saying "Different studies of dry eye yielded mixed findings among blast-exposed subgroups…."	Thank you for the suggestion. This has been addressed.
64.	2	31. Table 6, p. 20, first row: What does 1.25 M letter size mean? Would the average reader know this?	We have updated the table to clarify this outcome.
65.	2	32. P. 24, line 13 "Compared to comparable controls" sounds a bit funny to the ear. Maybe you can describe some characteristics of how the controls are comparable? Perhaps something like, "….compared to a control group without a TBI history that had similar characteristics…"	Thank you for the suggestion. This has been addressed.
66.	2	33. Table 11 – repeat column headings across pages	Thank you for the suggestion. This has been addressed.
67.	2	34. Page 26, For the Lew, 2011 reference, no need to spell out the NSI 22 again, already identified in Bulson 2012 row.	Thank you for the suggestion. This has been addressed.
68.	2	35. Page 26, Stelmack 2009 reference. No need to spell out NSI-22	Thank you for the suggestion. This has been addressed.
69.	2	36. Page 28, Table 12, please copy column headings across pages. Page 29, Alvarez 2012 row (patient sensitivity to direct light" - in the p-value column, Bonferroni is misspelled.	Thank you for the suggestion. This has been addressed.
70.	2	37. Page 31, line 17 – unless the study specifically identifies these as "ongoing post-concussive symptoms" I wouldn't refer to them as that, since we can't be certain that symptoms are related to concussion, which I think this phrase implies. Maybe use the term "current symptoms" instead?	Thank you for the suggestion. The document has been edited to reflect this throughout.
71.	2	38. Page 32, lines 1-2: Instead of "ongoing post-concussive symptoms" consider something else, like "current symptoms"	Thank you for the suggestion. The document has been edited to reflect this throughout.
72.	2	39. Page 32, line 18, Prevalence estimates OF(?) a broad group…? (Is "of" missing?)	Thank you for the suggestion. This has been addressed.
73.	2	40. Page 32, line instead of "many comorbid conditions," what about "multiple"?	Thank you for the suggestion. This has been addressed.
74.	2	41. Page 32, line 37: I think there can be a period after "studies," rather than a colon.	Thank you for the suggestion. This has been addressed.
75.	2	42. Page 32, line 37-38: I'd suggest using a term other than "ongoing post-concussive symptoms." In fact, that might be a point to make for future research directions – conducting longitudinal studies to determine whether symptoms following TBI persist over time, and for how long.	Thank you for the suggestion. The document has been edited to reflect this throughout.
76.	2	43. Page 32, line 39, "ongoing post-concussive symptoms" – maybe consider "Veterans with a TBI history who may have persistent TBI-related symptoms".	Thank you for the suggestion. The document has been edited to reflect this throughout.
77.	2	44. Page 33, lines 4-5 "ongoing post-concussive symptoms" – consider using "and who are experiencing current symptoms"	Thank you for the suggestion. This has been addressed.

	Reviewer	Comment	Response
78.	2	45. Page 36, Should read: Terri K. Pogoda, PhD Research Health Scientist Center for Healthcare Organization and Implementation Research VA Boston Healthcare System Boston, MA	Thank you for the suggestion. This has been addressed.
79.	3	In addition to quality of data concerns due to generalizability of population and setting, there is also much heterogeneity in methodology between studies. This may account for a large percentage of variability seen across the reports. This is particularly true in testing for dry eye and with visual fields. Automated visual field testing (Humphrey or Octopus) has not been validated in brain injury patients, and modifications to the testing protocols should be described and justified in detail if used. In dry eye, no single test is sufficient for a diagnosis; that is why the Dry Eye Workshop in 2007 defined a battery of tests for research quality studies. Some studies did not define testing methodology at all. Possible reasons that prevalence estimates in unscreened military personnel may be artificially low include: reluctance to complain; desire to remain with teammates; intermittent symptomatology, such as intermittent diplopia; lifestyle modifications to adapt to dysfunctions, such as not reading because of near vision problems; or having been told that there is nothing wrong with their vision previously after taking a high-contrast visual acuity test, which is relatively insensitive to many of the reported vision problems in TBI. Despite assertions to the contrary in the report, not all inpatients within PRC were moderate or severe TBI; one third of the Palo Alto group were mild TBI who presented in ambulatory status, wishing workup for TBI after having been told by the military that there was nothing wrong with them. Palo Alto did stratify examinations by TBI Severity Rating, and have found no correlations in quality of life or dry eye (published) or afferent visual function (unpublished). A major area of weakness in current TBI Vision literature is lack of longitudinal data and visual outcomes	We agree, and have added information related to methods in the tables and text.
80.	4	This does not give much guidance to the field on where the gaps exist. What is the point of this exercise if recommendations on the type studies that are needed to improve the science or the healthcare of this condition? What about imaging studies to verify that central fiber loss or EEG studies indicating physiological loss that could consistent with visual dysfunction? Or potential studies that demonstrate therapies to overcome these deficits? The field as well as VA Central Office need that kind of objective input from a evidence synthesis review to make strategic research and funding decisions.	We are not able to address some of those questions due to the scope of this report and key questions, but agree that they may be very relevant to VA leadership.
81.	5	I would like to see better differentiation of studies looking at symptom report vs. confirmed clinical diagnosis (p9 line 32-37) as this has important implications for administrators looking at screening implications. VHA has a large data set of mandatory visual exams from TBI patients during an inpatient PRC stay. It is critical that this important data set be studied and published in order for VHA to determine the effectiveness and importance of this policy.	We have edited this section for clarity.
82.	6	There is no discussion of the possibility of progression of visual dysfunction after TBI – I know of no study yet published, but this is a big area of concern, especially in light of CTE where progressive dementia occurs over time after concussion.	We have included suggestions of longitudinal research in the FRN section of this report.

	Reviewer	Comment	Response
83.	7	This is a well done report. The breadth of the criteria is wide and thoroughly addresses the spectrum of problems encountered by our Veterans with TBI. The apparent discrepancy between the numbers of presenting individuals with various problems is well explained on the basis of clinical setting and natural recruitment bias. The relatively rare nature of the visual problems seen in the large data base study is explainable on the basis of emphasis of care being rendered that was not focused on vision assessment but also due to the expected lower rate of problem identification that is seen when surveying ICD entries. This begs the question for a prospective study to establish the actual prevalence rate of these problems since a more detailed vision assessment is likely to be informative, but this needs to be done for a large population not already pre-selected based on a priori vision criteria.	Noted, and we have added to the FRN section of this report.
84.	8	Entire document – capitalize the word “Veterans” throughout document; consistency	Thank you for the suggestion. The document has been edited to reflect this throughout.
85.	8	Entire document – correct capitalization of term “Service members” throughout document for consistency. “S” in Service should be capitalized.	Thank you for the suggestion. The document has been edited to reflect this throughout.
86.	8	Cover page – Notwithstanding the acknowledgement on page 4, would it be appropriate to include list of names of those that provided editorial / review assistance for the report.	We generally do not list the names of peer reviewers, but have included a list of TEP members and stakeholders who also review the report.
87.	8	Page 1, 1st paragraph, lines 3-6, first sentence – comment - need to include reference for the stats cited in the sentence that reads, “Approximately 1.7 million people experience…”	We include these references in the body of the report, though our formatting removes references from the executive summary.
88.	8	Page 1, 1st paragraph, line 6 – edit - suggest changing “vision” to “visual functioning”	Thank you for the suggestion. This has been addressed.
89.	8	Page 1, first paragraph, line 9 – edit - recommend adding “occupational and physical therapists, primary care providers” after “rehabilitation specialists.”	Thank you for the suggestion. This has been addressed.
90.	8	Page 1, Key Question 2, line 15 – edit – recommend changing “vision clinics” to “eye care clinics.”	Thank you for the suggestion. This has been addressed.
91.	8	Page 4, 1st paragraph, line 5 – edit - insert Dr. Barker’s title at the VCE after his name. His title is, “Associate Director, Research, Rehabilitation and Reintegration, Vision Center of Excellence.”	Thank you for the suggestion. This has been addressed.
92.	8	Page 9, 3rd paragraph, lines 24-31 – comment / recommendation – In reference to the study by Dougherty and colleagues, the severity of TBI was included in the study. The paper reports 8.9% were diagnosed with an ocular or visual disorder within 12 months of the blast injury. The odds of visual dysfunction increased with the severity of TBI. Recommend reviewing the Dougherty study to ensure data from it was accurately used and is accurately quoted in the report.	We have reexamined this study and report updated results in this revised report.
93.	8	Page 10, Table 1 – question – Are totals able to be calculated, i.e., total patients with some type of visual dysfunction?	We have presented this information in text in the revised report.
94.	8	Page 11, last paragraph – comment – This comment refers to both key questions; therefore, recommend repeating this language for Key Question 2 or place this paragraph after the paragraph on “Rating the Body of Evidence” on page 6 of the report.	We have included quality and methods considerations for both key questions.

	Reviewer	Comment	Response
95.	8	Page 15, 2nd paragraph, lines 13-15 – edit – sentence starting with, "The authors report…" delete "a moderating effect of blast exposure, with" and "reported" and rewrite sentence to read, "The authors report higher frequencies for blast-exposed inpatients than non-blast exposed inpatients, but lower frequencies for blast-exposed outpatients compared to non-blast exposed outpatients."	Thank you for the suggestion. This has been addressed.
96.	8	Page 15, 2nd paragraph, line 16 – comment / edit - referring to the word "similar" in this sentence…does this refer to other investigators findings or differences between blast & non-blast? Also, it may be noted that these differences may be due to selection bias as outpatients may have more visual demands. Recommend deleting the word "similar" on line 16 and insert "to be similar" between "dysfunction" and "for blast" on line 17.	We have clarified this paragraph.
97.	8	Page 15, 2nd paragraph, lines 16-17 – edit – replace "refraction dysfunction" with "refractive errors."	We have made this change.
98.	8	Page 32, last paragraph, line 40 – edit - delete the word "diagnosed."	Thank you for the suggestion. This has been addressed.
99.	8	Page 33, line 2 – edit - replace "infrequent, generally occurring in less than 1% of patients" with, "diagnosed with a frequency of 7.3% for disorders of accommodation and refractive errors and a frequency of less than 1% for other visual dysfunctions." Please refer to above comment regarding the Dougherty paper to check this sentence for accuracy.	Thank you for the suggestion. This has been addressed.
	Optional Dissemination and Implementation Questions		
100.	***5. Are there any VA clinical performance measures, programs, quality improvement measures, patient care services, or conferences that will be directly affected by this report? If so, please provide detail.***		
101.	1	1. The report is directly relevant to VA optometry and ophthalmology services as well as PRC and PNS programs or any program addressing veterans with TBI.	Noted.
102.	1	2. It is also applicable to neuropsychology and others who rely on assessments that include reading or near tasks as the presence of undetected visual dysfunction or visual loss has the potential to generate misleading test results.	Noted.
103.	1	3. Relevant to the DoD/VA Vision Center of Excellence	Noted.
104.	1	4. Relevant to VA Rehabilitation Research & Development and Health Services Research &Development.	Noted.
105.	1	5. The American Academy of Optometry, American Academy of Ophthalmology, and Association for Research on Vision and Ophthalmology (ARVO) would be receptive audiences for this information.	Noted.
106.	3	Not sure.	Noted.
107.	4	The way the report is currently written, the effect will be minimal.	Noted.
108.	5	There is currently a directive requiring Optho exam of all Veterans with inpatient rehabilitation stays at the PRCs with a TBI diagnosis. This directive is expiring and I believe the national Ophthalmology program will be promoting a clinical practice recommendation/guideline moving forward.	Noted.
109.	6	All blind rehabilitation centers within the VA will have an interest in this report. There will be an ARVO symposium on visual dysfunction and TBI chaired by Dr. John Clark John I Clark [clarkji@u.washington.edu]* that will be held in Denver first week of May 2015.	Noted.

	Reviewer	Comment	Response
110.	7	At present the eye care services (optometry and ophthalmology) of the VA would benefit from the results of this study in support of their efforts to detail recommended eye/vision assessments and the referral criteria for such assessments	Noted.
111.	8	Continual modification or rescinding of VA Directive 2008-065 (published 10/20/08).	Noted.
	6. Please provide any recommendations on how this report can be revised to more directly address or assist implementation needs.		
112.	1	Given that all studies recommend specific vision screening for mTBI patients this report could well echo that recommendation perhaps specifically targeting applicable services (optometry, ophthalmology, and the Polytrauma System of Care, to mention a few).	Though we try not to make clinical recommendations in our reports, we are hoping to collaborate on dissemination efforts such as cyber-seminars with TEP members and stakeholders who are better able to make clinical recommendations
113.	2	I will defer to the experts to determine how the findings impact the directive for PRCs to have ocular health and visual functioning examinations performed by optometrists or ophthalmologists.	Noted.
114.	3	Emphasize the research gaps	We have updated the FRN section of this report.
115.	4	See my suggestions under #4. At this point, I do not see any benefit to VA clinicians or investigators who would be the consumers of this review.	Noted.
116.	5	It would be helpful to include a description of eye care within VHA and provide some detail about the ability to treat and manage the listed diagnosis in this review (i.e. can every VA ophthalmologist and optometrist diagnose and treat convergence insufficiency or does a primary care clinician need to refer to a tertiary center). It would also be helpful to more clearly state that additional research is needed to establish referral guidelines for visual symptom complaints as the reader may assume that any complaint would trigger a referral to Eye clinic. In addition if there are any recommendations for Primary care providers to implement prior to referral there should be a reference included. The Office of Specialty care may want to consider implementing (or at least recommending) a national consult template for Eye clinics to direct the ordering clinician to identify Veterans with h/o TBI.	We have plans to address these clinical questions in a cyber-seminar with TEP members and stakeholders, and also updated the FRN section of this report to address some of these concerns.
117.	8	Well written and constructed. Minor comments, edits and revisions noted in item #4 above.	Noted.
	7. Please provide us with contact details of any additional individuals/stakeholders who should be made aware of this report.		
118.	2	Polytrauma/Blast-Related Injuries QUERI, PM&R Program Office	Noted.
119.	3	N/A	Noted.
120.	4	COL Dallas Hack 'dallas.c.hack.mil@mail.mil'	Noted.
121.	5	DCoE Vision Center of Excellence and Primary Care in VHA if not already involved.	Noted.
122.	6	VA Rehabilitaton Journal and possibly published in that journal	Noted.
123.	7	Dr John Townsend Optometry Consusltant and Dr Glenn Cockerham Ophthalmology Consultant	Noted.

	Reviewer	Comment	Response
124.	8	Mary Lynch, MD – mary.lynch4@va.gov Glenn Cockerham, MD – glenn.cockerham@va.gov John Townsend, MD – john.townsend@va.gov Robert Sergott, MD – rcs220@comcast.net Amy Chomsky, MD – amy.chomsky@va.gov Randy Kardon, MD – randy.kardon@va.gov Robert Ruff, MD – Robert.ruff1@va.gov Gregory Goodrich, PhD – Gregory.goodrich@va.gov	Noted.