McMaster University | Health Forum

# Rapid Evidence Profile appendices

# Transcranial photobiomodulation therapy for traumatic brain injury (TBI)

## 8 April 2026

[MHF product code: REP 101]

## Appendices



## Appendix 1: Methodological details

We use a standard protocol for preparing rapid evidence profiles (REPs) to ensure that our approach to identifying research evidence is as systematic and transparent as possible in the time we are given to prepare the profile.

### Identifying research evidence

For this REP, we searched Health Systems Evidence, PubMed and ACCESSSS for evidence syntheses, single studies and protocols. All searches were conducted on 9 March 2026.

We searched Health Systems Evidence using filters for brain injury and a date limit of the past 10 years.

In PubMed, we used an open text search for (("low level" AND "light" AND "therapy") OR "low level light therapy" OR "photobiomodulation") AND (("brain" AND "injuries") OR "brain injuries" OR ("brain" AND "injury") OR "brain injury")), combined with MeSH search terms for "low level light therapy," "brain injuries," as well as exclusions for editorial and comment publication types and a date limit of the past 10 years. The link provides access to the full search strategy.

In ACCESSSS, we used an open text search for (("photobiomodulation" OR "light therapy") AND "brain injury")) with a date limit of the past 10 years. The link provides access to the full search strategy.

Each source for these documents is assigned to one team member who conducts hand searches (when a source contains a smaller number of documents) or keyword searches to identify potentially relevant documents. A final inclusion assessment is performed both by the person who did the initial screening and the lead author of the rapid evidence profile, with disagreements resolved by consensus or with the input of a third reviewer on the team. The team uses a dedicated virtual channel to discuss and iteratively refine inclusion/exclusion criteria throughout the process, which provides a running list of considerations that all members can consult during the first stages of assessment.

During this process we include published, pre-print and grey literature. We do not exclude documents based on the language of a document. However, we are not able to extract key findings from documents that are written in languages other than Chinese, English, French, Portuguese or Spanish. We provide any documents that do not have content available in these languages in an appendix containing documents excluded at the final stages of reviewing. We excluded documents that did not directly address the research questions and the relevant organizing framework.

## Jurisdictional scan

For each REP, we work with the requestors to collectively decide on what jurisdictions to examine based on the question posed. For this REP, we examined transcranial photobiomodulation (tPBM) therapy for traumatic brain injury (TBI) programs and research projects from relevant government and professional association websites within the 'Five Eyes' countries (Australia, Canada, New Zealand, the United Kingdom and the United States). While we do not exclude content based on language, where information is not available in English, Chinese, French, Spanish or Portuguese, we attempt to use site-specific translation functions or Google Translate. A full list of websites and organizations searched is available upon request. A section in the report documents the types of approaches used by different jurisdictions and for various health services. Details from the Canadian and international jurisdictional scans can be found in Appendix 3.

# Appendix 2: Details about each identified single study

| Dimensions of organizing framework | Declarative title and key findings | Study characteristics | Equity considerations |
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| • Wavelength range<br>  ○ 800–900 nm<br>• Treatment time<br>  ○ 5–20 minutes<br>• Number of sessions<br>  ○ 1–3<br>• Frequency of sessions<br>  ○ Daily<br>• Setting of sessions<br>  ○ Clinical setting<br>• Patient eligibility<br>  ○ Type of traumatic brain injury<br>  ▪ Moderate<br>  ○ Age<br>  ▪ 18–29<br>  ▪ 30–44<br>  ▪ 45–60<br>  ▪ 60+<br>• Outcomes<br>  ○ Health outcomes | Transcranial low-level light therapy is safe and feasible after moderate traumatic brain injury and produces significant changes in diffusion magnetic resonance imaging (MRI) measures of brain recovery (1)<br>• This study assessed the feasibility and safety of low-level light therapy (LLLT) after moderate traumatic brain injury, as well as the effects of LLLT on brain neuroreactivity using MRI and post-concussion questionnaires<br>• Participants<br>  ○ 68 men and women (18–79 years; mean age 50.49) with acute, nonpenetrating, moderate traumatic brain injury (TBI) were randomized to LLLT or sham treatment (33 to LLLT and 35 to sham therapy)<br>• Methods<br>  ○ LLLT was provided through a custom-made helmet and was started within 72 hours after the TBI<br>  ▪ Consisted of eight clusters of 20 near-infrared (NIR) light-emitting diodes<br>  ▪ The LEDs emit at a centre wavelength of 810 nm with a bandwidth of 30 nm<br>  ▪ Provided an incident fluence of approximately 43 J/cm2 (0.036 W/cm2 x 20 minutes x 60 seconds/min = 43.2 J/cm2) to the scalp per 20-minute session<br>  ▪ Based on known scalp/skull transmission of NIR light in cadavers, approximately 3% (or 1.3 J/cm2) of the incident fluence reached the cortical surface of the brain<br>  ○ Treatment was divided into three sessions of 20 minutes duration with at least 12-hour intervals between the therapy sessions<br>  ○ Sham therapy was delivered using the same helmet with the light-emitting diodes remaining off<br>  ○ Following the first helmet application, a baseline MRI was performed to assess acute brain trauma<br>  ▪ Two follow-up scans, one early (–2-3 weeks post-trauma) and one late (~3 months post-trauma), were performed to assess subacute stages of recovery through brain diffusion measures<br>  ○ Clinical assessments were performed using the Rivermead Post-Concussion Symptoms Questionnaire (RPQ) at baseline, 14 days, three months, and six months after the trauma<br>• Outcomes<br>  ○ Of the LLLT group, 28 participants completed at least one LLLT session, with no side effects relating to the treatment reported<br>  ○ At 3 months follow up, MRI results showed significant differences over time between the treatment and sham groups in three brain structure measures (radial diffusivity (RD), mean diffusivity (MD) and fractional anisotropy (FA), (RD: 0.013; 95% CI 0.006–0.019; P < .001; MD: 0.008; 95% CI 0.001–0.015; P = .03; FA: −0.018; 95% CI −0.026 to −0.010; P < .001)) | Relevance rating: High<br><br>Publication date: September 2020<br><br>Jurisdiction studied: U.S.<br><br>Methods: Randomized, single-centre, prospective, double-blind, placebo-controlled parallel-group trial | None identified |

| Dimensions of organizing framework | Declarative title and key findings | Study characteristics | Equity considerations |
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| | ○ Participants in the LLLT group reported fewer post-concussion symptoms with lower RPQ scores, but the difference was not statistically significant<br>• This study provides human evidence that light therapy engages neural substrates that play a role in the pathophysiologic factors of moderate TBI and suggests that diffusion imaging is a biomarker of therapeutic response | | |
| • Wavelength range<br>○ 800–900 nm<br>• Treatment time<br>○ 5–20 minutes<br>• Number of sessions<br>○ 1–3<br>• Frequency of sessions<br>○ Daily<br>• Setting of sessions<br>○ Clinical setting<br>• Patient eligibility<br>○ Type of traumatic brain injury<br>▪ Moderate<br>○ Age<br>▪ 18–29<br>▪ 30–44<br>▪ 45–60<br>▪ 60+<br>• Outcomes<br>○ Health outcomes | Low-level light therapy administered shortly after moderate traumatic brain injury increased early resting-state brain connectivity but did not significantly improve clinical symptoms compared with sham treatment (2)<br>• The purpose of the study was to investigate the effects of low-level light therapy on resting-state functional connectivity (RSFC) in the brain of patients recovering from moderate TBI using functional MRI across different stages of recovery (acute, subacute and late-subacute)<br>• Participants<br>○ The study included 38 patients with moderate TBI and 23 healthy control participants; among the TBI participants, 17 received LLLT and 21 received sham treatment<br>○ The median age of both treatment groups was 50 years (IQR 25–67), while the control group had a median age of 42 years (IQR 32–54)<br>○ Participants with TBI were recruited from the Massachusetts General Hospital emergency department between 2015 and 2019<br>○ Participants were eligible if they had moderate traumatic brain injury, defined as a Glasgow Coma Scale score of 9–12 or a score of 13–15 with abnormal CT findings, such as hemorrhagic contusions, intracranial hemorrhage, skull or facial fractures, or subgaleal hematoma<br>• Methods<br>○ Low-level light therapy was delivered using a helmet device that emitted near-infrared light with a wavelength of 810 nm and a bandwidth of 30 nm<br>○ Each treatment session lasted approximately 20 minutes, and participants received three treatment sessions, each separated by at least 12 hours<br>○ Treatment began within 72 hours of the traumatic brain injury<br>○ The sham treatment group underwent the same procedure with the helmet device but without active light emission, ensuring that participants and most research staff remained blinded to treatment allocation<br>○ The helmet device contained eight clusters of 20 NIR light-emitting diodes (LEDs) positioned around the scalp to deliver light to multiple brain regions<br>○ Participants with traumatic brain injury underwent resting-state functional MRI scans at three follow-up time points, including the acute phase (within one week after injury), the subacute phase (two to three weeks)<br>○ Clinical outcomes were assessed using the Rivermead Post-Concussion Symptoms Questionnaire (RPQ), which measured the severity of post-concussion symptoms at each MRI visit | Relevance rating: High<br><br>Publication date: May 2024<br><br>Jurisdiction studied: Boston, U.S. (Massachusetts General Hospital)<br><br>Methods: Secondary analysis of prospective single-site double-blinded sham-controlled study | None identified |

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| | ○ Resting-state functional connectivity was also assessed through blood-oxygen-level dependent (BOLD) signals obtained during functional MRI scans, allowing researchers to measure the correlation of neural activity between brain regions<br>• Outcomes<br>○ The study found that seven brain region pairs demonstrated greater changes in functional connectivity in the LLLT group compared with the sham group between the acute and subacute recovery phases, with Fisher z-transformed differences ranging from 0.37 to 0.45 (95% CI 0.20–0.67) and false discovery rate-adjusted P values between 0.010 and 0.047<br>○ Connectivity generally increased in the LLLT group but decreased in the sham group during this early recovery phase<br>○ From the subacute to late-subacute phase, 13 brain region pairs in the sham group showed increased connectivity, which the researchers interpreted as a potential natural healing process<br>○ Despite these imaging findings, no significant differences were found in clinical outcomes between the LLLT and sham groups, with RPQ score differences ranging from −3.54 to −0.59 and P values between 0.44 and 0.99<br>• Researchers suggest LLLT did not produce significant improvements in clinical symptom outcomes and larger studies with longer follow-up are needed to determine the clinical benefits of LLLT for TBI recovery | | |
| • Wavelength range<br>○ 600–700 nm<br>○ 800–900 nm<br>• Treatment time<br>○ 5–20 minutes<br>• Number of sessions<br>○ 1–3<br>• Frequency of sessions<br>○ Daily<br>○ Multiple times per week<br>• Setting of sessions<br>○ Clinical setting<br>• Patient eligibility<br>○ Type of traumatic brain injury<br>▪ Mild<br>○ Age<br>▪ 18–29<br>▪ 30–44<br>▪ 45–60<br>▪ 60+<br>• Outcomes | Six weeks of transcranial photobiomodulation therapy did not significantly improve concussion symptoms or neurocognitive performance compared with placebo therapy in patients with persistent post-concussion symptoms (3)<br>• The purpose of the study was to evaluate the effectiveness of transcranial photobiomodulation (tPBM) as a treatment for patients experiencing persistent post-concussion symptoms<br>• Participants<br>○ A total of 53 participants were enrolled in the study, and 48 participants completed the clinical trial and were included in the final analyses after five participants withdrew (three from the control group and two from the treatment group)<br>○ Participants were 11 years of age or older (mean age of 22 years) and were receiving clinical care for persistent post-concussion symptoms (average of 225 days post-injury at the time of enrolment)<br>○ Most injuries occurred during sports, exercise, or similar activities, with soccer being the most common sport associated with concussion among sport-related injuries<br>○ Loss of consciousness occurred in 13% of participants, while 35% experienced post-traumatic amnesia at the time of injury<br>• Methods<br>○ Participants were randomly assigned to tPBM therapy or placebo therapy using a random number generator sequence<br>○ Participants two treatment sessions per visit, each lasting 10 minutes<br>○ Treatments occurred three times per week and the treatment period lasted six weeks total<br>○ Visits were scheduled with approximately 48 hours between sessions | Relevance rating: High<br><br>Publication date: May 2024<br><br>Jurisdiction studied: U.S.<br><br>Methods: Randomized, double-blind, placebo-controlled trial | None Identified |

| Dimensions of organizing framework | Declarative title and key findings | Study characteristics | Equity considerations |
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| ○ Health outcomes | ○ Transcranial photobiomodulation was delivered using two MedX Health Console Model 1100 LED therapy units<br>▪ Each unit delivered light through three cluster heads that measured approximately 2 inches in diameter, contained nine visible red LEDs (633 nm wavelength), and contained 52 near-infrared LEDs (870 nm wavelength)<br>▪ Two consoles were used simultaneously, providing six cluster heads in total<br>▪ The cluster heads were placed at specific scalp locations across the forehead and scalp to deliver light transcranially<br>▪ The therapy used red and near-infrared wavelengths, which are believed to stimulate mitochondrial cytochrome-c oxidase activity and improve cellular energy metabolism in neurons<br>○ Participants in the placebo group received treatment using identical MedX Health Console units fitted with placebo cluster heads<br>▪ The placebo cluster heads were applied in the same locations and sequence as the active treatment devices<br>▪ The consoles were labelled “A” or “B,” and the treatment assignment code was hidden until the study was completed<br>▪ The devices were covered during treatment so that participants and investigators could not see whether light was emitted, maintaining the double-blind design<br>○ Outcomes were assessed were the change in Post-Concussion Symptom Scale (PCSS) and Post-Concussion Assessment and Cognitive Testing (ImPACT) scores at baseline (study entry), three weeks of treatment, and at six weeks of treatment (completion of therapy)<br>○ Clinical assessments were PCSS, to measure symptom severity, and Immediate ImPACT to produce composite scores for verbal memory, visual memory, processing speed and reaction time<br>• Outcomes<br>○ After three weeks of treatment, self-reported concussion symptoms measured by the PCSS total score improved in both groups, but the difference between the treatment group (mean improvement = 9.86) and the control group (mean improvement = 7.22) was not statistically significant (P = 0.566)<br>○ After six weeks of treatment, the control group showed greater improvement in PCSS scores (mean change = 14.63) compared with the treatment group (mean change = 7.86), although this difference was not statistically significant (P = 0.251)<br>○ Cognitive symptom scores and depression scores also improved in both groups, but there were no statistically significant differences between groups at either three weeks or six weeks of treatment<br>○ After three weeks of treatment, the placebo group demonstrated significantly greater improvement in visual–motor speed performance compared with the treatment group (P = 0.023) | | |

| Dimensions of organizing framework | Declarative title and key findings | Study characteristics | Equity considerations |
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| | ○ After six weeks of treatment, the placebo group demonstrated significantly greater improvement in visual memory compared with the treatment group (P = 0.008)<br>○ There were no significant differences between groups in verbal memory or reaction time at either time point<br>• The study concluded that transcranial photobiomodulation therapy did not produce significant improvements in concussion symptoms or neurocognitive outcomes compared with placebo treatment in patients with persistent post-concussion symptoms | | |
| • Wavelength range<br>○ 800–900 nm<br>• Wave type<br>○ Continuous<br>• Treatment time<br>○ 5–20 minutes<br>• Number of sessions<br>○ Ongoing use<br>• Frequency of sessions<br>○ Multiple times per week<br>• Setting of sessions<br>○ Clinical setting<br>• Patient eligibility<br>○ Type of traumatic brain injury<br>▪ Mild<br>○ Co-morbid conditions<br>▪ Mental health conditions (e.g., depression, PTSD)<br>▪ Neurological conditions<br>▪ Musculoskeletal conditions (e.g., chronic pain)<br>▪ Other conditions (e.g., sleep disorders, vision/hearing loss)<br>○ Age<br>▪ 18–29<br>▪ 30–44<br>▪ 45–60<br>▪ 60+<br>• Outcomes | Eighteen tPBM sessions improved cognition and reduced post-injury symptoms – including sleep issues, physical symptoms, pain and PTSD – supporting its potential as a symptom-relief intervention (4)<br>• This study investigated the effects of transcranial photobiomodulation (tPBM) on patients with mild TBI (mTBI)<br>• Sample<br>○ 17 patients (eight females and nine males) with mTBI for at least 8 months, between 18 and 80 years old (mean age: 60.25) who were recruited from the outpatient clinic of the Department of Neurosurgery at Prince of Wales Hospital between May 2023 and April 2024 and were randomized to tPBM or sham treatment (nine to tPBM and eight to sham therapy)<br>• Methods<br>○ tPBM device<br>▪ The tPBM intervention used a custom device with 81 LEDs emitting 810 nm continuous-wave light<br>▪ LEDs (~1 $cm^2$) were positioned over prefrontal, parietal, and temporal regions (FpZ, Fp1, Fp2, F7, F8, T7, T8, Fz, F3, F4, Cz, C3, C4, P3, P4)<br>▪ Each 12-minute session delivered 30 $mW/cm^2$ and 1.8 $J/cm^2$ per minute via nine LED clusters, totaling 16.2 J per cluster/minute<br>▪ To prevent overheating, 12 one-minute stimulations used 1–2 clusters at a time, totalling 324 J per session (irradiance: 30 $mW/cm^2$, fluence: 21.6 $J/cm^2$)<br>▪ The sham intervention used an identical non-emitting device that produced matching beeping sounds to maintain participant blinding<br>○ Baseline included standardized neuropsychological tests, questionnaires, and the Visual Working Memory Span Task (VWMST) with functional near-infrared spectroscopy (fNIRS) recording<br>○ Each intervention lasted six weeks (18 sessions), followed by a baseline-identical assessment and a one-week washout before the second intervention<br>○ Participants and administrators were blinded to the crossover; however, the outcome assessor was not, due to managing tPBM device technicalities<br>• Outcomes<br>○ 23 patients were initially randomized and allocated to real (12) or sham tPBM (11); however, six participants dropped out | Relevance rating: High<br><br>Publication date: October 2025<br><br>Jurisdiction studied: China<br><br>Methods: Randomized placebo-controlled trial | None identified |

| Dimensions of organizing framework | Declarative title and key findings | Study characteristics | Equity considerations |
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| ○ Health outcomes | ○ No participants reported serious discomfort or adverse effects during or after the intervention<br>○ Impact of tPBM on cognitive efficiency<br>▪ VWMST visual span showed a marginal condition difference ($F(2, 32) = 3.20$, $p = 0.05$, $\eta p^2 = 0.17$). Performance improved significantly from baseline only after real tPBM ($t(16) = 2.95$, $p < 0.01$, $d = 0.72$), while differences between baseline/sham ($p = 0.09$) and sham/real intervention ($p = 0.86$) were non-significant<br>▪ Reaction time showed a significant condition-by-span interaction ($F(14, 224) = 1.85$, $p = 0.03$, $\eta p^2 = 0.10$). Sham improved over baseline at spans 2 and 4–6, while the real tPBM intervention improved reaction times at spans 2, 4, 5, 7 and 9 ($p < 0.04$)<br>▪ At span 9, real tPBM was significantly faster than both baseline ($p < 0.01$) and sham ($p = 0.02$), whereas the baseline-to-sham difference was non-significant ($p = 0.31$)<br>▪ Oxygenated hemoglobin (HbO) data showed no significant effects ($p > 0.23$), suggesting the real tPBM intervention improved performance without increasing cognitive effort, which indicates enhanced neural efficiency<br>○ Impact of tPBM on cognitive function<br>▪ Neuropsychological assessment showed significant total learning gains ($F(2, 32) = 7.66$, $p < 0.01$, $\eta p^2 = 0.32$), where real tPBM significantly outperformed both sham ($p = 0.04$, $d = 0.53$) and baseline ($p < 0.01$, $d = 0.81$)<br>▪ Test (HKLLT) delayed recall and Five-Point Test (FPT) unique designs ($p < 0.01$, $\eta p^2 \geq 0.27$)<br>▪ While both sham and real tPBM significantly improved performance over baseline ($p < 0.02$), no significant differences existed between them ($p > 0.56$), nor for Category Fluency Test (CFT), Digit Span Test (DST) or Shape Trail Test (STT) ($p > 0.07$)<br>○ Impact of tPBM on sleep, physical post-concussion symptoms, and post-traumatic stress disorder (PTSD) symptoms<br>▪ Subjective sleep quality showed a significant condition difference ($F(2, 32) = 7.45$, $p < 0.01$, $\eta p^2 = 0.31$); real tPBM significantly improved sleep quality compared to both baseline and sham ($p < 0.01$, $d = 0.74$), while no difference existed between baseline and sham ($p = 1.00$); global and other Pittsburgh Sleep Quality Index (PSQI) subscale scores remained non-significant ($p > 0.29$)<br>▪ RPQ physical symptoms showed a significant main effect ($F(2, 32) = 3.69$, $p = 0.04$$, $\eta p^2 = 0.19$); real tPBM significantly improved symptoms over baseline ($p = 0.02$, $d = 0.61$), though no significant differences existed between baseline and sham ($p = 0.13$) or sham and real conditions ($p = 0.21$)<br>▪ Visual Analog Scale (VAS) pain intensity showed a significant main effect ($p = 0.04$, $\eta p^2 = 0.23$); real tPBM significantly reduced pain versus baseline ($p = 0.03$), while sham and real-versus-sham comparisons showed only non-significant trends ($p = 0.06$) | | |

| Dimensions of organizing framework | Declarative title and key findings | Study characteristics | Equity considerations |
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| | ▪ PTSD symptoms (PCL-5) showed a significant main effect ($p = 0.02$, $\eta p^2 = 0.21$); only real tPBM significantly improved symptoms over baseline ($p < 0.01$, $d = 1.03$), while sham and real-versus-sham differences were non-significant ($p=0.19$)<br>○ No significant carryover effects were found ($p = 0.17–0.86$)<br>○ All tests (PSQI, PCL-5, VAS, RPQ) reached the minimal clinically important difference (MCID), confirming that the statistically significant improvements were also clinically significant<br>○ Significant correlations were found between improvements in RPQ and both PCL-5 ($r = 0.57$, $p = 0.02$) and VAS ($r = 0.56$, $p = 0.02$), linking reduced post-concussion symptoms with improved PTSD and pain outcomes; no other significant correlations were found among behavioral or cognitive assessments ($p = 0.05$)<br>○ Significant learning effects likely influenced outcomes ($d = 0.55–0.93$), with HKLLT delayed recall showing significant improvements ($p = 0.05$) after sham tPBM; non-significant results ($p = 0.07$) for other measures likely reflect limited power | | |
| • Wavelength range<br>○ 800–900 nm<br>• Treatment time<br>○ 5–20 minutes<br>• Frequency of sessions<br>○ Multiple times per week<br>• Setting of sessions<br>○ Clinical setting<br>• Patient eligibility<br>○ Type of traumatic brain injury<br>▪ Moderate<br>○ Age<br>▪ 18–29<br>▪ 30–44<br>▪ 45–60<br>▪ 60+<br>• Outcomes<br>○ Health outcomes | The study indicates a potential benefit of LLLT, which lowered mIns/NAA in the late subacute phase, while the sham group showed a significant increase (5)<br>• The study aimed to evaluate the metabolic effects of low-level light therapy in patients with moderate traumatic brain injury using MR spectroscopic imaging across acute (within one week), subacute (two to three weeks), and late-subacute (three months) stages of recovery<br>• Methods<br>○ Sample: 68 patients (38 men and 30 women) with acute-moderate TBI were initially recruited in the emergency department of the Massachusetts General Hospital (MGH); however, only MR spectroscopic imaging data from 34 (15 LLLT, 19 sham) were included in the final analysis after exclusions and loss to follow-up (18 men and 16 women with average age of 51.7 Sham and 45.9 LLLT)<br>○ Eligible patients had moderate TBI within three days, defined by a Glasgow Coma Scale (GCS) score of 9–12, or GCS 13–15 with abnormal imaging findings.<br>○ Patients were randomized (tPBM (half) or placebo (the other half)) from December 2015 to July 2028<br>○ The device:<br>▪ a custom-built LLLT helmet delivering near-infrared light via LEDs evenly distributed along the inner surface, with a central wavelength of 810 nm, 30 nm bandwidth, and an irradiance of 36 mW/cm²<br>▪ treatment began within 72 hours of injury and was delivered at three time points, with 20-minute sessions spaced at least 12 hours apart<br>▪ both groups underwent helmet application; sham treatment used inactive LEDs with fans on<br>▪ only the researcher coordinator was unblinded<br>▪ Magnetic Resonance Imaging (MRI) scans were performed at acute (≤1 week), subacute (two to three weeks), and late-subacute (three months) stages post-injury<br>• Outcomes | Relevance rating: High<br><br>Publication date: March 2026<br><br>Jurisdiction studied: U.S.<br><br>Methods: Single-centre, prospective, double-blind, placebo, randomized, controlled, parallel-group trial | None identified |

| Dimensions of organizing framework | Declarative title and key findings | Study characteristics | Equity considerations |
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| | ○ Cross-sectional treatment comparisons:<br>▪ during the late-subacute phase, mIns/NAA levels were significantly lower in the LLLT group compared with the sham group -0.31; 95% CI -0.50 to -0.13; PHolm = .019); mIns/NAA represents the combined effect of elevated neuroinflammation (mIns) and decreased neuronal/axonal health (NAA)<br>○ Temporal comparisons:<br>▪ in the sham group, mIns/NAA in the corpus callosum increased over time, with a significant rise from the acute to late-subacute phase (0.19; 95% CI 0.09–0.29; PHolm = .005)<br>▪ mIns/NAA levels remained stable in the LLLT group, with no significant differences observed across time points (all PHolm > .74)<br>▪ no significant differences were observed between treatment groups over time (all PHolm > .14) | | |
| • Wavelength range<br>○ 800–900 nm<br>• Wave type<br>○ Continuous<br>• Treatment time<br>○ 20 minutes +<br>• Number of sessions<br>○ 3–5<br>• Frequency of sessions<br>○ Multiple times per week<br>• Setting of sessions<br>○ Community or home-based setting<br>• Patient eligibility<br>○ Age<br>▪ 18–29<br>• Outcomes<br>○ Health outcomes | Transcranial photobiomodulation protects against neuroinflammation and axonal injury in National Collegiate Athletic Association (NCAA) Division I football athletes exposed to repetitive head acceleration events (RHAE) (6)<br>• This study assessed the effects of transcranial photobiomodulation (tPBM) on neuroinflammatory signalling and axonal integrity in athletes exposed to RHAE over a single NCAA Division I football season, as measured by diffusion MRI metrics (restricted diffusion imaging (RDI) and quantitative anisotropy (QA))<br>• Participants<br>○ 24 male NCAA Division I football athletes (ages not specified)<br>○ Randomized into two groups: 12 received active tPBM, 12 received sham PBM<br>○ Player position details were withheld to preserve confidentiality; exposure profiles were analyzed:<br>▪ High frequency / low strain (e.g., linemen)<br>▪ Moderate frequency / moderate strain<br>▪ Low frequency / high strain (e.g., skill/speed positions)<br>• Methods<br>○ tPBM delivery: custom transcranial helmet with clusters of NIR LEDs<br>▪ Wavelength: 810 nm ± 15 nm<br>▪ Incident fluence: ~43 J/cm² per 20-minute session (0.036 W/cm² × 20 min × 60 s/min)<br>▪ Cortical fluence: ~1–1.5 J/cm² after accounting for scalp/skull transmission<br>○ Treatment frequency: Three sessions per week, 20 minutes each<br>○ Sham tPBM: Identical helmet with LEDs turned off<br>○ Diffusion MRI scans at baseline and post-season:<br>▪ RDI: biomarker of immune cell infiltration/neuroinflammation<br>▪ QA: biomarker of axonal integrity/microstructural connectivity<br>○ Supplementary analyses: Assessed impact of positional exposure on RDI and QA changes within the sham group<br>• Outcomes | Relevance rating: High<br><br>Publication date: January 2026<br><br>Jurisdiction studied: U.S. (NCAA Division I collegiate athletics setting)<br><br>Methods: Single-season, randomized, sham-controlled trial, using pre- and post-season diffusion MRI to assess the effects of transcranial PBM on neuroinflammation and axonal integrity | None identified |

| Dimensions of organizing framework | Declarative title and key findings | Study characteristics | Equity considerations |
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| | ○ Active tPBM group:<br>▪ RDI remained stable or decreased over the season, indicating reduced neuroinflammation<br>▪ QA remained stable or slightly improved, suggesting preserved axonal integrity<br>▪ Effects were most prominent in "cone of vulnerability" brain regions, including frontal white matter and deep subcortical structures prone to repetitive impacts<br>▪ No adverse events reported<br>○ Sham tPBM group:<br>▪ High frequency / low strain positions exhibited significant increases in RDI and QA over the season (RDI increase $p < 0.05$; QA increase: $p < 0.05$), consistent with neuroinflammatory and axonal stress responses<br>▪ Moderate and low frequency/strain positions showed smaller or negligible changes<br>○ tPBM may complement existing neuroprotective strategies:<br>▪ Nutritional: DHA and long-chain omega-3 supplementation stabilizes membranes, attenuates RDI elevations<br>▪ Equipment-based: advanced helmets, Guardian Caps reduce macroscopic forces but do not affect subcellular pathways<br>▪ PBM acts at the cellular level by modulating mitochondrial cytochrome c oxidase, reducing inflammation, and supporting axonal integrity<br>• Limitations<br>○ Small sample size limits statistical power and generalizability<br>○ Lack of noncontact athlete comparison group; effects cannot be solely attributed to RHAE<br>○ No direct measurement of RHAE exposure (e.g., game snaps, accelerometer data)<br>○ Variability in tPBM dose delivery due to hair type, scalp pigmentation, and helmet fit<br>○ Positional differences likely influence RDI/QA outcomes; high frequency / low strain athletes show greater susceptibility to microstructural changes<br>• This study provides preliminary, human evidence that transcranial PBM is a safe, non-invasive and feasible neuroprotective intervention for collision sport athletes<br>○ It reduces neuroinflammatory signalling, preserves axonal integrity and may act prophylactically to mitigate long-term neurological consequences of RHAE<br>• Future studies should incorporate:<br>○ larger sample sizes and multisite cohorts<br>○ longitudinal, multi-season follow-ups<br>○ direct RHAE exposure metrics (accelerometer-based impact monitoring)<br>○ functional outcome measures (cognition, mood, sleep, physical performance) | | |

## Appendix 3: Details from the jurisdiction scan of 'Five Eyes' countries

| Jurisdiction | Dimensions of organizing framework | Key findings about programs or investments in the 'Five Eyes' |
|---|---|---|
| Canada | • Wavelength range<br>  ○ 600–700 nm<br>  ○ 700–800 nm<br>  ○ 800–900 nm<br>• Treatment time<br>  ○ 5–20 minutes<br>• Number of sessions<br>  ○ 3–5<br>• Frequency of sessions<br>  ○ Multiple times per week<br>• Setting of sessions<br>  ○ Clinical setting<br>  ○ Age<br>  ▪ 18–29<br>  ▪ 30–44<br>  ▪ 45–60<br>  ▪ 60+<br>• Outcomes<br>  ○ Health outcomes | Kivo light therapy is a commercial organization that provides red and near-infrared photo biomodulation for persons with concussions and traumatic brain injuries<br>• The organization explicitly mentions Veterans as a key population of service, but does not provide specific details related to Veterans<br>• Safety considerations for red and near-infrared light therapy include using devices with verified wavelengths, consulting neurologist for severe disorders, and not exceeding recommended times described below<br>• The organization provides proposed parameters for use:<br>  ○ Wavelength: 630–670 nm for red and 810–900 nm for near-infrared<br>  ○ Irradiance: 10–100 mW/cm<br>  ○ Energy dose: 1–10 j/cm per session<br>  ○ Session length: 10–30 mins<br>  ○ Frequency: three/week for four to eight weeks<br>  ○ No recommendations provided for type of traumatic brain injury or other details on patient eligibility<br>• The organization proposed that red and near infrared light therapy can support by boosting cellular energy, improving blood flow to delivery oxygen and nutrients throughout the brain, easing inflammation, and supporting brain connectivity |
| United States | • Setting of sessions<br>  ○ Clinical setting | The PBM (photobiomodulation) Foundation is an organization located in the United States that supports the research and application of photobiomodulation<br>• The organization references Veterans and military supports for traumatic brain injury as a key population in their overview and highlights two studies using red light therapy to improve symptoms in Veterans with Gulf War Illness<br>  ○ Scalp application to improve thinking and memory in Veterans with Gulf War Illness<br>  ○ General Gulf War Illness symptoms<br>  ○ The organization states that there are currently 505 active trials, some of which may be applicable to Veterans |
| | • Setting of sessions<br>  ○ Clinical setting<br>• Patient eligibility<br>  ○ Type of traumatic brain injury<br>  ▪ Mild<br>  ▪ Moderate<br>  ▪ Severe<br>• Outcomes<br>  ○ Health outcomes | The Concussion Alliance provides information on light therapy photobiomodulation<br>• The organization refers to an ongoing study for military members and Veterans<br>• Positive effects associated with light therapy include increased cerebral blood flow, increased energy production, increased neuroprotection, and reduced inflammation<br>• The organization advises against at home therapies and recommends that individuals interested in the treatment volunteer to be a part of formal research studies<br>• The organization references Vielight as the only photobiomodulation device used in research and is also available to the public<br>• This device falls under the Food and Drug Administration (FDA) category of "low risk devices" so generally cannot be claimed under medical insurance |
| | • Treatment time<br>  ○ 20 minutes +<br>• Number of sessions<br>  ○ 1–3<br>• Frequency of sessions | The Neurorehabilitation Lab at Boston University offers photobiomodulation therapy for Veterans with traumatic brain injury<br>• The United States Department of Veterans Affairs provided an update on this intervention<br>• The program is supported in collaboration with VHA Center for Compassionate Care Innovation<br>• Most Veterans included in the study had symptoms for at least six months<br>• The intervention starts in clinic and then is followed by three 30-minute sessions/week over the course of two weeks |

| Jurisdiction | Dimensions of organizing framework | Key findings about programs or investments in the 'Five Eyes' |
|---|---|---|
| | ○ Multiple times per week<br>• Setting of sessions<br>○ Clinical setting<br>○ Community or home-based setting<br>• Patient eligibility<br>○ Type of traumatic brain injury<br>▪ Mild<br>▪ Moderate<br>▪ Severe<br>• Outcomes<br>○ Health outcomes | • The intervention has shown no adverse events |
| | • Treatment time<br>○ 20 minutes +<br>• Number of sessions<br>○ 5–10<br>• Frequency of sessions<br>○ Multiple times per week<br>• Setting of sessions<br>○ Clinical setting<br>○ Community or home-based setting<br>• Patient eligibility<br>○ Type of traumatic brain injury<br>▪ Mild<br>▪ Moderate<br>▪ Severe | In September 2025, the United States Department of Defence awarded a grant to the University of Utah and New York University to trial photobiomodulation in Veterans with traumatic brain injuries<br>• To date, there is no data available for this study and a protocol could not be identified<br>• The study will involve patients using the device for 25 minutes a day for five to six days/week |
| | • Setting of sessions<br>○ Clinical setting<br>• Patient eligibility<br>○ Type of traumatic brain injury<br>▪ Moderate<br>▪ Severe<br>• Outcomes<br>○ Health outcomes | The University of Utah is currently recruiting for a study looking at photobiomodulation for Veterans with traumatic brain injury<br>• This program explores moderate to severe traumatic brain injury<br>• Projected outcomes will be related to brain health, cognitive function and physical performance<br>• No additional details were identified |
| United Kingdom | • Setting of sessions<br>○ Clinical setting | Medical Research Council (MRC) Device Development Funding<br>• A project titled "A device for direct application of photobiomodulation in traumatic brain injury (ADAPT)" has been funded through the U.K. Medical Research Council Innovation Acceleration Account (MRC-IAA)<br>• The project focuses on developing medical devices capable of delivering photobiomodulation directly to injured neural tissue and translating laboratory findings into clinical therapeutic technologies for brain injury |
| | • Setting of sessions<br>○ Clinical setting<br>• Patient eligibility | Researchers at the University of Birmingham are conducting studies on near-infrared photobiomodulation for traumatic brain injury |

| Jurisdiction | Dimensions of organizing framework | Key findings about programs or investments in the 'Five Eyes' |
|---|---|---|
| | ○ Type of traumatic brain injury<br>▪ Mild | • Their work investigates how transcranial light therapy can reduce neuroinflammation, apoptosis and neuronal damage following mild TBI<br>• Laboratory studies using animal models have shown that near-infrared wavelengths (e.g., 810 nm) improved cognitive performance and reduced inflammatory markers after brain injury<br>• No additional details could be found |
| New Zealand | Not applicable | No findings were identified specifically for transcranial photobiomodulation (tPBM) as a therapy TBI in military/Veterans |
| Australia | • Setting of sessions<br>○ Clinical setting<br>• Outcomes<br>○ Health outcomes | The Brain Foundation Australia: UWA Light Stimulation Project<br>• The Brain Foundation Australia funded a project at the University of Western Australia that explores using light stimulation after TBI to promote neurotrophins and brain cell survival<br>○ A research grant of roughly $38,000 Australian was received by a team by Dr. Jamie Beros<br>• Important distinctions:<br>○ This project uses light to stimulate neurological recovery, similar in principle to tPBM, but doesn't follow all the international tPBM protocols (e.g., precise wavelengths, doses, and delivery through the skull)<br>○ It is more accurately described as a neuromodulation study using light, rather than a full-scale tPBM clinical trial<br>• This demonstrates that research interest exists, but it's still at a project level rather than a national program level |

## Appendix 4: Documents excluded at the final stages of reviewing

| Document type | Hyperlinked title |
|---|---|
| Evidence synthesis | Photobiomodulation in acute traumatic brain injury: A systematic review and meta-analysis |
| Evidence synthesis | Transcranial photobiomodulation in the management of brain disorders |
| Evidence synthesis | Can transcranial photobiomodulation improve cognitive function? A systematic review of human studies |
| Evidence synthesis | Can transcranial photobiomodulation improve cognitive function in TBI patients? A systematic review |
| Single study | Pulsed transcranial red/near-infrared light therapy using light-emitting diodes improves cerebral blood flow and cognitive function in Veterans with chronic traumatic brain injury: A case series |
| Singe study | Home-based photobiomodulation treatment for cognitive and neuropsychiatric symptoms in TBI |

## References


1. Figueiro Longo MG, Tan CO, Chan S-t, et al. Effect of transcranial low-level light therapy vs sham therapy among patients with moderate traumatic brain injury: A randomized clinical trial. *JAMA Network Open* 2020; 3(9): e2017337-e2017337.
2. Chan S-t, Mercaldo N, Figueiro Longo MG, et al. Effects of low-level light therapy on resting-state connectivity following moderate traumatic brain injury: Secondary analyses of a double-blinded placebo-controlled study. *Radiology* 2024; 311(2): e230999.
3. Taylor AM, Mannix R, Zafonte RD, Whalen MJ, Meehan WPI. A randomized, double-blind, placebo-controlled clinical trial evaluating transcranial photobiomodulation as treatment for concussion. *Medicine & Science in Sports & Exercise* 2024; 56(5): 822-827.
4. Lee T-L, Chan DY-C, Chan DT-M, Cheung M-C, Shum DH-K, Chan AS-Y. Transcranial photobiomodulation improves cognitive function, post-concussion, and PTSD symptoms in mild traumatic brain injury. *Journal of Neurotrauma* 2025; 42(19-20): 1695-1707.
5. Ratai E-M, Wenke MR, Mercaldo N, et al. Low-level light therapy effect on metabolites measured by MR Spectroscopy in patients with moderate traumatic brain injury: A double-blind, randomized, placebo-controlled clinical trial. *American Journal of Neuroradiology* 2026; 47(3): 699-707.
6. Lindsey HM, Esopenko C, Jain D, et al. Transcranial photobiomodulation promotes neurological resilience in current collegiate American football players exposed to repetitive head acceleration events. *Journal of Neurotrauma* 2026: 08977151251403554.



Whitelaw H, Waddell K, Sivanesanathan T, Dass R, Grewal E, Osorio D, Wilson MG. Rapid evidence profile #101: Transcranial photobiomodulation therapy for traumatic brain injury (TBI). Hamilton: McMaster Health Forum; 8 April 2026.

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