Neurocognitive Effects of Repetitive Low-Level Blast (rLLB) Overpressure Exposure in Humans – Addendum 1

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Context

This report is an Addendum to the initial Rapid Evidence Assessment (REA) published in January 2026. The original REA examined the evidence published in the five years preceding September 2025 on repetitive low-level blast exposure and its potential physiological, neurological, cognitive, and behavioural effects in humans.

This Addendum updates that evidence base by incorporating newly published literature released between January 2025 and 7 April 2026. It is intended to identify whether recent evidence materially strengthens, weakens, or otherwise modifies the conclusions of the original REA.

The aims of the original REA were to:

1. Systematically review the contemporary evidence base (peer-reviewed and grey literature).
2. Assess the quality of the new evidence.
3. Consider how the new evidence adds or detracts from the existing evidence base.
4. Highlight areas for future research that address the identified gaps.

Summary of findings

The updated search identified 876 records, of which 308 records underwent title and abstract screening and 30 were assessed at full text level. Following deduplication, exclusion of studies already captured in the original REA, and full-text review, 16 new peer-reviewed publications met the inclusion criteria and were included in this Addendum. These comprised 13 human studies and 3 animal studies, supplemented by 3 items of grey literature focused on blast overpressure risk mitigation and monitoring guidance.

Overall, the new evidence does not materially change the conclusions or confidence rating of the initial REA. The additional studies provide further support for biological plausibility and strengthen consistency across several domains, including neuroinflammatory, vascular, axonal, biomarker, imaging, vestibular, sensory, and symptom-based findings. However, the evidence remains limited by observational study designs, variable exposure definitions, reliance on self-report or occupational proxies, small or selected samples, and important confounding from post-traumatic stress disorder, depression, sleep disturbance, chronic pain, prior concussion or mild traumatic brain injury, and other concurrent exposures.

All newly included studies were assessed as providing very low certainty evidence. The Addendum therefore should be interpreted as an incremental update to the evidence base, rather than a shift in causal interpretation. Current evidence continues to support an association between repetitive low-level blast exposure and a range of physiological, neurological, cognitive, behavioural, sensory, and neuropsychiatric outcomes, but it does not establish that repetitive low-level blast exposure alone causes a distinct clinical syndrome, nor does it identify validated diagnostic tools, safe exposure thresholds, or blast-specific treatment pathways.

Updated search results

The literature search was replicated in full using the same search strings applied in the original review (see Appendix 6 of the original report).

The search update was conducted in seven bibliographic databases, covering the period from January 2025 to April 7th, 2026.

The following databases were searched. Search strings were applied consistently with the original review methodology:

Database	Platform	Raw Records Retrieved
PubMed	NLM / NCBI	173
Embase	Ovid	113
Cochrane Library (EBM)	Wiley	44
Scopus	Elsevier	373
CINAHL	EBSCOhost	57
PsycINFO	APA / EBSCOhost	109
ProQuest Dissertations & Theses	ProQuest	7
Total		**876**

Following identification, all records were deduplicated and cross-referenced against publications already captured in the original search to ensure no overlap.

- Stage 1: Cross-database deduplication: Records retrieved across multiple databases were merged and duplicates identified.
- Stage 2: Cross-search deduplication: Remaining records were cross-referenced against the full publication list from the original review, and any previously identified studies were excluded.

Following retrieval, 876 records underwent deduplication, 308 underwent title/abstract screening and 30 were considered for full text inclusion.

A total of 16 studies met all the inclusion criteria and underwent data extraction and quality assessment (Figure 1).

Peer Reviewed Publications

A total of 16 peer-reviewed publications underwent data extraction, quality appraisal, content review, analysis and interpretation (Table 2). The findings are presented below.

Animal Studies

Study Design and Models

The additional animal studies (n=3) use controlled experiments, with two in rodent and one in chinchilla. Compared to studies reviewed earlier in in the initial report, there appears to be an increasing trend across studies to provide more exhaustive methodological description of the characteristics of blast exposure used. These studies use defined exposure intervals and cumulative dosing to examine change over time of outcomes and dose-response relationships with greater precision. While helpful to understand how exposure to blast may cause various changes in the nervous system, each of these studies must be interpreted with caution in regards to applicability to human blast exposure (that is, they constrained by indirectness) particularly in replicating complex occupational exposure environments and long-term human outcomes (1–3).

Mechanistic Domains

Neuroinflammation and Immune Response

Neuroinflammation continues to emerge as a central and persistent response to repetitive exposure. Sustained microglial activation and cytokine dysregulation are observed, supporting a prolonged neuroimmune response rather than an isolated short-term effect on brain tissue. While variability in direction and magnitude of inflammatory markers persists, the overall consistency across studies is consistent with the previously reviewed studies. Methodological variability and small sample sizes, however, continue to limit the ability to precisely translate animal data to human clinical treatment and recovery (1,2).

Vascular and Blood-Brain Barrier (BBB) Dysfunction

Additional evidence supports vascular involvement, including perivascular inflammation and structural changes consistent with BBB disruption. These findings are aligned with a vascular-glial interaction model described in the primary review, although their persistence and clinical implications remain uncertain. Direct translation of this animal data to human pathology must be done with caution (1).

Axonal and White Matter Injury

Evidence of axonal disruption following repetitive exposure remains consistent, supporting white matter vulnerability as a recurring problem. However, variation in measurement methods and limited longitudinal modelling restrict conclusions about progression or recovery over longer timeframes (1,2).

Neurodegenerative Pathways

Tau-related signalling suggests potential overlap with neurodegenerative pathways. However, these findings remain preliminary and highly model-dependent, and there is currently no direct translational evidence linking repetitive exposure to progressive neurodegenerative disease (1).

Electrophysiology and Excitability

Altered neuronal excitability and electrophysiological instability have been observed following repetitive exposure. These findings provide a plausible mechanistic link between structural injury and functional disturbance, although direct clinical correlations have not yet been established (2).

Mitochondrial and Metabolic Dysfunction

Metabolic disruption and mitochondrial dysfunction are consistent with a broader bioenergetic stress response. These findings align with existing hypotheses regarding metabolic vulnerability but remain exploratory and require further validation (1).

Behavioural and Functional Outcomes

Behavioural outcomes, including anxiety-like behaviours, memory impairment, and motor dysfunction, are broadly consistent with underlying structural and molecular findings. These patterns mirror domains observed in human studies, supporting cross-species coherence, while remaining indirect proxies for human cognitive and neuropsychiatric function (1,2).

Intervention and Mitigation Studies

One chinchilla study reported that liraglutide may reduce blast-related auditory injury, with effects varying by blast intensity, ear protection status, and timing of administration. The findings support

further investigation of targeted mitigation strategies for hearing outcomes, but remain limited to an animal model and cannot be generalised to broader neurological effects (3).

Key Additive Value

The additional animal studies strengthen the internal coherence of mechanistic pathways identified in the primary review, particularly across neuroinflammatory, vascular, and axonal domains. However, they do not materially reduce indirectness or improve certainty of evidence, and their contribution remains supportive rather than determinative.

Human Studies

Study Design Characteristics

The additional human studies remain predominantly observational, including cross-sectional analyses, cohort studies, and limited longitudinal datasets. While some studies incorporate larger samples or advanced techniques such as imaging and biomarker panels, the fundamental limitations associated with observational design remain unchanged (4–16).

Measuring Exposure

Exposure characterisation continues to rely largely on proxy measures, including occupational role and self-reported exposure. Some incremental improvement is observed through the use of structured exposure windows; however, objective dosimetry remains limited. This ongoing imprecision represents a key source of indirectness and constrains interpretation of dose-response relationships (4,13,15,16).

Outcome Domains

Neurocognitive and Behavioural

Some cohorts demonstrate subtle differences in working memory, delayed recall, learning, or processing speed, but effects are generally small, heterogeneous, and often remain within expected performance ranges. Subjective symptom burden is more consistently elevated than objective cognitive impairment, particularly where blast or mTBI occurs in combat or other high-stress contexts. Interpretation remains complicated by psychiatric symptoms, sleep disturbance, pain, and other deployment-related factors, although recent occupational blast studies suggest that some cognitive effects may not be fully mediated by mental health alone. (5,6,12).

Neuroimaging

Structural and functional neuroimaging studies report white matter, cortical morphometric, and network-level connectivity changes following repetitive blast exposure. However, findings remain heterogeneous and difficult to interpret because blast exposure often co-occurs with diagnosed concussion, combat exposure, psychological trauma, PTSD symptoms, depression, sleep disturbance, hearing injury, and other occupational exposures. Current evidence supports biological plausibility, but not a single consistent imaging signature or causal pathway (7,14,15).

Biomarkers

Biomarker studies report acute post-exposure increases in markers of astroglial and axonal injury, including glial fibrillary acidic protein (GFAP) and neurofilament light (NfL). Some high-exposure cohorts also show evidence of elevated resting or pre-task biomarker levels, suggesting possible chronic or cumulative neurobiological stress. These findings support biological plausibility, but

remain limited by variability, uncertain specificity, and insufficient validation for clinical decision-making (6,8,16).

Sensory and Vestibular Outcomes

One study reported hearing and vestibular effects following blast exposure, including measurable hearing threshold changes and symptom provocation during vestibular/ocular motor testing. However, the relationship between these findings and broader cognitive or neurological outcomes remains unclear (8).

Sleep and Neuropsychiatric Outcomes

Across the human studies, psychiatric and sleep-related factors remain major interpretive confounders. In Lopez et al (12), adjustment for lifetime TBI events statistically attenuated psychiatric outcome effect sizes, although the associations remained significant. Objective cognitive differences were also small, and psychiatric symptom burden explained more variance in cognitive performance than mTBI history itself. Overall, the evidence supports a multidimensional clinical picture in which blast exposure, injury context, PTSD, depression, sleep disturbance, chronic pain, and neurobehavioural symptoms interact, rather than a simple exposure-outcome pathway attributable to blast alone (11,12).

Dose-Response and Cumulative Exposure

For two studies, cumulative exposure showed only limited and context-dependent associations with outcomes. Low-level blast exposure was not a strong independent predictor of cognitive performance, but appeared to modify risk in specific subgroups, particularly where PTSD or deployment-related mTBI was also present. Interpretation remains constrained by retrospective exposure estimation, possible exposure misclassification, and confounding from combat context and psychiatric comorbidity (4,13).

Interventional Evidence

Exploratory mitigation approaches suggest that modification of exposure conditions may influence physiological outcomes. These findings remain preliminary and insufficient to inform clinical or operational practice (15).

Key Additive Value

The additional human studies increase consistency of observed associations across symptom, biomarker, and imaging domains and provide early indications of longitudinal effects. However, they do not materially resolve key limitations relating to causality, exposure quantification, or specificity.

Cross-Cutting Observations

Convergence

Only partial convergence is observed across animal and human studies in domains such as neuroinflammatory signalling, axonal injury, and biomarker responses. While these findings support the biological plausibility of cumulative injury processes, important differences in exposure models, study design, and translational applicability limit the strength of direct cross-species comparison (1–3,6,16).

Divergence

Animal studies provide more controlled evidence of plausible biological mechanisms, but these findings do not translate directly into clear clinical conclusions in humans. Differences in blast exposure conditions, study design, outcome measurement, and confounding from PTSD, depression, sleep disturbance, pain, and prior mTBI remain central limitations of the evidence base.

Interpretive Guidance and Analysis

The additional studies do not materially change the overall certainty of the evidence, which remains very low across the newly included studies. Although the new literature adds support for biological plausibility and shows some consistency across mechanistic, biomarker, imaging, and symptom domains, these findings should be interpreted cautiously.

The main reason for low confidence is that many human studies cannot clearly separate the effects of repetitive low-level blast exposure from other factors that commonly occur in the same populations. These include prior concussion or mild traumatic brain injury, combat exposure, PTSD, depression, sleep disturbance, chronic pain, hearing injury, substance use, and other occupational exposures. These factors can independently affect cognition, mood, sleep, symptoms, biomarkers, and functional outcomes. As a result, even where associations are observed, it remains uncertain whether blast exposure is the primary cause, a contributing factor, or a marker for a broader exposure and health profile.

Additional limitations also remain. Exposure is often estimated using occupational role, self-report, or cumulative exposure proxies rather than objective dosimetry. Study populations are frequently small or selected, outcome measures vary between studies, and many findings are not replicated across independent cohorts. Animal studies provide useful mechanistic information, but their blast conditions and biological models do not directly reproduce complex human military and occupational exposures.

Accordingly, this Addendum should be interpreted as an incremental extension of the evidence base. It strengthens biological plausibility but does not establish causation, define safe exposure thresholds, identify a blast-specific clinical syndrome, or justify new policy-relevant thresholds.

The GRADE (Grading of Recommendations Assessment, Development, and Evaluation) assessment indicates very low confidence in the newly included studies. This means the findings may suggest possible associations between repetitive low-level blast exposure and health outcomes, but they are not strong enough to draw firm conclusions. Confidence is reduced because many studies used small or selected samples, measured exposure imprecisely, relied on observational designs, and could not fully separate blast effects from PTSD, depression, sleep disturbance, chronic pain, prior mTBI, or other military exposures. The evidence therefore supports biological plausibility and further research, but does not establish causation, diagnostic thresholds, or blast-specific treatment pathways.

Individual GRADE assessments for each paper are presented in Table 3.

Grey Literature

The updated grey literature consists of three United States military guidance or policy documents addressing blast overpressure risk management. These documents are not primary scientific or

experimental studies and do not directly answer the central review question regarding the neurocognitive effects of repetitive blast overpressure exposure in humans. Their main contribution is operational rather than evidentiary.

The documents reflect a precautionary approach to risk mitigation, including exposure monitoring, standoff distances, Personal Protective Equipment requirements, baseline cognitive testing, and principles similar to keeping exposure "as low as reasonably achievable". These measures are sensible given current uncertainty and potential concern, but they should not be interpreted as confirming causal neurocognitive harm or defining safe exposure thresholds. Overall, the grey literature demonstrates how some military organisations are translating concern about repeated blast exposure into governance and exposure-control procedures, but it adds limited direct evidence about human neurocognitive outcomes.

Impact on Research Questions

The impact of the additional studies was assessed against the research questions as outlined in the initial report. These are outlined below.

Research question	Response	Updates
How is LLB overpressure exposure defined?	Low-level blast (LLB) overpressure exposure refers to exposure to blast pressure waves that are below thresholds typically associated with acute blast injury or clinically diagnosed traumatic brain injury. These exposures commonly arise from military weapons systems (e.g. breaching charges, artillery, mortars, heavy firearms) and generally involve peak overpressures in the approximate range of 1–6 psi, although higher values are occasionally reported in training or operational contexts. LLB exposure does not usually produce immediate, overt neurological injury but may exert subclinical physiological stress on the brain.	No material change. Additional studies are consistent with existing definitions and do not refine exposure thresholds or conceptual framing.
What criteria are used to define repetitive LLB (rLLB) exposure (e.g., duration/frequency/intensity)?	There is no universally accepted definition of rLLB. In the literature, rLLB is operationalised variably using proxies such as occupational role (e.g. breacher, instructor), self-reported blast counts, duration in high-risk roles, or inferred cumulative exposure during training cycles or careers. Frequency, cumulative dose (blast count or impulse), and career duration are more commonly used than precise intensity thresholds. This lack of standardisation is a major limitation of the evidence base.	No change. Continued reliance on proxy exposure measures reinforces lack of standardisation and remains a key limitation.

Research question	Response	Updates
What assessment process is recommended for individuals presenting with acute or chronic cognitive signs and symptoms associated with rLLB exposure?	The report supports a holistic, multimodal clinical assessment rather than a blast-specific diagnostic test. Recommended assessment integrates clinical history (including blast exposure history), symptom inventories, neuropsychological screening, vestibular and balance assessment, mental health screening (PTSD, depression, anxiety), sleep assessment, and pain evaluation. rLLB exposure should be considered within existing mTBI and mental health pathways rather than as a standalone diagnosis.	No change. Additional studies support continued use of multimodal, non-specific assessment approaches.
What is the reliability and validity of the cognitive assessments designed to assess acute or chronic signs/symptoms associated with rLLB overpressure exposure with respect to (i) clinical history; (ii) alternative diagnoses; and (iii) comorbid diagnoses?	The evidence indicates limited reliability and validity of existing cognitive assessments for isolating rLLB effects. Neuropsychological tests, symptom questionnaires, eye-tracking, balance testing, imaging, and biomarkers demonstrate sensitivity to change but poor specificity. Results are strongly influenced by clinical history, comorbid PTSD, depression, sleep disturbance, chronic pain, and prior impact-related mTBI. No assessment tool has been validated to reliably distinguish rLLB effects from alternative or comorbid diagnoses.	No change. Additional studies reinforce limited specificity and strong influence of comorbid conditions.
Which military roles are associated with higher levels of rLLB overpressure exposure during (i) training; and (ii) deployment?	High-risk roles consistently include breachers and explosive entry personnel, artillery and mortar crews, heavy-weapons operators, special operations forces, and instructors in blast-intensive training environments. Exposure occurs both during training and deployment, with instructors and career specialists demonstrating the highest cumulative exposure profiles.	No change. Occupational risk patterns remain consistent with prior findings.

Research question	Response	Updates
What individual, occupational, or environmental factors may protect against the development of cognitive impairment following rLLB overpressure exposure?	Protective factors remain incompletely defined. Based on human observational evidence and occupational guidance, plausible protective factors include reduced cumulative exposure, adequate recovery intervals between exposures, modification of training practices, exposure monitoring, and management of modifiable health factors such as sleep disturbance, mental health conditions, chronic pain, and substance use. Evidence for hearing and head protection is mainly relevant to sensory and exposure-mitigation outcomes, rather than proven prevention of cognitive impairment. Animal studies provide limited mechanistic support that physical mitigation and modulation of inflammatory pathways may reduce some blast-related effects, but these findings do not translate directly to human cognitive protection.	Minor reinforcement. The additional human literature provides limited support for exposure reduction, monitoring, and management of comorbid factors as prudent risk-reduction measures. The additional animal studies provide indirect mechanistic support for mitigation strategies, but overall evidence remains preliminary and insufficient to identify confirmed protective factors for cognitive impairment.
Does rLLB overpressure exposure increase susceptibility to clinically diagnosed neurological, psychiatric, or medical conditions?	Human evidence suggests an association between rLLB exposure and increased symptom burden, prior or diagnosed mTBI, and some neuropsychiatric outcomes. However, the evidence does not establish that rLLB exposure independently increases susceptibility to clinically diagnosed neurological, psychiatric, or medical conditions. This is because blast exposure often occurs alongside other important contributors to symptoms and diagnosis, including prior head injury, combat exposure, PTSD, depression, sleep disturbance, chronic pain, hearing injury, and other occupational exposures. These factors may explain, modify, or amplify observed associations.	No material change. The additional studies reinforce that associations exist in some exposed groups, particularly where blast exposure is cumulative or occurs with prior mTBI or PTSD. However, causality remains unestablished, and current evidence does not support attributing increased diagnostic susceptibility to rLLB exposure alone.
What are the mechanisms by which rLLB overpressure exposure is proposed to affect cognitive functioning in humans?	Animal and translational evidence supports mechanisms including axonal injury, neuroinflammation, vascular and blood-brain barrier disruption, altered neuronal excitability, mitochondrial dysfunction, and neuroimmune activation. These mechanisms provide biological plausibility for observed human symptoms but do not yet establish direct causal pathways in humans.	Reinforced. Additional animal and human biomarker studies strengthen understanding of existing mechanistic pathways of injury (neuroinflammation, axonal injury, metabolic dysfunction).

Research question	Response	Updates
What brain structures and cognitive processes are affected by rLLB overpressure exposure in humans (neuropathology, neuroimaging, biomarkers)?	Human studies implicate frontal and subcortical networks, white matter tracts, vestibular and oculomotor systems, and salience/default mode networks. Neuroimaging and biomarker studies suggest involvement of axonal and glial pathways, though findings are inconsistent and confounded.	No change. Findings remain consistent but heterogeneous and confounded.
What is the underlying neuropathology associated with rLLB overpressure exposure in humans?	Direct neuropathological evidence in humans is extremely limited. Imaging and biomarker findings suggest possible microstructural white matter changes, neuroinflammatory activity, and metabolic alterations. Animal studies demonstrate more definitive axonal, vascular, and glial pathology, but translation to human disease remains uncertain.	No change. Animal evidence is strengthened, but human evidence remains indirect and insufficient.
How are cognitive changes assessed following rLLB overpressure exposure?	Assessment relies on symptom reporting, neuropsychological testing, vestibular and balance measures, eye-tracking, and research-grade biomarkers or imaging. No validated rLLB-specific diagnostic framework exists; assessments are best interpreted longitudinally and in clinical context.	No change. No new validated approaches identified.
What acute cognitive signs and symptoms are associated with rLLB overpressure exposure in humans?	Acute effects include transient cognitive slowing, attention deficits, headache, dizziness, balance disturbance, visual or oculomotor changes, and short-term biomarker elevations. These effects often resolve over hours to days.	Reinforced. Additional biomarker and functional data support transient physiological and cognitive changes.
What chronic cognitive signs and symptoms are associated with rLLB overpressure exposure in humans?	Chronic findings in high-exposure cohorts include persistent headaches, concentration difficulties, irritability, sleep disturbance, mood dysregulation, and subtle executive or attentional deficits. These are often intertwined with psychiatric and pain comorbidities.	Reinforced. Increased consistency of symptom clusters, but attribution remains uncertain due to confounding.

Research question	Response	Updates
How can rLLB-related symptoms be distinguished from other cognitive or psychiatric conditions (differential diagnosis)?	Current evidence does not support a reliable method for distinguishing rLLB-related symptoms from other cognitive, neurological, or psychiatric conditions. Reported symptoms such as poor concentration, memory difficulty, irritability, sleep disturbance, headache, dizziness, mood symptoms, and fatigue are non-specific and overlap substantially with PTSD, depression, anxiety, sleep disorders, chronic pain, substance use, neurodegenerative disease, and impact-related mTBI. No clinical test, imaging finding, biomarker, or symptom profile has been validated as specific to rLLB exposure.	No change. This remains a central finding of the review. Additional studies reinforce that rLLB exposure should be considered as one possible contributor within a broader clinical assessment, but attribution to rLLB alone is not supported by current evidence. Differential diagnosis should therefore prioritise comprehensive assessment of alternative and comorbid explanations rather than seeking a blast-specific diagnostic signature.
Is there any evidence that rLLB overpressure exposure is associated with mTBI (or signs and symptoms of same) in humans?	Epidemiological data suggest that individuals in high blast-risk roles have higher rates of diagnosed mTBI and post-concussive symptoms. However, rLLB may act as a risk modifier rather than an independent cause.	No change. Evidence continues to support risk modification rather than causation.
Is there any evidence that rLLB overpressure exposure is associated with neurodegenerative conditions (or signs and symptoms of same) in humans?	Evidence is insufficient to establish an association between rLLB overpressure exposure and neurodegenerative conditions in humans. Some animal studies using low-level blast ranges, including exposures approximating the 1-6 psi range, report biological changes that are plausibly relevant to neurodegenerative pathways, such as neuroinflammation, axonal injury, vascular or blood–brain barrier disruption, and tau-related signalling. However, these findings are mechanistic and model based. They do not demonstrate progressive neurodegenerative disease in humans, nor do they establish that rLLB exposure causes conditions such as dementia, chronic traumatic encephalopathy, Parkinsonian syndromes, or other neurodegenerative disorders.	No change. The additional animal evidence provides limited support for biological plausibility, including in some lower-overpressure models, but human evidence remains insufficient, inconsistent, and very low certainty. Current evidence does not establish a causal or diagnostic link between rLLB exposure and neurodegenerative disease.
What treatment or management strategies are recommended for individuals presenting with acute or chronic cognitive signs and symptoms associated with rLLB exposure?	No rLLB-specific treatments are recommended. Management should follow established guidelines for mTBI, PTSD, depression, sleep disorders, and chronic pain, using multidisciplinary, symptom-focused care.	No change. No new therapeutic evidence identified.

Research question	Response	Updates
What is the safety and efficacy of the treatment or management strategies for individuals presenting with acute or chronic cognitive signs and symptoms associated with rLLB overpressure exposure?	Standard rehabilitation and mental health treatments are considered safe and effective for symptom management. Interventions such as hyperbaric oxygen therapy or supplements lack sufficient evidence for routine use.	No change. Evidence base unchanged.
What prevention strategies are proposed or in use to reduce rLLB exposure or its effects?	Strategies include minimising unnecessary repetitive exposures, modifying training practices, improving documentation and surveillance, piloting blast sensors in training, and monitoring emerging international guidance. No safe exposure thresholds have been established.	Minor reinforcement. Emerging mitigation approaches noted, but no definitive or scalable strategies established.
What rehabilitation approaches are used for rLLB-related cognitive impairment?	Rehabilitation mirrors mTBI care: cognitive rehabilitation, vestibular therapy, psychological interventions, sleep management, and pain management. Evidence specific to rLLB is limited.	No change. No new rLLB-specific rehabilitation evidence.
What is known about long-term wellbeing and quality of life impacts for individuals with rLLB-related cognitive symptoms?	Long-term wellbeing and quality of life impacts in blast-exposed populations appear to be shaped more by the broader clinical picture than by rLLB exposure alone. Persistent cognitive symptoms commonly occur alongside PTSD, depression, anxiety, sleep disturbance, chronic pain, headache, vestibular symptoms, hearing problems, substance use, prior concussion or mTBI, and other deployment or occupational stressors. These conditions can independently reduce function, work participation, relationships, and quality of life, and may also amplify perceived cognitive difficulties. Current evidence does not allow the long-term effects of rLLB exposure to be separated reliably from these overlapping contributors.	No change. This remains a key finding. The additional studies support a lifetime brain-health and wellbeing approach, but do not establish that rLLB exposure alone drives long-term quality of life outcomes. Assessment and management should therefore focus on the full burden of comorbid physical, psychological, sleep, pain, sensory, and functional problems rather than attributing persistent symptoms solely to blast exposure.

Research question	Response	Updates
What is the quality and certainty of the evidence used to address the research questions?	Overall certainty remains very low to low. Human studies are limited by observational designs, imprecise exposure measurement, confounding, small or selected samples, and inconsistent outcome measures. Animal studies, including some using blast overpressure ranges approximating 1–6 psi, provide limited support for biological plausibility by showing changes in pathways such as neuroinflammation, axonal injury, vascular disruption, electrophysiological change, and biomarker responses. However, these studies remain indirect because animal exposure conditions, dosing patterns, and measured outcomes do not fully reproduce human occupational or military exposure settings.	No material change. The additional evidence modestly strengthens biological plausibility, including from some low-overpressure animal models, but does not materially improve certainty. Current evidence supports possible mechanisms and associations, not causation, validated diagnostic criteria, safe exposure thresholds, or threshold-based policy.

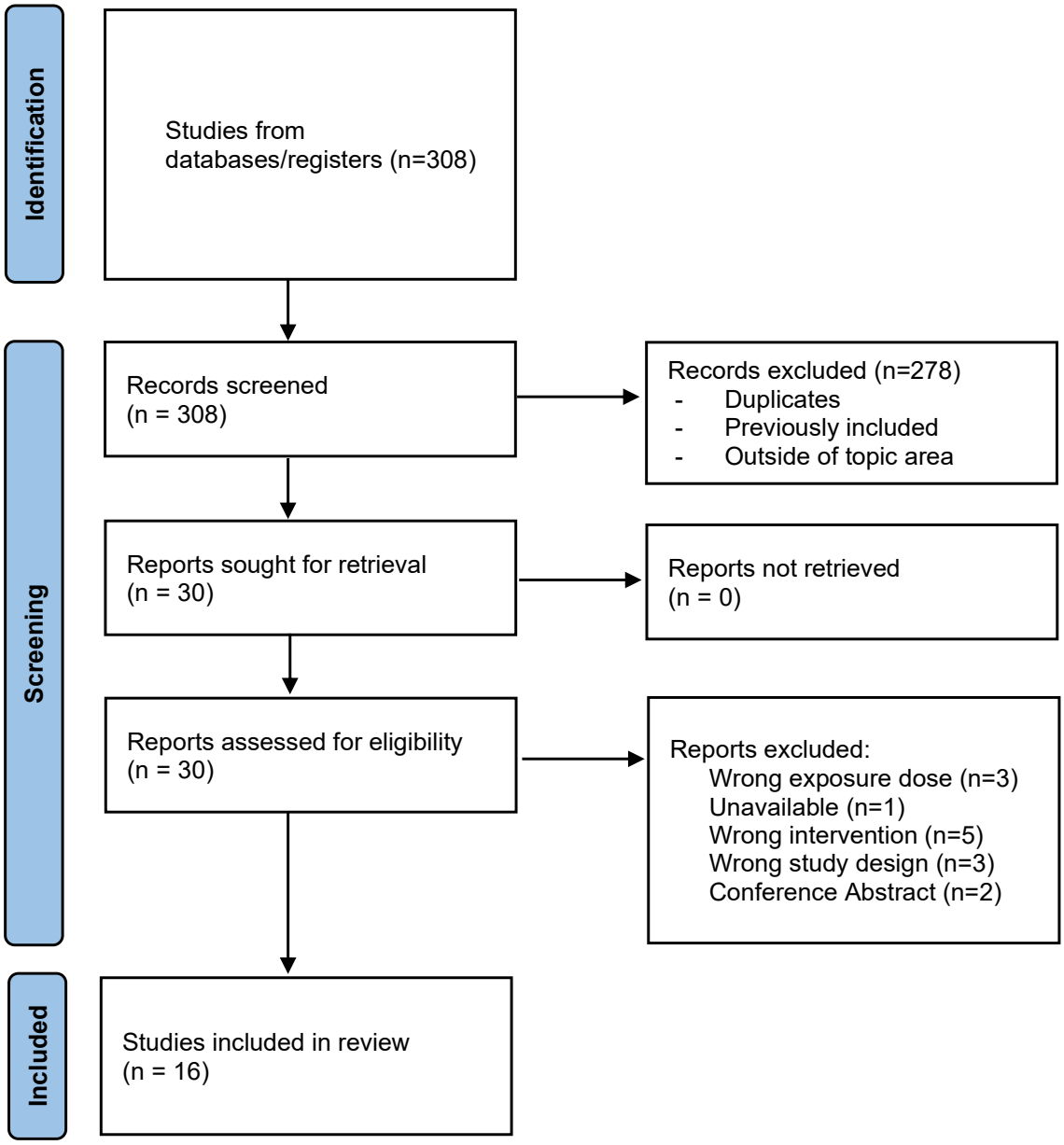

Figure 1 - PRISMA Flowchart

Table 2 - Outline of Peer Reviewed Literature

Study ID	Title (citation)	Population	Setting	Country
Wang 2025	Associations Between Blast Exposures and Intestinal Permeability and Neurotrauma Symptoms During Mortar Fire Military Tactical Training Operations	Human	31 service members (22 mortarmen exposed to low-level blast; 9 controls) during mortar fire training; exposures measured with sensors	USA
Tseng 2026	Tau biomarkers in Special Operations Forces with repeated blast exposure: A cross-sectional study	Human	ReBlast pilot study of active-duty SOF with PET-MRI and blood sampling	USA
Solar 2025	Widespread cortical morphological alterations are associated with repetitive blast exposure independent of concussion history	Human	Hospital for Sick Children, Toronto; current/former CAF or RCMP personnel	Canada
Martindale 2025	Cumulative and Contextual Effects of Low-Level Blast Exposure on Cognitive Function in Military Personnel: Interactions With PTSD and Mild TBI	Human	Multi-site DOD/VA research centres (LIMBIC-CENC)	USA
Lopez 2025	Context Matters: Influence of Injury Context on Long-Term Psychiatric and Cognitive Outcomes in Combat Veterans With Mild Traumatic Brain Injury History	Human	LIMBIC-CENC secondary analysis of baseline data	USA
Lipov 2025	Treating Post-Traumatic Stress Disorder in Canadian Special Operation Forces Command with Ketamine Plus Cervical Sympathetic Blockade	Human	Single private clinic: Stella Center Headquarters, Westmont, Illinois, USA	USA
Lempke 2025	Psychological Health of Female Service Members and Veterans Associated With Mild Traumatic Brain Injury History: A LIMBIC-CENC Study	Human	Long-term Impact of Military-relevant Brain Injury Consortium–Chronic Effects of Neurotrauma study across 10 U.S. military/veteran healthcare sites	USA
Lam 2026	One is not like the other: Examining the neural response to repetitive low-level blast exposure in experienced military personnel	Human	Canadian military breacher/sniper training with fMRI scans	Canada
Kranfli 2025	Using the Modified Vestibular/Ocular Motor Screening Tool to Identify Blast Exposure Effects in Military Service Members	Human	Prospective cohort of 42 male service members training with mortars and 15 male controls across three visits	USA
Franke 2025	Auditory event-related potentials show both auditory and non-auditory associations with chronic mild traumatic brain injury	Human	LIMBIC-CENC PLS sites in Richmond and Minneapolis	USA
DiBattista 2026	Integrated Blood Biomarker and Neurobehavioural Signatures of Latent Neuroinjury in Experienced Military Breachers Exposed to Repetitive Low-Intensity Blast	Human	CFSME and DRDC Toronto; breachers vs controls	Canada
DiBattista 2025	The impact of repetitive exposure to low-level blast on neurocognitive function in Canadian Armed Forces' breachers, snipers, and military controls	Human	Canadian Armed Forces breachers and snipers compared with age- and sex-matched controls	Canada
Dark 2026	Plasma Biomarkers, Brain Volume, and Cognitive Performance in Service Members and Veterans With mTBI: A LIMBIC-CENC Study	Human	Long-Term Impact of Military-Relevant Brain Injury Consortium–Chronic Effects of Neurotrauma Consortium (LIMBIC-CENC) multicenter study	USA
Wright 2025	Repetitive Blast Exposure Drives Chronic Pain in Female Rats	Rat	Female Sprague–Dawley rats subjected to repeated blasts in a laboratory at Virginia Tech using an Advanced Blast Simulator	USA
PerezGarcia 2025	Minocycline partially reverses established PTSD-related behavioral traits in rats exposed to repetitive low-level blast injury	Rat	Two cohorts of rats exposed to three 74.5 kPa blasts once per day for 3 days; treated with minocycline or vehicle at 8–8.5 months post-blast	USA

Jiang 2025	Effects of Liraglutide on Mitigation of Hearing Loss After Repeated Blast Exposures: A Summary of Studies in Animal Model of Chinchilla	Chinchilla	Chinchilla models exposed to low (3–5 psi) or high (15–25 psi) blast overpressure with open or earplug-protected ears; liraglutide administered pre- or post-blast	USA

Table 3 – GRADE Assessment Table

Study ID	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrades & Downgrades	Overall GRADE
Wright 2025	Moderate	Moderate	High	Moderate	Unclear	Downgrade 1 level	Very Low
Wang 2025	Moderate	Moderate	Moderate	High	Unclear	Downgrade 2 levels	Very Low
Tseng 2026	Moderate	Moderate	Moderate	High	Low	Downgrade 2 levels	Very Low
Solar 2025	Moderate	Moderate	Moderate	Moderate	Unclear	Downgrade 2 levels	Very Low
PerezGarcia 2025	Moderate	Moderate	High	Moderate	Unclear	Downgrade 1 level	Very Low
Martindale 2025	Moderate	Moderate	Moderate	Low	Low	Downgrade 1 level	Very Low
Lopez 2025	Moderate	Moderate	Moderate	Low	Unclear	Downgrade 1 level	Very Low
Lipov 2025	High	High	High	High	High	Downgrade 2 levels	Very Low
Lempke 2025	Moderate	Low	Moderate	Moderate	Unclear	Downgrade 2 levels	Very Low
Lam 2026	Moderate	Low	Moderate	Moderate	Low	Downgrade 2 levels	Very Low
Kranfli 2025	Moderate	Moderate	Moderate	Moderate	Unclear	Downgrade 2 levels	Very Low
Jiang 2025	Moderate	Moderate	High	High	Unclear	Downgrade 2 levels	Very Low
Franke 2025	Moderate	Low	Moderate	Moderate	Low	Downgrade 2 levels	Very Low
DiBattista 2026	Moderate	Low	Moderate	Moderate	Low	Downgrade 2 levels	Very Low
DiBattista 2025	Moderate	Moderate	Moderate	Moderate	Low	Downgrade 2 levels	Very Low
Dark 2026	Moderate	Moderate	Moderate	Moderate	Low	Downgrade 2 levels	Very Low

Note: Downgrading decisions were applied in accordance with GRADE guidance and reflect considerations of risk of bias, indirectness, inconsistency, and imprecision across the contributing evidence.

Table 4 - Grey Literature

ID	Title	Year	Country	Organisation	Source Type	URL	Summary
GL_1	Blast Overpressure - Risk Mitigation for Maximum Performance	2026	USA	US Army	Opinion	https://www.lineofdeparture.army.mil/Journals/Engineer/Engineer-Archive/2026-E-Edition/Blast-Overpressure/	This document outlines military guidance on blast overpressure (BOP), covering exposure risks, injury thresholds, and health effects, including cumulative neurocognitive impacts. It emphasises mitigation via exposure limits, PPE, standoff distances, and cognitive monitoring, with leadership responsibility for risk management and clinical follow-up.
GL_2	DoD Blast Overpressure Reference and Information Guide (D-BOP RIG)	2024	USA	US Department of Defense	Technical Guidance / Reference	https://health.mil/BrainHealthRisk	This technical guide provides empirically derived blast overpressure data across weapon systems, including measured peak pressures and minimum standoff distances based on a 4 psi threshold. It operationalises As Low As Reasonably Achievable (ALARA) principles, integrates PPE requirements, and presents exposure contours and mitigation parameters for training and operational environments.
GL_3	Department of Defense Requirements for Managing Brain Health Risks from Blast Overpressure	2024	USA	US Department of Defense	Policy / Directive	https://denix.osd.mil/auth/soh/programs/bop/	This memorandum establishes DoD-wide policy for managing blast overpressure exposure, defining a 4 psi threshold for initiating risk controls and mandating cognitive baseline testing, exposure tracking, PPE use, and training modifications. It formalises system-level governance, surveillance, and risk mitigation strategies to protect brain health while maintaining operational readiness.

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