McMaster University | Health Forum

Rapid Evidence Synthesis

Examining the association between individuals who are occupationally exposed to repetitive low-level blasts and experience mid- to long-term TBI-like symptoms

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Context

- Low-level blast exposure, defined as repeated exposure to explosive or other forces below the threshold for immediate clinical symptoms, has emerged as a significant health concern for active military personnel and Veterans, given its potential for causing cumulative neurological damage.
- Many active service members and Veterans exposed to these types of low-level forces report experiencing symptoms in the mid- to long-term that are similar to those experienced by people with a diagnosed traumatic brain injury (TBI).
- These symptoms include blurred vision, loss of balance, difficulty sleeping, and memory and concentration problems, to name a few.
- However, definitions of what qualifies as low-level blast exposure, including threshold pressure levels, frequency of exposure, and cumulative thresholds, as well as the specific exposure patterns that lead to the onset of these symptoms, remain unclear.
- This rapid evidence profile aims to further examine the association between exposure to repetitive low-level blasts and other forces and the experience of TBI-like symptoms.

Box 1: Evidence and other types of information

+ Global evidence drawn upon

Evidence syntheses selected based on relevance, quality and recency of search

+ Forms of domestic evidence used (🍁 = Canadian)

Data analytics

Evaluation

+ Other types of information used

Jurisdictional scan (five countries: AU, CA, NZ, UK, US)

***Additional notable features**

Prepared with input from one active military service member and one Veteran

Prepared with input from a subject-matter expert

Prepared in six business days using an 'all hands on deck' approach

Questions

1) What is the association between occupational exposure to repetitive low-level blasts (or other repetitive sub-concussive forces) and experiencing medium- to long-term (six months or greater) effects of symptoms consistent with traumatic brain injury?

High-level summary of key findings

- We identified 41 evidence documents, of which 25 were highly relevant, including three evidence syntheses and 22 single studies.
- Generally, the highly relevant evidence documents report an association between high occupational risk for low-level blasts (as an indicator for repetitive sub-concussive exposure) and worse symptoms on the Neurobehavioural Symptom Inventory, as well as for tinnitus and hearing impairments, headaches, and sleep impairments.

- However, the literature presented mixed results across all symptom categories, likely influenced by the heterogeneity of how studies defined and measured exposure, as well as small sample sizes.
- Additionally, 16 out of 22 highly relevant single studies were cross-sectional, meaning that exposure and outcome data were collected at the same point in time, so a true temporal relationship (where exposure clearly precedes outcomes) cannot be established, further obscuring the potential mechanism driving the association between repetitive sub-concussive exposures and medium- to long-term mild traumatic brain injury (mTBI) symptoms.
- The relationship between high occupational risk (e.g., for breachers, mortarmen, gunners) and experiencing symptoms is non-specific, with years in service, combat experience, and number of deployments often identified as variables with significant interaction effects.
- Further, the role of post-traumatic stress disorder (PTSD) in this relationship remains unclear (mediator, enhancer, or confounder), with some studies reporting that PTSD may attenuate the statistical significance of the association between repetitive sub-concussive exposures and symptoms.
- No biomarkers or brain imaging changes could specifically be linked to symptoms, nor is there consensus on biomarkers that are sufficiently sensitive to detect subtler brain changes.
- In the jurisdictional scan, clinical practice guidelines were identified in three of the five 'Five Eye' countries and had significant similarities in definitions of mTBI.
- No guidelines and reimbursement policies specifically described sub-concussive exposures; however, there is ongoing work by the NATO Science and Technology Organization to develop clinical practice guidelines to mitigate military occupation brain health risks from repetitive blast exposure, due later in 2025.

Box 2: Approach and supporting materials

At the beginning of each rapid evidence profile and throughout its development, we engage a subject matter expert and citizen partner – in this case a Veteran and an active serving member – who help us to scope the question and ensure relevant context is taken into account in the summary of the evidence.

We identified evidence addressing the question by searching Health Systems Evidence, PubMed and Web of Science. All searches were conducted on 30 May 2025. The search strategies used are included in Appendix 1. We identified jurisdictional experiences by hand searching government and stakeholder websites for information relevant to the question from five countries including Australia, Canada, New Zealand, United Kingdom, and United States.

In contrast to our rapid evidence profiles, which provides an overview and insights from relevant documents, this rapid evidence synthesis provides an in-depth understanding of the evidence.

We appraised the methodological quality of evidence syntheses that were deemed to be highly relevant using the first version of the AMSTAR tool. AMSTAR rates overall quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality, medium-quality evidence syntheses are those with scores between four and seven, and low-quality evidence syntheses are those with scores less than four. The AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to evidence syntheses pertaining to delivery, financial, or governance arrangements within health systems or implementation strategies.

A separate appendix document includes:

- methodological details (Appendix 1)
- key findings from included evidence syntheses and primary studies (Appendix 2)
- details about each identified evidence synthesis (Appendix 3)
- details about each identified single study (Appendix 4)
- details from the jurisdictional scan (Appendix 5)
- documents that were excluded in the final stages of review (Appendix 6)
- references.

This rapid evidence synthesis was prepared in the equivalent of six days of a 'full-court press' by all involved staff.

Framework to organize what we looked for

- Type of exposure
  - Blast
    - Primary (i.e., resulting from high pressure or overpressure created by explosions)
    - Secondary (i.e., resulting from strong winds following the blast wave that propel fragments and debris towards the body)
    - Tertiary (i.e., resulting from strong blast winds and pressure gradients that can accelerate and cause blunt force injury)
    - Quaternary (i.e., resulting from other explosive products and from exposure to toxic substances that can cause burns, blindness, and inhalation injuries)
    - Quinary (i.e., resulting from post-detonation environmental contaminants including chemical, biological, and radiological substances)
  - Non-blast
    - Impact injuries (i.e., non-blast related collision between head and a stationary or moving object)
    - Acceleration injuries (i.e., non-blast injuries resulting from the brain being suddenly forced to speed up and slow down within the skull)
    - Recoil injuries (i.e., injuries sustained as a result of backward force produced during the use of medium to large calibre shoulder fired weapons)
  - Additional dimensions of exposure
    - Number of exposures
    - Intensity of exposures (psi)
    - Time between exposures
- Sensory effects of mTBIs
  - Blurred vision, saccadic dysfunction, and vestibulo-ocular reflex challenges
  - Sensitivity to light
  - Tinnitus
  - Changes in ability to taste or smell
- Cognitive and mental health effects of mTBIs
  - Memory or concentration problems
  - Ongoing problems with speech
  - Dizziness, loss of balance, or proprioception issues
  - Mood changes
  - Depression
  - Anxiety
  - Suicide (including ideation and risk)
  - Difficulty sleeping
  - Fatigue
- Possible effect modifiers
  - Stage in a military career
    - Early
    - Mid
    - Late
  - Biological sex
    - Male
    - Female
  - Setting
    - Training
    - Deployment

        - Operations
    - Time to return to high-risk activities
    - Nature of protective equipment available (including the consistency with which it is worn and whether it fits correctly) (e.g., helmet, mouthguard, hearing protection)
    - Co-morbid PTSD or mental health conditions
    - Other co-morbid chronic conditions
- Causality criteria
    - Temporal relationship (e.g., exposure must precede the occurrence of the outcome)
    - Strength of association (e.g., association should meet statistical significance to demonstrate that it was not simply a chance occurrence)
    - Dose-response relationship (e.g., evidence that increasing exposure increases the risk of the outcome)
    - Consistency of evidence (e.g., similar or the same results generated by studies using different methods in different settings)
    - Specificity (e.g., the exposure is the only cause of the outcome that can be shown)
    - Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)

What we found

We identified 41 evidence documents, of which we determined 25 to be highly relevant, including:
- three evidence syntheses
- 22 single studies.

Coverage by and gaps in existing evidence syntheses and domestic evidence

Generally, the highly relevant evidence documents report an association between high occupational risk for low-level blasts (as an indicator for repetitive exposure to sub-concussive forces) and worse symptoms on the Neurobehavioural Symptom Inventory for post-concussive symptoms. Specific symptoms of significance vary throughout the literature. The lack of longitudinal study design, heterogeneity in studies, small sample sizes, and tendency for the literature to mix exposures (e.g., blast exposure and recoil from high-calibre weapon use) and populations (e.g., military occupational specialties) may be a key reason for some of the mixed findings and the inability to establish a causal relationship. Additionally, the role of PTSD in the association between repetitive sub-concussive exposures and medium- to long-term symptoms remains unclear due to the large overlap in symptoms. Additional symptoms that may be associated with high lifetime exposure to sub-concussive forces, especially in service members and Veterans with more years of service, include tinnitus/ear ringing, sleep disorders, headaches, and slower reaction times, although more research is needed on these associations.

The included evidence documents covered all causality criteria, with most of the included documents providing evidence of the causality criteria for 1) strength of association (i.e., finding statistically significant associations between sub-concussive forces and experiencing symptoms), and 2) biological plausibility (though the majority of findings in this section relate to physical changes in the brain and have not been shown to be definitive biomarkers of sub-concussive forces). We found limited evidence that provided explicit insight about the remaining causality criteria of temporal relationship, dose response relationship, consistency of evidence, and specificity.

Studies were determined to be highly relevant if they examined mid-term effects of sub-concussive forces in military service members without a prior history of TBI. Highly relevant studies had to examine mid- to long-term effects of exposure, defined as six months or more. While we identified 25 studies that met this criteria, we also identified an additional 12 studies that examine the immediate impacts of exposure to sub-concussive forces, many of which identify related symptoms but did not undertake longer term follow-up. These have not been included in detail in the report but are available in the appendices.(1-12)

The 25 highly relevant evidence documents examined the following exposures:

- 10 addressed the effects of sub-concussive blasts on breachers (three focused on symptoms and seven on reported changes from brain imaging)
- one addressed the symptoms of blast exposure or high-calibre weapon use among artillerymen (referred to as ‘gunners’ within the study)
- 13 addressed the effects of sub-concussive blast exposure (unspecified) on military personnel generally
- one addressed the effects of acceleration/deceleration on military paratroopers.

Seventeen studies used proxy measures for exposure, such as occupational risk for blast exposure based on military occupational specialty (e.g., breachers, mortarmen), or involved retrospective reporting, such as blast/TBI/paratrooper jump exposure interviews or the calculation of a Generalized Blast Exposure Value from the frequency of exposure to various weapon systems.(13-29) The Generalized Blast Exposure Value tool considers a subset of exposure variables to offer a more standardized representation of units of blast exposure experienced over a lifetime, aiding in comparisons between studies since exposure and low/high level exposure thresholds are classified differently across the literature. Generalized Blast Exposure Values are unitless, with values greater than or equal to 200,000 (which participants with significant heavy arms usage, artillery, or explosion exposure typically score) generally considered as high lifetime exposure and values less than 200,000 as low lifetime exposure (which participants with significant light arms usage typically score).(25; 26)

Included studies generally categorize exposures as being either low or high and distinguish between the two by using pressure measurements (pounds per square inch, psi). However, the safety threshold that is used in most studies (4 psi) was established for hearing safety, not organ/brain injury protection. The variety in measures and thresholds for low-level blast exposure complicates establishing a true association between repetitive sub-concussive exposures and medium- to long-term outcomes.

Objective exposure measures (e.g., body-worn blast gauges or accelerometers) were inconsistently used in the evidence and typically used to measure short-term outcomes. Though we categorized it as being medium relevance for this rapid evidence synthesis, we did identify one study that includes a variety of recommendations for establishing a safety threshold (e.g., daily firing limits) and blast exposure measurement, including the use of body-worn sensors designed to track an individual’s cumulative exposure and a unit’s daily cumulative impulse thresholds, as well as the use of simulation technology to offer hands-on practice for certain tasks in high-risk occupations without exposing service members to additional blast exposure.(1) Daily firing limits and safety thresholds were urgently recommended based on the study’s trial findings that protective equipment (e.g., ear protection, helmets, ballistic body armour, blast attenuation devices) and practices (e.g., ducking before firing the mortar) do not significantly impact health outcomes without additional protections.(1) Lastly, one study was identified regarding body-worn blast gauges being used to measure cumulative exposure during training; however, it was not included in this rapid review since outcomes have not been reported yet, only the initial exposure measurements.(30)

Four sources were identified that studied the effects of slamming exposures, but none met the inclusion criteria for this rapid review since they investigated musculoskeletal outcomes rather than symptoms consistent with TBIs, as well as more severe levels of exposures instead of low-level or sub-concussive repetitive exposures.(31-34)

Drawing conclusions from the identified evidence documents is further hindered by the lack of a consistent definition for sub-concussive exposures. In the highly relevant evidence documents, at least four different conceptualizations exist:

- a retrospective cohort study noted that trainers exposure can be greater than six blast events per day, one to two days a week, with eight to 20 breaching courses per year, over the course of seven to 10 years of military experience in this high-risk occupation (breaching experience instructor in this study) (23)

- a cross-sectional study defines repetitive sub-concussive exposure as controlled blast exposure typically less than 3 psi, according to the Canadian Army Doctrine, that occurs during routine military training that is experienced over months or years (9)
- a cross-sectional study defines repetitive sub-concussive exposure in military paratroopers as mild brain impacts that do not meet clinical criteria for concussion or mTBI but involve mechanical forces transferred to the brain (24)
- a longitudinal study classified sub-concussive exposures when neurological symptoms do not emerge after a single exposure, but rather from cumulative/repetitive blast overpressures and impulses, recoils, and parachuting. (29)

Finally, the included evidence identifies additional challenges in supporting our understanding of the mechanism between exposure and outcomes, including the undetermined role of PTSD and the inconsistent use of mTBI as a variable in the available literature, with some studies using an mTBI diagnosis (based on the Glasgow Coma Scale) as an inclusion criteria to assume the presence of both exposure and outcomes, while others excluded participants with a history of concussion and/or moderate/severe TBIs.(35-37) The same is true for recent blast exposure within the last 24–72 hours, with some studies not filtering for this potential confounder and others excluding participants with recent blast exposure. For this synthesis, documents were only included as being highly relevant when they explicitly focused on sub-concussive forces.

Key findings from included evidence documents

To help answer the question, we have provided two different ‘ways in’ to the identified evidence. The first way in is through the medium- to long-term effects from repetitive sub-concussive exposures documented in the literature. These have been presented in synthesis form below given very few of the included documents examined homogeneous exposures and military occupations. However, table 1 in Appendix 2 does separate out the findings by exposure and by military occupation. The second way in is through five causal criteria that help to provide an understanding of whether a true causal relationship can be determined. The same highly relevant evidence documents are described in both ‘ways in,’ but two highly relevant documents appear only in the causal criteria (biological plausibility) section related to brain imaging changes.

Overview of findings related to symptoms of repetitive sub-concussive exposures

In general, 23 highly relevant evidence documents report on the following five subthemes of symptoms and health effects related to repetitive sub-concussive exposure:
- neurobehavioural symptoms
- hearing, vision, and vestibular symptoms
- headaches and pain
- sleep
- neuropsychological and affective symptoms.

<u>Neurobehavioural symptoms</u>

Two evidence syntheses (recent medium-quality and older low-quality) and 10 single studies (two recent retrospective cohort, eight recent cross-sectional) report mixed findings about the association between repetitive sub-concussive exposure and neurobehavioural symptoms.(13; 15; 18; 20; 21; 24; 27; 38-42) Generally, higher exposure was associated with higher cognitive, somatic, and emotional sub-scale scores on the Neurobehavioural Symptom Inventory measure for both active service members and Veterans compared to non-blast exposed controls, including for memory (e.g., delated recall, challenges with immediate recall and visual retention), concentration, and communication problems.(13; 15; 18; 40-42) Additionally, one recent cross-sectional study reported that experienced breachers had elevated neuronal-derived extracellular vesicle concentrations of tau and this elevated biomarker was associated with higher Neurobehavioural Symptom Inventory scores.(27) However, one older low-quality evidence synthesis and a recent cross-sectional study report that the statistical significance between high exposure and worse neurobehavioural functioning may be attenuated once PTSD is accounted for, with PTSD symptoms having a large cumulative effect alongside blast exposure.(20; 38)

Studies included in an older medium-quality evidence synthesis that reported mixed results on cognitive domains of health.(39) This finding is consistent with other evidence documents we identified. While one recent cross-sectional study found that participants with blast exposure performed worse on tasks requiring cognitive-motor integration,(15) no cognitive effects were found in an older low-quality evidence synthesis or in a second recent cross-sectional study, after relevant covariates were considered, including years of service, education, race, and combat exposure.(21; 38)

With respect to energy levels, a recent cross-sectional study found that blast exposure was associated with lower energy scores and worse perceptions of functional musculoskeletal performance compared to non-blast exposed controls.(15) Military deployment was also significantly associated with lower energy levels, as well as greater concussive scores and greater PTSD symptoms. Evidence documents described the need for additional research to further understand these relationships.(13; 21; 40)

Lastly, a recent cross-sectional study investigated the acceleration-deceleration and impact exposures experienced by paratroopers, finding that paratroopers showed significantly slower reaction times in the alerting network compared to health controls.(24)

Hearing, vision, and vestibular difficulties

One older low-quality evidence synthesis and five single studies found an association between blast exposure and sensorineural hearing loss and auditory symptoms.(13; 22; 25; 38; 40-42) High occupational risk was associated with hearing problems experienced over time, with a significant interaction effect between high occupational risk and more years of service for hearing problems and tinnitus/ear ringing in two recent retrospective cohort studies.(13; 40) Tinnitus without measurable hearing loss was referred to as ‘hidden hearing loss’ and was common in many of the evidence documents.(9; 42; 43)

One recent cross-sectional study reported that poor oculomotor behaviour in the blast-exposed group of breachers and ‘gunners’ (operators of high-calibre weapons) with 10–15 years of experience was also correlated with higher reported symptom severity on a concussion-assessment questionnaire.(22) The symptoms reported in this study and others found similar associations between blast exposure and vestibular symptoms (e.g., balance, coordination, reduced time and movement velocity on postural limits of stability tests), ocular motor behaviours (e.g., slower and more variable eye tracking movements), blurred vision, light sensitivity, eye strain, and vision problems more generally, as well as change in taste/smell and sensitivity to noise.(22; 25; 38; 41; 42)

Headaches and pain

One recent medium-quality evidence synthesis and three single studies (one recent retrospective cohort study, two recent cross-sectional studies) found that individuals with blast exposure (or high occupational risk) reported higher levels of headaches than control groups.(13; 22; 39; 42)

However, there is uncertainty in the included literature about when headaches appear (e.g., whether immediately following exposure or over the longer term) and at what point in a military career individuals are most at risk. One recent medium-quality evidence synthesis found that increased headaches tended to be most prevalent in the acute timeframe, rather than as a lasting effect of blast exposure.(39) One recent retrospective cohort study reports that the association between high-risk occupations and headaches differs throughout a military service member’s career. The study reported low-levels of risk for headache among baseline and early-career service members, but identified an increased risk of headaches for mid-career service members.(13) The study also noted that occupational risk was associated with lower risk of migraines at baseline.(13)

Sleep

Five single studies (three recent retrospective cohort studies, two recent cross-sectional studies) found mixed results for the effects of repetitive sub-concussive blasts on sleep and fatigue. In some studies, high occupational risk/blast exposure increased risk of sleep disorders and decreased risk in others.(13; 19; 20; 22; 40) In two recent cross-sectional studies, blast-exposed participants had higher symptom severity, including sleep impairment and fatigue, compared to those with low-/no blast exposure.(20; 22) In contrast, a recent retrospective cohort study reported that the relationship between high-occupational risk and reduced risk of impaired sleep was only significant at baseline and early career, not at mid-career.(13) Additionally, the same study found that occupational risk predicted significantly lower risk of fatigue at baseline, early career, and mid-career time points but the effect attenuated significantly over time. The study notes that this potentially indicates that repetitive sub-concussive exposure may have a cumulative effect on fatigue and sleep disorders. However, it was noted that service members in high-risk occupations may be less likely to receive formal diagnoses in general.

Two studies note that the effect of PTSD on the association between sub-concussive forces and sleep is unknown, with one study reporting PTSD to be a confounding variable, while the other reported an independent association with persistent sleep problems even after accounting for mTBI history, PTSD, and depression.(19; 20)

Neuropsychological and affective symptoms

Six single studies (two recent retrospective cohort studies, four recent cross-sectional studies) found that repetitive low-level blast exposure is associated with irritability, PTSD symptoms, depression, and alcohol misuse, although the effect of PTSD as a mediating or confounding variable remains uncertain.(13; 15; 19; 20; 25; 41) One recent retrospective cohort study and two recent cross-sectional studies found that PTSD was often involved in the relationship between high blast exposure and post-concussive symptoms, having significant synergistic effects with other psychological co-morbidities (e.g., depression, alcohol misuse) and affective symptoms linked to increased risk of experiencing post-concussive symptoms.(19; 20) Additionally, a recent retrospective cohort study reported that higher occupational risk was significantly associated with greater risk of behavioural health conditions, anxiety disorders, alcohol abuse/dependence, and PTSD.(13) Military deployments and increased combat exposure are also associated with these greater PTSD symptoms, potentially influencing the relationship between blast exposure and neuropsychological effects.(15; 20) Lastly, two recent cross-sectional studies reported higher levels of irritability in participants with high occupational blast exposure (e.g., breachers or GBEV ≥200,000).(25; 41)

Overview of findings related to causal criteria

Temporal relationship

A key limitation from the included evidence is the reliance on cross-sectional studies, which capture data (both the exposure and the outcome) at a single point in time. This makes it very difficult to determine a temporal relationship between repetitive exposure to sub-concussive forces and experiencing particular symptoms. Further, it is particularly difficult to establish the timeline of symptom onset and to control for other confounding variables, especially since the exposure is cumulative over months to years.

Of the 20 highly relevant single studies, only four were cohort studies that can be used to establish a temporal relationship. The remaining 16 were cross-sectional studies and one case-control study. The included cohort studies examined:

- the association between occupational risk for low-level blast exposure and clinically diagnosed TBIs and the symptoms typically experienced with them (13)

- the association between low-level overpressure and serum levels of neurotrauma biomarkers and concussion-like symptoms (40)
- early amyloid B deposition in the brain of those exposed to repeated sub-concussive blast injury (44)
- whether the mechanism of injury (blast versus impact) affects the likelihood of persistent sleep problems in post-deployment military populations.(19)

The first cohort study found service members with higher occupational risk and length of time serving were significantly more likely to receive a TBI diagnosis and to experience co-morbid conditions including cognitive challenges, headache, hearing problems, communication disorders, non-headache pain, and sleep disorders.(13) The study found that occupational risk was associated with significantly greater risk of cognitive problems and communication disorders in early and mid-career service members.(13) The study also noted that there was a trend for increased association with hearing problems the longer an individual was serving, but a weakening association with non-headache pain and sleep disorders over time.(13)

Two cohort studies identified changes taking place in the brain and found military personnel with low-level overpressure exposure, but no diagnosed brain injury, had greater levels of blood biomarkers associated with neurological damage (amyloid B levels, UCH-L1, tau) compared to the matched controls.(40; 44) Amyloid B accumulation was found among grenade and breacher instructors in four regions, including the inferomedial frontal lobe, praecuneus, anterior cingulum, and superior parietal lobule.(44)

The final cohort study found blast-related injury was more strongly associated with persistent sleep problems than impact-related injuries.(19) However, the study noted that the greater predictor of persistent sleep problems was reported sleep trouble at return from deployment.(19)

<u>Strength of association</u>

In addition to the four cohort studies above, we identified one older medium-quality evidence synthesis and seven cross-sectional studies that provide findings on strength of association. Although, it should be noted that there is significant heterogeneity in the populations included across the eight studies (e.g., many different types of military specialties), the exposures (e.g., number of sub-concussive forces, type of sub-concussive forces, context in which they take place – training or deployment), as well as in the outcomes examined (e.g., many different symptoms assessed using different tools). In addition, most of the included cross-sectional studies had small sample sizes of between 18–40 active military members or Veterans, though two recent cross-sectional studies were an exception, including between 130 and 282 military service members and Veterans.(20; 21) These two factors (heterogeneity in studies and small sample sizes) may be in part responsible for some of the mixed findings identified in the section above on symptoms and in specific reporting of strength of association below.

Findings from the evidence synthesis and cross-sectional studies indicate statistically significant associations between:
- Canadian breachers with repetitive sub-concussive blast exposure (up to a maximum of six blasts a week) and lower energy scores (p=0.022), worse perceptions of functional musculoskeletal performance (p=0.016), greater somatic symptoms (p=0.004), and more attention and memory challenges (p=0.001) compared to other Canadian Armed Forces members with no blast experience (15)
- breaching experience of instructors and prolonged reaction time, as well as slower movement velocity, compared to a matched control group of engineers with minimal to no exposure to sub-concussive forces (41)
    - high lifetime exposure (determined through the Generalized Blast Exposure Value tool) resulting in some alteration but not loss of consciousness, low-levels of PTSD, and worse symptom scores across the Neurobehavioural Symptoms Inventory (p=0.013) compared to those with low-lifetime blast exposure and low-levels of PTSD (20)
- military breachers or gunners exposed to long-term (10–15 years) low-level blasts or high calibre weapon usage and impaired oculomotor behaviour including slower eye movements (visual reaction speed: p=0.03; saccadic velocity:

p=0.027), more frequent stopping points when following a target (fixation percentage: p<0.001), and higher rates of variation (smooth pursuit variance: p=0.049; eye-target velocity error: p=0.04) as compared to other military members with different occupations (22)

- paratroopers (acceleration-deceleration exposure) and slower reaction times (p=0.001 for no cue; p<0.001 for double cue conditions), as well as for attentional resource allocation and inhibition control in the executive control network (p=0.008) (24)
  - high-level blast exposure (determined by the Generalized Blast Exposure Value tool) and poorer results on the neurobehavioural symptoms severity composite (p=0.036) and its sub-scales of somatic (p=0.04) and cognitive (p=0.043) outcomes compared to those with low-level blast exposure.(18)

Findings from the evidence synthesis and cross-sectional studies identified no statistically significant association between:

- breaching experience of instructors and lower vestibular scores or visual scores on a sensory organization test (41)
- breaching experience of instructors and balance (measured through endpoint excursion, maximal excursion, and directional control) (41)
- lifetime blast exposure among military service members and Veterans and differences in attention, working memory, processing speed, executive functioning, and general cognition.(21)

Dose-response relationship

One older-medium-quality evidence synthesis and three cross-sectional studies provide findings related to dose-response relationships. Each of the five evidence documents note that within their samples, those with more exposure to sub-concussive forces had increased negative outcomes. However, the thresholds about what constitutes "many" exposures differs by study, as does the exposure itself (e.g., how sub-concussive exposure is defined).

The first cross-sectional study provides insights into repetitive exposures, noting that among 181,000 Marines recurrent occupational overpressure exposure heightened the future risk of developing an mTBI from a subsequent blast. This finding indicates that there may be a priming effect following a single blast exposure in deployed settings.(45) Another study (that did not meet the inclusion criteria for this rapid review) also investigated this priming effect related to the impact of subsequent blast exposure on biomarkers in people who have previously been diagnosed with an mTBI.(10)

The remaining evidence synthesis and two cross-sectional studies identify dose-response relationships for specific outcomes. The older medium-quality evidence synthesis included one study of 573 deployed service members that found a dose-response relationship between blast exposure and hearing loss.(38)

Another recent cross-sectional study found that participants with high-level blast exposure (determined by the Generalized Blast Exposure Value tool) had poorer results on the neurobehavioural symptoms severity composite measure (p=0.036) and its sub-scales related to somatic (p=0.04) and cognitive (p=0.043) outcomes compared to those with low-level blast exposure.(18)

Finally, a recent cross-sectional study of 984 service members found those with a lifetime blast exposure of greater than 200,000 Generalized Blast Exposure Value units were significantly different than the low-blast exposure group (less than or equal to a score of 200,000), with the five most significant symptoms being change in taste/smell, numbness, sensitivity to noise, irritability, and vision problems.(25)

Consistency of evidence

Among included evidence syntheses and single studies, determining evidence consistency is challenging due to many occupational exposure sources (low-level blasts, high-calibre weapons, parachuting, among others), methodological differences in quantifying military exposures, and difficulty controlling for confounding factors in deployment and training.

These challenges are noted in the included literature of this rapid evidence profile, where included studies identify conflicting findings, notably around outcomes related to attention.

Two evidence syntheses and one recent cross-sectional study provide findings related to the consistency of evidence.

The first older medium-quality evidence synthesis notes finding mixed effects of repetitive low-level blasts in military and police training, with some studies reporting changes to cognition, biomarkers, and headaches, while others only identified these effects in the acute or post-acute phase of exposure.(39)

The remaining three findings pertain to consistency within the broader evidence base. One recent medium-quality evidence synthesis found repetitive exposure to low-level blasts resulted in changes to select biomarkers, including UCH-L1, peripheral inflammatory markers, and APP, but noted that these effects were not consistently replicated within the literature.(13) Additionally, one recent cross-sectional study found no evidence to suggest that there was an impact of blast exposure on neurocognitive functioning in military service members, and notes that these findings diverge from past studies that have suggested blast exposure is related to deficits in reaction time and attention.(21)

Specificity

Within the included studies, two issues concerning specificity were raised. The first has to do with concerns around the measurement of sub-concussive exposures, particularly regarding the measurement and calculation of threshold levels for sub-concussive forces. Findings from one recent medium-quality evidence synthesis address this issue, noting that the persistence of select health outcomes, such as headaches, were not experienced beyond the acute window, but it is unknown if this is due to the non-existence of a causal relationship with low-level blast exposure, or challenges with blast exposure measurement.(39)

The remaining documents – one older low-quality evidence synthesis and two cross-sectional studies – speak to a second issue of specificity, which is the overlap between symptoms of sub-concussive blast exposure and symptoms of PTSD. In one older low-quality evidence synthesis, co-existing PTSD symptoms were found to explain some of the behavioural and emotional symptoms observed after blast-related exposure, with blasts potentially exacerbating PTSD symptoms.(38) One cross-sectional study found that when controlling for PTSD, the association between cumulative blast exposure and overall symptom severity was attenuated, particularly for emotional and mood related (affective) symptom domain.(27) Similarly, a second recent cross-sectional study found blast exposure effects were evident when PTSD symptoms were minimal, with high blast exposure participants showing consistently worse neurobehavioral outcomes than low blast exposure participants. However, when clinically significant PTSD symptoms were present, blast exposure effects were largely obscured, with meaningful differences between high and low blast exposure groups only emerging among participants with the highest symptom burden (six or more clinically elevated measures).(20)

Biological plausibility

In addition to the two cohort studies noted in the section on temporal relationships and two cross-sectional studies highlighted in the strength of association section,(17; 24; 40; 44) two evidence syntheses and eight cross-sectional studies looked at physical changes in the brain using a range of different measures.(14; 16-18; 23; 26; 39; 42; 43) However, none of the included measures could specifically be linked to symptoms. Further, there is no research consensus on biomarkers that are sufficiently sensitive to detect subtler brain changes, nor is there consensus on timing for biomarker sampling given the cumulative effect of exposures.

One recent medium-quality evidence synthesis included six studies that measured various biomarkers (e.g., T-tau, neurofilament light chain, glial fibrillary acidic protein, S-100 calcium binding protein B, CSF/serum albumin ratio, UCH-L1, TNFα, IL-6, IL-10, APP, spectrin breakdown products 150), but the findings were mixed or were noted in the synthesis as not being consistent with existing literature. As an example, one of the studies from this evidence synthesis suggested that blast magnitude is connected to an increase in UCH-L1 and subsequently increased postural sway and changes in one cognitive measure, but another study found no change in UCH-L1 from baseline in breachers during and after training.(39) Another recent low-quality evidence synthesis also found inconsistent evidence of changes in biomarkers (e.g., UCH-L1, peripheral inflammatory markers, APP) after sub-concussive blast exposure.(43)

Physical changes in the brain identified in the cross-sectional studies, include:

- higher levels of anti-glial fibrillary acid protein, immunoglobin M, and immunoglobin B (circulating antibody profiles) in breachers compared to non-exposed controls (14)
  - neuronal slowing in the right fronto-temporal lobes and sub-cortical regions, as well as functional dysconnectivity in the posterior default mode network after controlling for concussion and traumatic stress history (18)
- changes to blood-based proteins and lipid molecules among servicemen with at least a six-month history of testing and trialling heavy weapons, including the neurofilament light chain and elevated c-reactive protein levels (42)
- elevated blood biomarkers of inflammation, extracellular matrix degradation, and blood-brain barrier disruption (myeloperoxidase, MMP-3, MMP-9, MMP-10, occludin, and syndecan-1) among breachers with a median seven years of breaching experience and 10 years of blast exposure as compared to a control group with limited blast exposure (23)
- statistically significant elevations of neuronal-derived extracellular vesicle tau concentrations in breachers with 400+ blast exposures and/or four or more years of breaching experience compared to age-matched military and law enforcement controls, where an association between the elevated tau concentrations and increased neurobehavioural symptom inventoryl scores of experienced breachers was observed (27)
  - Non-statistically significant changes were observed in serum and neuronal-derived extracellular vesicle concentrations of NF-L and Aβ42, as well as serum concentrations of tau compared to controls (27)
- increased cortical thickness in the left rostral anterior cingulate cortex (a region that helps to modulate cognition and emotion) among U.S. special operations breachers (with at least 10 years of experience) compared to those with limited blast exposure (26)
- neuroinflammation in the cerebellum and medio temporal brain regions, reductions in cortical thickness, and volumetric brain tissue loss at higher Generalized Blast Exposure Value (16)
- greater cortical thickness in the occipital lobes, higher default mode network activity, and differences in measures of white matter tract integrity (e.g., fractional anisotropy and radial diffusivity) in breachers compared to non-blast exposed controls.(17)

The final cross-sectional study that identified elevated blood biomarkers of inflammation, extracellular matrix degradation, and disruptions to the blood brain barrier was noted as being consistent with existing blast models and other previously conducted human studies.(23)

Key findings from jurisdictional scans

We conducted a jurisdictional scan for clinical practice guidelines and reimbursement policies relevant to repetitive sub-concussive forces in each of the ‘Five Eye’ countries – Australia, Canada, New Zealand, United Kingdom, and United States. We also undertook a review of the North Atlantic Treaty Organization’s Science and Technology Organization, given there has been a significant focus on this topic.

Clinical practice guidelines were identified in three of five countries – Canada, United Kingdom, and United States.

The guidelines from the ‘Five Eye’ countries share many commonalities including similar definitions of mTBI or concussion (see table 1).

Table 1. Definitions of mTBI from Canadian, U.K., and U.S. guidelines (adapted from NATO technical report)

Country	Canada	U.K.	U.S.
Definition of mTBI in clinical guidelines	Any of the following diagnostic definitions: • a score of between 13–15 on the Glasgow coma scale • normal structural imaging • alteration of consciousness and mental state up to 24 hours • post-traumatic amnesia lasting 0–1 day • persistence of physical symptoms (e.g., headache, nausea), cognitive symptoms (e.g., memory problems, confusion, disorientation), and emotional and behavioural symptoms (e.g., mood swings, anxiety)	• Loss of consciousness for 30 minutes or less and/or alteration of consciousness for a moment up to 24 hours late and/or post-traumatic amnesia for less than 24 hours • Transient neurological abnormality • Glasgow Coma Score no lower than 13 after 30 minutes	A new onset or worsening of any of the following clinical signs: • any period of loss of or a decreased level of consciousness • any loss of memory for events immediately before or after the injury • any alteration in mental state at the time of the injury • neurological deficits that may or may not be transient • intracranial lesion TBIs are the result of external forces include any of: • being struck by an object • the head striking an object • the brain undergoing acceleration or deceleration without external trauma to the head • a foreign body penetrating the brain • forces generated from events such as blasts or explosions

Guidelines from both Canada and the U.K. apply a symptom-based approach, whereby individuals who have concerns about mTBI are responsible for self-reporting. The U.S. uses an event-based approach, in which military personnel who are within 50 meters of a blast event or other potentially concussive event are required to undergo medical evaluation. In both the U.K. and U.S. guidelines, roles in the treatment and management of mTBIs are included, but Canadian guidelines have not been developed in a way that describes specific roles of healthcare providers in the assessment, treatment, and management of post-concussive symptoms. Other elements of the clinical guidelines pertain primarily to neurocognitive evaluations, exertion testing, and requirements prior to returning to active service. No elements in the guidelines address Veterans specifically, though the U.S. guidelines include clinical recommendations for treatment options.

In addition to the clinical practice guidelines, we identified information on benefits and reimbursements for health services in three of the ‘Five Eye’ countries – Australia, Canada and the U.S. In Australia, we identified that a Statement of Principle relevant to blast injuries had been developed in 2020 and is used to connect military services to compensation and treatment coverage. The explosive blast injury principle covers any physical injury resulting from explosive blasts including direct effects of overpressure waves, flying debris, or being thrown against an object by the force of the blast. No mention is made of sub-concussive forces and the principle requires that the blast is sustained during operational service, peacekeeping, hazardous service, war-like service, or non-war like service but does not include training. Separate principles have been established for concussion, acute mTBI (but does not include ongoing/persistent effects) and moderate to severe TBI.

For Veterans Affairs Canada, the following factors are accepted to cause or aggravate mTBI and can be considered alongside evidence to assist in establishing a relationship to service for the receipt of benefits or entitlements:
- the head being struck by an object
- the head striking an object
- the brain undergoing an acceleration or deceleration movement without direct external trauma
- an explosion or a blast
- experiencing repeated concussive or sub-concussive forces at the time of clinical onset or aggravation of mild TBI symptoms
  - experiencing a consecutive mTBI, defined as receiving a subsequent mTBI before fully recovering from a previous head injury at the time of clinical onset or aggravation of mTBI symptoms
  - inability to obtain appropriate clinical management of mTBI.

Additional medical conditions included in Veterans Affairs Canada entitlement/assessment are post-traumatic headaches, post-traumatic migraines and non-specific dizziness.

In the U.S., Veterans are eligible for medical care and health services needed to provide the standard of care supported by the established clinical guidelines. In addition, Veterans Affairs disability compensation benefits program may provide additional benefits for presumptive conditions for which some exposures (e.g., blasts) are relevant.

In addition to identifying the documents above, the NATO technical report includes sections related to the prevention of mTBI in military populations, noting the importance of education and training. Further, we identified two ongoing processes within NATO Science and Technology Organization. The first is the development of clinical practice guidelines to mitigate military occupational brain health risks from repetitive blast exposure (due later in 2025). The second is the ongoing development of guidelines for the evaluation of personal protective material and systems against blasts.

Next steps based on the identified evidence

- A considerable challenge in the literature is the lack of consensus on the definition of sub-concussive exposures and the tendency to group exposures for all high-risk military occupational specialties together, creating challenges for analysis.
- As a result, the establishment of specific scales, thresholds, or definitions to distinguish the difference between sub-concussive exposures and mTBI exposures is a critical next step, for both research and policy efforts.
- Additionally, greater efforts need to be made to tease apart the outcomes based on the type of exposure and occupation of the participants, with future research clearly reporting findings from homogenous exposures/military occupational specialties and differences between and within groups (see Appendix 2).
- Integrating methods in future research that better monitor an individual's cumulative exposure, such as through body-worn sensors, would add greatly to improving the level of certainty in the evidence base.
- Improved efforts within studies to disentangle different types of exposure would help to further understand how risk differs across military roles.
- Additional research efforts could focus on generating evidence to establish causal relationships between repetitive sub-concussive exposure and mid- to long-term mTBI symptoms; for example:

    - for the causal criteria of temporality, longitudinal research is needed
    - to strengthen the association, larger sample sizes are needed to increase the power of statistical calculations
    - for the causal criteria of specificity, further research on the role of PTSD in this relationship is needed, as well as the collection of contextual data about the exposure (e.g., setting, time in service, existing health conditions) to better specify what outcomes are observed in each occupational specialty.
- These next steps could be aided by collaborative efforts between jurisdictions (e.g., high-speed boat operators from the militaries of NATO countries participate in a study to increase the sample size, as well as the specificity in the type of exposure/a more homogenous population, rather than sampling active service members across all occupational specialties from the Canadian Armed Forces).
- To further understand the influence of PTSD, future research could specifically evaluate the relationship between repetitive sub-concussive blast exposure and mental health symptoms.
    - Notably, aiming to understand how the severity of mental health experiences peak and plateau across a service member or Veteran's career and lifetime with increased deployments and/or combat exposure can help to minimize potential confounding variables in the relationship between repetitive sub-concussive blast exposure and medium- to long-term symptoms.

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