Rapid Evidence Synthesis appendices

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

8 August 2025

[MHF product code: RES 132]

Appendices

Appendix 1: Methodological details

Background to the rapid evidence synthesis

This rapid evidence synthesis mobilizes both global and local research evidence about a question submitted to the McMaster Health Forum's Rapid Response program. Whenever possible, the rapid evidence synthesis summarizes evidence drawn from existing evidence syntheses and from single research studies in areas not covered by existing evidence syntheses and/or if existing evidence syntheses are old or the science is moving fast. A systematic review is a summary of studies addressing a clearly formulated question that uses systematic and explicit methods to identify, select, and appraise research studies, and to synthesize data from the included studies. The rapid evidence synthesis does not contain recommendations, which would have required the authors to make judgments based on their personal values and preferences.

The Forum produces timely and demand-driven contextualized evidence syntheses such as this one that address pressing health and social system issues faced by decision-makers (see our website for more details and examples). This includes evidence syntheses produced within:
- days (e.g., rapid evidence profiles or living evidence profiles)
- weeks (e.g., rapid syntheses that at a minimum include a policy analysis of the best-available evidence which can be requested in a 10-, 30-, 60- or 90-business-day timeframe)
- months (e.g., full evidence syntheses or living evidence syntheses with updates and enhancements over time).

This rapid evidence synthesis was prepared over a six-business day timeframe and involved six steps:
1) submission of a question from a policymaker or stakeholder (in this case, Veterans Affairs Canada)
2) engaging subject matter expert and citizen partner
3) identifying, selecting, appraising, and synthesizing relevant research evidence about the question
4) conducting and synthesizing a jurisdictional scan of experiences about the question from other countries and Canadian provinces and territories
5) drafting the rapid synthesis in such a way as to present concisely and in accessible language the research evidence
6) finalizing the rapid evidence synthesis based on the input of at least two merit reviewers.

Engaging subject matter experts

At the beginning of this rapid evidence synthesis and throughout its development, we engaged subject matter experts and two individuals with lived experience (one active serving member of the Canadian Armed Forces and one Veteran), who helped us to scope the question and ensure relevant context is considered in the summary of the evidence.

Identifying research evidence

For this RES, we searched Health Systems Evidence, PubMed, and Web of Science for:
1) evidence syntheses
2) single studies.

In Health Systems Evidence, we used the filter for "military personnel, Veterans and their families" combined with search terms for: "(blast OR overpressure OR explosion OR explode OR recoil)".

In PubMed, we limited the search to the past ten years and used the search terms: ("blast" OR "explo*" OR "over pressure" OR "recoil") AND ("repeat" OR "repetitive" OR "multiple") AND ("military" OR "Veteran" OR "Military Personnel"[Mesh]).

In Web of Science, we limited the search to the past 10 years and used the search terms: ("blast" OR "explo*" OR "over pressure" OR "recoil") AND ("repeat" OR "repetitive" OR "multiple") AND ("military" OR "Veteran" OR "Navy" OR "Army" OR "Air Force").

Each source for these documents is assigned to one team member who conducts hand searches (when a source contains a smaller number of documents) or keyword searches to identify potentially relevant documents. A final inclusion assessment is performed both by the person who did the initial screening and the lead author of the rapid evidence profile, with disagreements resolved by consensus or with the input of a third reviewer on the team. The team uses a dedicated virtual channel to discuss and iteratively refine inclusion/exclusion criteria throughout the process, which provides a running list of considerations that all members can consult during the first stages of assessment. Excluded documents are listed in Appendix 6.

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

Assessing relevance and quality of evidence

We assess the relevance of each included evidence document as being of high, moderate, or low relevance to the question.

Two reviewers independently appraise the methodological quality of evidence syntheses that are deemed to be highly relevant using the first version of the AMSTAR tool. Two reviewers independently appraise each synthesis, and disagreements are resolved by consensus with a third reviewer if needed. AMSTAR rates overall methodological quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality. High-quality evidence syntheses are those with scores of eight or higher out of a possible 11, medium-quality evidence syntheses are those with scores between four and seven, and low-quality evidence syntheses are those with scores less than four. It is important to note that the AMSTAR tool was developed to assess evidence syntheses focused on clinical interventions, so not all criteria apply to those pertaining to health-system arrangements or implementation strategies. Furthermore, we apply the AMSTAR criteria to evidence syntheses addressing all types of questions, not just those addressing questions about effectiveness, and some of these evidence syntheses addressing other types of questions are syntheses of qualitative studies. While AMSTAR does not account for some of the key attributes of syntheses of qualitative studies, such as whether and how citizens and subject matter experts were involved, researchers' competency, and how reflexivity was approached, it remains the best general quality-assessment tool of which we're aware. Where the denominator is not 11, an aspect of the tool was considered not relevant by the raters. In comparing ratings, it is therefore important to keep both parts of the score (i.e., the numerator and denominator) in mind. For example, an evidence synthesis that scores 8/8 is generally of comparable quality to another scoring 11/11; both ratings are considered 'high scores.' A high score signals that readers of the evidence synthesis can have a high level of confidence in its findings. A low score, on the other hand, does not mean that the evidence synthesis should be discarded, merely that less confidence can be placed in its findings and that it needs to be examined closely to identify its limitations. (Lewin S, Oxman AD, Lavis JN, Fretheim A. SUPPORT Tools for evidence-informed health Policymaking (STP): 8. Deciding how much confidence to place in a systematic review. *Health Research Policy and Systems* 2009; 7(Suppl1): S8.)

Identifying clinical practice guidelines and reimbursement policies from 'Five Eye' countries

For each REP, we work with the requestors to collectively decide on what countries to examine based on the question posed. For this REP, we examined clinical practice guidelines and reimbursement policies from 'Five Eyes' countries (Australia, Canada, New Zealand, United Kingdom, and United States). We also examined consensus reports from NATO's Human Factors and Medicine Panel. We search relevant government and agency websites responsible for national defense and Veterans. While we do not exclude content based on language, where information is not available in English, Chinese, French, Spanish, or Portuguese, we attempt to use site-specific translation functions or Google Translate. A full list of websites and organizations searched is available upon request.

Appendix 2: Key findings from included evidence syntheses and primary studies

Exposure type	Military occupational specialty	Key findings from highly relevant included documents

Blast	Breachers	*Symptoms*
		• One recent cross-sectional study found as compared to a control group made up of other Canadian Armed Forces members, military breachers with blast exposure (possibly exposed to a maximum of six blasts a week) had lower energy scores (p= 0.022), worse perceptions of functional musculoskeletal performance (p=0.016), greater concussive symptoms including somatic (p=0.004), cognitive (p=0.004), and emotional (p=0.001), and more attention and memory challenges (p=0.001) (1)
		  ○ Further, the study found that having a previous history of concussions was uniquely associated with musculoskeletal related functional disturbances (p<0.001), while deployment was associated with greater concussive scores (p<0.001), lower energy levels (p=0.006) and greater PTSD symptoms (p<0.001) (1)
		• One recent cross-sectional study found experienced breachers had significantly prolonged reaction time compared to controls (p=0.048) and significantly slower movement velocity compared to controls (p=0.039) (2)
		  ○ The study found no statistically significant results between breaching experience and vestibular scores or visual scores on a sensory organization test (2)
		  ○ Similarly, no significant differences were found for endpoint excursion, maximal excursion, or directional control, though both groups showed high rates of abnormal maximal excursion (2)
		• One recent cross-sectional study of 25 military personnel with lengths of service between 10 and 15 years found significant differences between ocular motor behaviours in blast exposed participants as compared to controls (3)
		  ○ The blast exposed group included breachers and 'gunners' (operators of high-calibre weapons)
		  ○ In particular, eye-tracking revealed slower eye movements, more frequent stopping points when following a target, and higher rates of variation (3)
		  ○ Poor oculomotor behaviour in the blast group also correlated with higher reported symptom severity on a concussion assessment questionnaire (3)
		
		Biomarkers/Brain imaging
		• One recent prospective cohort study of nine male grenade and/or breacher instructors without a history of concussion showed abnormal amyloid β accumulation at PET after injury when compared to the control participants (4)
		  ○ Four brain regions showed significant increased deposition, including inferomedial frontal lobe, precuneus, anterior cingulum, and superior parietal lobule (4)
		• One recent cross-sectional study of 20 U.S. special operations breachers (with at least four years of experience) identified differences in neuroimaging compared to controls with limited lifetime exposure to blasts, namely an association between blast exposure and an increased cortical thickness in the left rostral anterior cingulate cortex, which helps to modulate cognition and emotion (5)
		  ○ The study also notes that in the small sample the severity of post-traumatic stress disorder (PTSD) symptoms was not associated with cumulative blast exposure, neither was co-existing PTSD attributable for the cortical thickness, functional connectivity, or quality of life (6)
		• One recent cross-sectional study identified significant neurovascular injury in breachers (with a median 7 years of breaching experience and 10 years of blast exposure) compared to controls and noted elevated blood biomarkers of inflammation, extracellular matrix degradation, and blood-brain barrier disruption (myeloperoxidase, MMP-3, MMP-9, MMP-10, occludin, and syndecan-1), which have also been observed in preclinical blast models (blood-brain barrier degradation and MMP activation) and previous human studies with similar populations and exposures (increased MMP-9 and occludin) (7)

Exposure type	Military occupational specialty	Key findings from highly relevant included documents
		○ These biological occurrences were not directly linked to health outcomes, but findings from the self-reported symptoms in this study included increased post-concussive symptoms and decreased energy (7) • One older medium-quality evidence synthesis examining the health impacts of repetitive low-level blasts in military and police during a breacher training course found mixed results among included studies, with some studies reporting changes to cognition, brain biomarkers, and reported symptoms such as headaches but only in the acute/post-acute phase of exposure (8) ○ However, the synthesis found that included studies reported differences in health outcomes between students and instructors, suggesting the possibility of a cumulative effect (8) • One recent cross-sectional study found that low-level blast exposure was associated with higher levels of anti-glial fibrillary acid protein, immunoglobin M and immunoglobin B, as well as two antibodies (anti-glial fibrillary acid protein ad anti-pituitary immunoglobin M and G) compared to non-exposed controls (9) ○ The study notes that these are relatively new findings within the literature (9) • One recent longitudinal study found that repetitive sub-concussive blast exposure was related to decreases in white and grey matter in the anterior and posterior midcingulate cortex of military breachers (10) ○ These are relatively new findings and no detail was provided on the type and frequency of blast exposure (10) • One recent cross-sectional study found that experienced breachers with 400+ blast exposures over their career had statistically significant elevated concentrations of neuronal-derived extracellular vesicle tau and Neurobehavioural Symptom Inventory scores, compared to age-matched military and law enforcement controls (11)
	Artillerymen/'gunners'	• One recent cross-sectional study of 25 military personnel with lengths of service between 10 and 15 years found significant differences between ocular motor behaviours in blast exposed participants as compared to controls (3) ○ The blast exposed group included breachers and 'gunners' (operators of high-calibre weapons) ○ In particular, eye-tracking revealed slower eye movements, more frequent stopping points when following a target and higher rates of variation (3) ○ Poor oculomotor behaviour in the blast group also correlated with higher reported symptom severity on a concussion assessment questionnaire (3)
	Special Operations Force (SOF)	*Biomarkers/brain imaging* • One recent cross-sectional study of 18 U.S. Special Operations Forces found a dose-response relationship between neuroinflammation (in the cerebellum and medio temporal brain regions), reductions in cortical thickness, and volumetric brain tissue loss at higher Generalized Blast Exposure Value (a metric developed to quantify cumulative blast exposure over a military career) thresholds (12) ○ Specifically, reduced levels of cortical thickness were reported in the anterior temporal lobe regions (12)
	Unspecified (general blast exposure)	*Symptoms* • One older medium-quality evidence synthesis found statistically significant associations between combat-related blast exposure and post-concussive syndrome, but these all involve higher-level exposures than sub-concussive military occupational blast (13) • One recent cross-sectional study of 181,000 U.S. Marines in military occupational specialities with high-risk for recurrent overpressure (e.g., field artillery, such as cannoneers; infantry, such as machine gunners) found that recurrent occupational overpressure exposure heightens the risk of mild traumatic brain injury (mTBI) following blasts, indicating that there may be a priming effect following a single blast exposure in deployed settings (14) ○ Further, among marines that experienced a blast during exposure, those in high-risk occupations were 45% more likely than those in low-risk occupations to sustain a probable mTBI (14) ○ The findings were not delineated for specific occupations; the results include a variety of military occupational specialties, such as combat engineer, field artillery, infantry, and Special Forces, which can include the roles of breachers, mortarmen, cannoneers, and machine gunners, among others

Exposure type	Military occupational specialty	Key findings from highly relevant included documents

		• One recent cross-sectional study of life-time blast exposure on neuropsychological functioning of 282 U.S. military service members and Veterans with and without a history of traumatic brain injury (TBI) found no statistically significant differences in attention and working memory, processing speed, executive functioning, memory, or general cognition.(15)
		  o Occupations categorized as high-risk included field artillery, infantry, Special Forces, etc.
		  o The finding that blast exposure does not impact neurocognitive functioning diverges from previous literature, which has suggested that blast exposure is related to deficits in reaction time and attention (15)
		• One recent cross-sectional study of Canadian Armed Forces members and Royal Canadian Mounted Police found participants with a high-level of blast exposure (determined by the Generalized Blast Exposure Value (GBEV) tool) had poorer somatic and cognitive outcomes than those in the low-level blast exposure group, after controlling for age, sex, psychological trauma and blast exposure (16)
		  o Military occupational specialties were not specified for high- compared to low-exposure groups (based on GBEV scores)
		• A large recent cross-sectional study found individuals with lifetime blast exposure of greater than 200,000 GBEV units (generally representing heavy arms, inclusive of shoulder-fired weapons, artillery, small and large explosives) were significantly different than the low-blast exposure group (less than or equal to a score of 200,000; generally representing light arms or no weapon exposure), with the five highest ratios being change in taste/smell, numbness, sensitivity to noise, irritability, and vision problems; participants frequently using heavy arms compared to light arms had higher blast exposure values, as well as higher signals of hearing loss, tinnitus, and change in taste/smell (17)
		• One recent retrospective cohort study of 2.2 million active-duty service members from the U.S. found higher occupational risk (determined based on occupation and length of time) was significantly more likely to receive a TBI diagnosis, co-morbid TBI conditions such as cognitive challenges, headache, hearing problems, communication disorders, non-headache pain, and sleep disorders/symptoms (18)
		  o Occupational risk was associated with significantly greater risk of cognitive problems and communication disorders among early career and mid-career service members, strong association of hearing problems over time, and weakening associations of non-headache pain and sleep disorders overtime (18)
		  o Higher occupational risk and time in service were also associated with greater risk of post-concussive syndrome and tinnitus at early and mid-career and a weakening strength of association between occupational risk and fatigue and migraines over the course of a career (18)
		  o Careers with high-occupational risk include general armour and amphibious, artillery and gunnery, aviation ordnance, general combat engineering, general combat operations control, explosive ordnance disposal/underwater demolition team, expeditionary medical services, general infantry, infantry, gun crews, seamanship specialists, military training instructors, missile artillery operating crew, rocket artillery and special forces
		  o Careers with moderate-occupational risk include ammunition repair, artillery repair, counterintelligence, general armament maintenance, general law enforcement, independent duty hospital services, operational intelligence, security guards, and tracked vehicles
		• One recent retrospective cohort study of military personnel (active-duty U.S. Army or law enforcement personnel who had routinely conducted heavy-wall breaching, used a 0.50-calibre sniper rifle, and/or participated in hand-grenade-throwing exercises during their career to date) reported experiencing ear ringing, memory problems, and sleep problems (19)
		  o It should be noted that approximately 34% of the cohort reported having a prior concussion (19)
		• One recent retrospective cohort study of U.S. deployed marines (specific occupations were not reported) examined whether the mechanism through which injury occurred resulted in differences in the experience of sleep disturbances and found that the association was strongest among those that previously reported sleep challenges prior to deployment, followed by those with a history of blast exposure, those with depression, and those with impact-induced injury (20)

Exposure type	Military occupational specialty	Key findings from highly relevant included documents

		• One recent cross-sectional study found active service members and Veterans (no specific occupation was noted) with high lifetime blast exposure and low levels of PTSD had worse symptom scores (based on the Neurobehavioural Symptoms Index) (p=0.013) as compared to those with low lifetime blast exposure (15)
		  ○ The study also identified statistically significant differences in sleep disturbance (p=0.013) and cognitive concerns (p=0.028), but when accounting for PTSD many of these findings were no longer significant (15)
		• One older medium-quality evidence synthesis included three studies reporting on auditory and vestibular effects from low-level blast exposure, all of which found positive associations between blast exposure and hearing challenges (13)
		  ○ This evidence synthesis included one study of 573 deployed service members and found a dose-response relationship between blast exposure and hearing loss (13)
		• One recent cross-sectional study found PTSD has a significant influence on neurobehavioural symptom reporting and can overshadow the effects of blast exposure (15)
		  ○ When comparing high and low blast exposure among U.S. service members with high levels of PTSD few symptoms remained statistically significant, namely total neurobehavioural symptoms (p=0.011) (but no differences on individual measures) and cognitive concerns generally (p=0.027) (15)
		  ○ The study notes that the effects of blast exposure are most apparent when PTSD is minimal (15)
		Biomarkers/Brain imaging
		• A recent cross-sectional study described above used magnetoencephalography on Canadian Armed Forces members and Royal Canadian Mounted Police and reported disrupted neuronal activity in participants with a greater history of repetitive sub-concussions, including neuronal slowing in the right fronto-temporal lobes and sub-cortical regions and functional dysconnectivity in the posterior default mode network after controlling for concussion and traumatic stress history (16)
		• 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 these effects were not consistently replicated (18)
		• One recent cross-sectional study identified changes to blood-based proteins and lipid molecules among servicemen with at least a six-month history of testing and trialling heavy weapons as compared to their matched controls (21)
		  ○ Changes included significant elevation in the neurofilament light chain and elevated c-reactive protein levels, suggesting systematic inflammation more generally as well as clinically meaningful alterations to 23 lipid molecules (21)
		  ○ However, the direct connection of this biological phenomenon to blast exposure and clinically relevant symptoms was not identified (21)
		  ○ One recent longitudinal study identified decreases in volume loss, white matter changes, and enlarged Virchow Robin spaces in military men with repetitive overpressure blast exposure in military men during operation and training (22)
		• One recent retrospective cohort study of military personnel with prior low-level overpressure exposure but no diagnosed brain injury found greater levels of blood biomarkers associated with neurological damage (e.g., amyloid B-42 levels, UCH-L1, tau) than their age-matched controls who had no prior history of blast exposure (19)
		  ○ Participants consistent of male, active-duty U.S. Army or law enforcement personnel who had routinely conducted heavy-wall breaching, using a 0.50-calibre sniper rifle, and/or who participated in hand-grenade-throwing exercises during their career to date (19)

Impact		No findings identified
Acceleration-deceleration	Paratroopers	*Biomarkers/Brain imaging* • A recent cross-sectional study reported that paratroopers exhibit significantly slower reaction times in the alerting network compared to healthy controls (which may be explained by the reduced cue-N1 amplitudes in the alerting network that were measured in the sub-concussive group)

Exposure type	Military occupational specialty	Key findings from highly relevant included documents
		○ The study identified no significant reaction time differences for orienting or executive control networks despite the sub-concussive group having reduced target-P3 amplitudes in the executive control network, which suggests deficits in attentional resource allocation and inhibition control (23)
Recoil		No findings identified
Slamming	High-speed boat operators	No findings identified • Research on 'slamming' exposures did not meet inclusion criteria due to their focus on musculoskeletal and pain outcomes, rather than mTBI-like symptoms, and/or on higher severity exposures, rather than repetitive sub-concussive exposures ○ However, this has been identified as an important area for future research

Appendix 3: Details about each identified evidence synthesis

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Additional dimensions of exposure ▪ Intensity of exposures (psi) ▪ Time between exposures • Sensory effects of mTBIs ○ Blurred vision, saccadic dysfunction, and vestibulo-ocular reflex challenges • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems ○ Dizziness, loss of balance, or proprioception issues • Possible effect modifiers ○ Biological sex ▪ Male ○ Setting ▪ Training • Causality criteria ○ Temporal relationship (e.g., exposure must precede the occurrence of the outcome) ○ Consistency of evidence (e.g., similar or the same results generated by studies using different	A systematic review of 18 studies investigating the health impacts of repetitive low-level blasts in military and police training settings generally found inconsistent results among 10 health outcome domains (8) • This systematic review studied military and police training/exercise settings where trainers and students repeatedly participated in breaching, firing artillery, mortars, grenades, and shoulder-fired weapons ○ Studies that recruited participants based on positive mild traumatic brain injury (mTBI) status were excluded from this systematic review since the potential impacts of low-level exposures were of interest, not retrospective analysis of blast exposure and mTBI history ○ Included studies had variable blast exposure, including psi and days of exposure (ranging from one day to years) • Acute effects of blast exposure were observed in many health outcome domains, but persistence beyond acute exposure window was not found ○ It is difficult to know whether this is due to blast exposure measurement challenges or a true lack of correlation between repetitive low-level exposure and chronic health effects ○ Students had high blast exposure in an acute period, whereas instructors had lower levels of blast exposure but sustained over a long period of time ○ Different health outcomes between students and instructors were reported, suggesting there may be a cumulative health effect that cannot be detected after acute exposure ○ However, studies that longitudinally assessed breachers did not report blast effects on long-term health • The health outcome domains from the studies were summarized as biomarkers (blood/CSF), cognitive, hearing, brain imaging, motor, neurologic, sleep, symptom complaints, vestibular, and vision ○ Six of the 18 included studies measured blood-based biomarkers, including T-tau, NFL, GFAP, S-100B, CSF/serum albumin ratio, UCH-LI, TNF(alpha), IL-6, IL-10, APP, and SBDP150, but findings of these studies are mixed ▪ Many of the biomarkers were only measured in one of the studies, so validation of findings is difficult, and even when	High	No	5/9	2019	None	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
methods in different settings) o Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)	the same biomarker was investigated across studies, findings were mixed • For example, one study suggested that blast magnitude is connected to an increase in ubiquitin carboxy-terminal hydrolase-L1, and this biomarker elevation is related to increased postural sway and one cognitive measure; however, another study found no change in UCH-L1 from baseline in breachers during and after training ▪ It was suggested that biomarkers measuring peak pressure, rather than total exposure, may be important since effects were only found at peak individual times o Six studies measured cognitive domains of health, but with mixed results, so the findings from this evidence synthesis support previous concussion literature that measures may not be sensitive enough to demonstrate a change in neurocognitive effects from blast exposure o Five studies utilized brain imaging, suggesting that peak overpressure may affect brain activation during a working-memory task, but only in the acute/post-acute phase of exposure since persistent changes were not evident o 12 studies measured symptom complaints, with increased headaches being the most prevalent in the acute timeframe, but a lasting effect of blast exposure was not found for any symptom reporting o Three studies evaluated hearing, three studies evaluated vestibular effects, one studied motor effects, one investigated sleep, one evaluated neurologic health, and one studied vision • Difficulties quantifying low-level blast exposure and heterogeneity of the study designs made it challenging to draw conclusions o Heterogeneity in the study designs included variance in the duration of the evaluation period, the strength and duration of blast exposure, the level of protective equipment used, the assessment metric for exposure (e.g., yes/no for lifetime blast exposure, subjective estimate of number of lifetime exposures, objective assessment using blast gauges), the outcome measures, and the inclusion and exclusion criteria o Improvements to blast gauge sensors were highlighted as a priority area of improvement for future studies to use this objective data to establish correlations with health outcomes						

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
	○ Automated algorithms could help standardize blast metrics by minimizing confounding variables (e.g., orientation) ○ The CONQUER study by the U.S. Army Special Operations Command aims to prioritize blast gauge data collection to better quantify and understand repetitive low-level blast exposure • All included studies were identified to have a high risk of bias						
• Type of exposure ○ Blast ○ Non-blast ▪ 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) • Sensory effects of mTBIs • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems ○ Dizziness, loss of balance, or proprioception issues • Possible effect modifiers ○ Setting ▪ Training • Causality criteria ○ Dose-response relationship (e.g., evidence that increasing exposure increases the risk of the outcome) ○ Consistency of evidence (e.g., similar or the same	There is evidence to support that low-level blast exposure has the potential to harm military members, with the most well-supported adverse outcome being self-reported symptomology (e.g., headaches and trouble hearing); however, many limitations still exist within the available literature (24) • The scoping review aimed to provide a broad overview of the interdisciplinary nature of blast research • The review defines low-level blast exposure as a form of overpressure that is typically below the strength of intensity of a high-level blast exposure and can result from firing heavy calibre weapons • The review included approximately 20 studies on human exposure to low-level blasts, of which approximately 11 reported exclusively on active-duty personnel • Significant variation was noted in the LLB exposure with some articles examining the impact of weapons such as Howitzers, bazookas, grenades, light anti-tank weapons, M4 Carbine rifles and C4 • Training programs that examined the effects of these exposures ranged from one day to three weeks, with most falling within a two-week duration, with an average weekly exposure of 40 to 50 LLBs ○ However, it was noted that instructors likely experience hundreds of low-level blasts per year • Estimated or measured overpressure also varied with several studies reporting exposures below the four psi threshold while others reported that overpressure exceeded the threshold for at least one subject • Results of studies suggest that low-level blast has the potential to cause harm, specifically adverse outcomes for brain perturbation, including axonal disruption, changes in neuromotor functioning, and impairments in working memory	High	No	4/10	2021	No	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
results generated by studies using different methods in different settings) ○ Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)	○ However, findings related to the relationship between overpressure exposure and hearing loss, and overpressure exposure and the vestibular system functioning • Select studies suggest provided evidence of changes in biomarkers including UCH-L1, peripheral inflammatory makers and APP, but these effects were not consistently replicated • Numerous limitations were noted in the included studies including the reliance on observational studies, small included populations, variability in definitions of low-level blast, the intentional use of low exposure in training settings, and variability in the exposure of individuals within the same environment						
• Type of exposure ○ Blast ○ 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) • Sensory effects of mTBIs ○ Tinnitus • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems	Though the review suggests that some behavioural and emotional symptoms following blast-related exposure may be explained by co-existing post-traumatic stress disorder (PTSD) symptoms, the primary take away is the relatively little high quality evidence on the effects of low-level blast exposure, particularly that does not require loss or alteration of consciousness (13) • The review found no research on the overall frequency of low-level military occupational blast exposure or guidelines about what constitutes safe exposure in training or similar settings. • No human studies examined the effects of low-level military occupational blasts on motor effects, neurosensory effects, neuropathologic effects, or visual effects • Two human studies of repeated low-level military occupational blast exposure were included, neither of which found cognitive effects • Included studies – mainly cross-sectional – suggest that behavioural and emotions symptoms following blast-related TBI (with or without loss of consciousness) may be explained by co-existing PTSD and that blasts may increase PTSD symptoms • Three included studies also identified an association between blast exposure and sensorineural hearing loss and auditory and vestibular symptoms • The review did not identify any early detection biomarkers that can reliably be used in humans	High	No	4/9	2019	No	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ Dizziness, loss of balance, or proprioception issues ○ Mood changes ○ Depression ○ Anxiety • Possible effect modifiers ○ 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 • Causality criteria ○ Temporal relationship (e.g., exposure must precede the occurrence of the outcome) ○ Consistency of evidence (e.g., similar or the same results generated by studies using different methods in different settings) ○ Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)							

Appendix 4: Details about each identified single study

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations

• Type of exposure
  ○ Blast
    ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions)
• Possible effect modifiers
  ○ Biological sex
    ▪ Male
  ○ Setting
    ▪ Training
    ▪ Operations
• 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)
  ○ Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)
	Repetitive overpressure blast exposures in military men during operation and training was related to decreases in volume loss, white matter changes, and enlarged Virchow Robin (VR) spaces (22)
	• The purpose of this study was to examine brain MRI findings in military members in operation or training with multiple repeated sub-concussive blast overpressure exposures
	• Participants were excluded if they had any previous neurological issues
	• A total of 92 male military members with a mean age of 31 (range 23 to 52 years), and an average of 9 years of blast exposure
	• The frequency of blast exposures was not described
	• Statistically significant decreases in volume loss (OR 1.083, 95% CI 1.678–1.731), white matter changes (OR 0.754, 95% CI 0.442–1.284), and enlarged VR spaces (OR 0.754, 95% CI 0.442–1.284 (OR 0.775, 95% CI 0.513–1.171)
	  ○ It remains unclear if these findings indicate neurodegeneration and risk for chronic traumatic encephalopathy (CTE)
	  ○ The finding about volume loss will require the identification of biomarkers that support this result
	  ○ Enlarged VR spaces were observed mostly in the posterior quadrants of the brain
	• Screening prior to blast exposure was conducted to minimize the confounding effect of structural lesions and several participants were found to have vascular abnormalities (cavernomas and developmental venous abnormalities (DVAs)) which may have occurred from repetitive exposure, or may be indicative of sampling bias
	  ○ 26.9% of the sample was found to have DVAs, when this age group in the general public only has an incidence of 9.6%, so further research is needed to understand influential factors and risk for progression or rupture in the military population
	  ○ Pre-screening MRIs in military populations was recommended
	• Challenges with maintaining the sample size and continuity of scans over the longitudinal five-year study proved difficult, alongside the limitation of no control group in this study
	• Future longitudinal research should conduct neuropsychological assessments (cognitive symptoms) annually alongside the MRI
		High	Publication date: May 2024
			
			Jurisdiction studied: Canada
			
			Methods: Longitudinal
				• Occupation

• Type of exposure ○ Blast	Repetitive sub-concussive blast exposure in military breachers was related to decreases in white and grey matter in the anterior and posterior midcingulate cortex (10)	High	Publication date: December 2024	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) • 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) ○ Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)	• The purpose of this study was to explore the relationship between cortical volume and white matter integrity in Canadian Special Operations Forces breachers with long-term exposure to repetitive sub-concussive blasts • Sub-concussive exposures were defined as such because "a single exposure does not result in neurological symptoms," examples included recoil from large calibre weapons, blast exposure from explosives, and parachuting, but only breachers were studied in this instance ○ Blast exposures were described as repetitive overpressures and impulses, which put acceleration, deceleration, and rotational forces on the brain • Data was collected using an MRI machine at two timepoints: baseline and either a one of two year follow-up • Data was available for a total of 62 participants • No information was provided on participant characteristics (e.g., length of career) or the type and number of blast exposures ○ Time (follow-up after one or two years) was used as a proxy measure for blast exposure, since all participants were active service members ○ Exposure to other sub-concussive forces (e.g., parachuting, hand-to-hand combat, high calibre weapons) was not measured, but is likely in this population and may influence the reported findings • Significant decreases in grey and white matter volume were seen in between timepoints (baseline and follow-up) • The functional anisotropy of white matter showed both increases and decreases, suggesting different pathologies corresponding to reductions • Reductions in grey matter were mostly seen in the anterior and posterior midcingulate cortex, regions that are vulnerable to trauma as they are positioned between hemispheres • However, changes in grey matter volume and functional anisotropy were not significant after a period of exposure of only one year		Jurisdiction studied: Canada Methods: Longitudinal	
• Type of exposure ○ Blast • Sensory effects of mTBIs ○ Blurred vision, saccadic dysfunction, and vestibulo-ocular reflex challenges ○ Tinnitus • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems ○ Ongoing problems with speech	Higher occupational risk and time in service were significantly associated with greater risk of traumatic brain injury (TBI), comorbid conditions, behavioural diagnoses, and blast associated conditions (18) • Data was extracted on health outcomes for approximately 2.2 million active-duty service members who had been serving for up to 10 years; analyses were controlled for sex and branch of service ○ Service members across multiple branches of service were included (Army, Air Force, Navy, and Marine Corps) ○ Hazard ratios are calculated with 95% confidence intervals and p<0.001 was used to determine statistical significance • No information was included on type of exposure	High	Publication date: December 2021 Jurisdiction studied: United States Methods: Retrospective cohort study	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ Dizziness, loss of balance, or proprioception issues ○ Mood changes ○ Depression ○ Anxiety ○ Difficulty sleeping ○ Fatigue • Possible effect modifiers ○ Stage in a military career ▪ Early ▪ Mid • Causality criteria ○ 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)	• Blast exposure was approximated based on occupation and time in service; baseline (<1 year), early career (1–7 years), and mid-career (7–10 years) ○ Note that using occupation as a proxy measure for low-level blast exposure may lead to confounding low-level blast with other factors such as operational tempo (the setting and intensity of blasts taking place) • Participants were grouped based on low, moderate, or high risk of low-level blast exposure based in their military occupation ○ High risk: general armour and amphibious; artillery and gunnery; aviation ordnance; general combat engineering; general combat operations control; explosive ordnance disposal/Underwater Demolition Team; expeditionary medical services; general infantry; infantry, gun crews, seamanship specialists; military training instructor; missile artillery operating crew; rocket artillery; and special forces ○ Moderate risk: ammunition repair, artillery repair, counterintelligence, general armament maintenance, general law enforcement, independent duty hospital services, operational intelligence, security guards, and tracked vehicles ○ Low risk: everything else • Participants in high-risk occupations were significantly more likely to receive a TBI diagnosis (HR=1.26–1.58), and participants with less years in service were significantly less likely to receive a TBI diagnosis (HR=0.71–0.92) ○ The interaction of high-risk occupations and more years in service were significantly associated with increased diagnosis of any TBI, mild TBI, moderate TBI, and unclassified TBI ○ Higher occupational risk was associated with greater risk of any, mild, and moderate TBI in early career service members (HR=1.19–1.52), and even more so in mid-career service members (HR=1.28–1.61) • High occupational risk was significantly associated with comorbid TBI conditions including greater risk of altered mental status, cognitive problems, communication disorders, headache, and hearing problems (HR=1.04–1.47); interactions of high occupational risk and more years in service were significant for cognitive problems, communication disorders, headache, hearing problems, non-headache pain, and sleep disorders/symptoms (HR=1.00–1.06) ○ Occupational risk was additionally significantly associated with reduced risk of non-headache pain, sleep disorders/symptoms, and vision problems (HR=0.90–0.98)			

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
	○ Occupational risk was associated with significantly greater risk of cognitive problems and communication disorders among early career and mid-career services members, significantly greater risk of headaches among mid-career service members (although the risk was significantly lower at baseline), stronger associations with hearing problems over time, and weakening associations of lower risk of non-headache pain and sleep disorders/symptoms over time ○ These findings are consistent with previous literature • Higher occupational risk was significantly associated with greater risk of behavioural health conditions, anxiety disorders, alcohol abuse/dependence, delirium/dementia, and post-traumatic stress disorder (PTSD) (HR=1.04–1.60) ○ Occupational risk was significantly associated with greater risk of any behavioural condition, anxiety disorders, and drug abuse/dependence among early and mid-career service members (although it was associated with lower risk at baseline), and was additionally associated with significantly greater risk of alcohol abuse/dependence, delirium/dementia, and PTSD in early and mid-career • Higher occupational risk and time in service, and the interaction between them, were additionally significantly associated with greater risk of post-concussive syndrome and tinnitus ○ Occupational risk was associated with greater risk of post-concussive syndrome and tinnitus at early and mid-career, and a weakening strength of association between occupational risk and fatigue and migraines over a career (although occupational risk was associated with lower risk of these outcomes at baseline) ○ This is one of the most consistent findings in the literature of low-level blast exposure and subsequent health outcomes			
• 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) ○ Non-blast	Marines with high occupational risk for recurrent occupational overpressure exposure (ROPE) are significantly more likely to have a probable mild traumatic brain injury (mTBI) following a blast exposure than marines with low occupational risk for ROPE (14) • Examines whether ROPE is a risk factor for TBI following blast exposure using Post-Deployment Health Assessments (PDHA) from 181,423 U.S. Marines • ROPE is defined as a low-level overpressure that may result from firing heavy calibre weapons or breaching charges • High risk for overpressure exposure was defined as an above atmospheric pressure wave generated by explosive or weapons such as	High	Publication date: June 2020 Jurisdiction studied: United States Methods: Cross-sectional with a retrospective exposure assessment	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
▪ 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) ○ Additional dimensions of exposure ▪ Number of exposures • Possible effect modifiers ○ Setting ▪ Deployment • Causality criteria ○ 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)	explosives, rocket-propelled grenades, shoulder-fired rockets, 0.50 calibre weapons, mortars, artillery, and some breaching rounds • Service members who were identified as having high occupational risk for ROPE were involved in ammunition and explosive ordnance disposal, field artillery, infantry, and tank and assault amphibious vehicles • Blast exposure potentially leading to TBI was assessed on the PDHA as: a blast/explosion, a vehicular accident, fragment/bullet wound above the shoulders, fall, or other • OR and RR of occupational risk on ROPE and blast exposures was calculated with 95% confidence intervals and p<0.001 • Findings indicated that blast exposure and high occupational risk of ROPE were associated with increased risk of mTBI independently and when co-occurring, indicating that repeated low-level exposure increases risk of mTBI following a blast exposure • Marines with high occupational risk were significantly more likely to report blast exposures for bullet/fragment wounds (OR=2.56), blasts (OR=1.90), vehicle crashes (OR=1.80), and falls (OR=1.46), but were less likely to report “other” exposures • Probable mTBI was significantly associated with a reported blast exposure, even in models adjusted for all other deployment exposures (OR for each deployment exposure is included in the full text) • Marines with high occupational risk for ROPE were 1.23 times more likely to have a probable mTBI (OR=1.30), and marines with high occupational risk who reported a blast exposure were 1.45 times more likely to have a probable mTBI (OR=1.59) • Marines with high occupational risk were 1.25 times more likely to have a probable mTBI after blast exposure than those without blast exposures (OR=1.34); conversely, marines with low occupational risk were less likely to have a probable mTBI after blast exposure			
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ 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	Military and law enforcement personnel who were exposed to low-level overpressure (LLOP) but had been medically cleared for service had greater levels of blood biomarkers associated with neurological trauma than age-matched controls, and elevated levels of certain biomarkers were associated with ear ringing, memory problems, and time in service (19) • The study examines blood biomarkers of neurological trauma among individuals who have been exposed to LLOP and reported concussion-like symptoms, but have been cleared to return to duty • LLOP is defined as a shock wave from pressure above normal atmospheric levels	High	Publication date: April 2021 Jurisdiction studied: United States Methods: Retrospective cohort study	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
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) • Sensory effects of mTBIs ○ Tinnitus • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems ○ Difficulty sleeping • Possible effect modifiers ○ Stage in a military career ▪ Early ▪ Mid ▪ Late ○ Biological sex ▪ Male ○ Setting ▪ Training ○ Time to return to high-risk activities • Causality criteria ○ 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) ○ Biological plausibility and coherence (e.g., the association between the exposure and outcome should be	• The exposure to LLOP from breachers is approximately 4-5 psi monthly or annually, hand grades lead to exposure of 0.5 psi many times/week, and 0.50 calibre rifles lead to exposure of 4 psi • Participants were military and law enforcement personnel who were involved in heavy-wall breaching, used a 0.50-calibre rifle, and/or participated in hand-grenade-throwing exercises on a regular basis; 30 participants were compared to 30 healthy civilian controls, and the remaining 76 were included in analysis of associations between biomarkers and self-reported symptoms and medical history • Participants were actively in training and recruited from training sites • Statistical significance was set at $p \leq 0.05$ and models were adjusted for age • Results showed that multiple blood biomarkers of neurological trauma were elevated in military and law enforcement participants compared to age-matched controls, and was associated with greater length of service • Concussion-like symptoms reported by participants included ear ringing, deafness, memory problems, concentration problems, and sleeping problems, and 26 reported prior concussion • Increased levels of biomarkers including tau and Ab-42 were significantly associated with time in service • Increased Ab-42 was significantly associated with ear ringing and memory problems			

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
plausible and consistent with current knowledge)				
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Additional dimensions of exposure ▪ Number of exposures • Possible effect modifiers ○ Setting ▪ Deployment ▪ Operations • 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)	Low-level repetitive blast exposure was associated with higher levels of anti-glial fibrillary acid protein, immunoglobin M, and immunoglobin B, suggesting that they may be biomarkers of exposure (9) • This study compared the relationship between circulating antibody profiles and low-level repetitive blast exposures in military breachers versus controls with no blast exposure • This study recruited breachers with occupational exposure to low-level primary blasts from overpressure • It was not possible to quantify the amount of blast overpressure; however, breachers were exposed to 8-20 course/week and were exposed to a maximum of six blasts/day • Occupational specialty was used as a proxy for blast exposure • Autoantibodies (e.g., glial fibrillary acid protein, myelin basic protein, and pituitary antigens) are a biomarker of injury to the central nervous system and can provide insights on to mechanisms following injury • The type, intensity, and time between blast exposure was not specified • Participants were primarily male (one female in control and two in breachers), and no differences in sex were analyzed • On average breachers had at least one blast exposure but had similar concussion histories to controls, however the exact number of exposures was not reported • Breachers also had more years of service (13.2 vs. 6.6 in controls), deployments (11 vs. 0), and years of explosives (11.1 vs. 0.5) • Military breachers with blast exposure demonstrated higher levels of the following antibodies than controls: ○ Anti-glial fibrillary acid protein: breachers (9.39 [7.9–10.5] µg/mL) versus controls 5.31 [4.2–6.7] ○ Anti-pituitary immunoglobin M and G: breachers 2.17 [1.2–5.4] µg/mL versus controls 0.40 [0.19–3.6] ○ These findings were relatively new in the literature	High	Publication date: December 2024 Jurisdiction studied: United States Methods: Cross-sectional	• Occupation
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems • Possible effect modifiers	Military breachers with low-level primary blast exposures demonstrate lower energy levels and perceptions of functional abilities and greater post-concussive symptoms and PTSD symptoms than military controls without blast exposure (1) • This study compared the neuropsychological and neurocognitive profiles of military breachers with low-level blast primary exposures and military controls without blast exposure • Key demographic details of participants include:	High	Publication date: December 2020 Jurisdiction studied: Canada Methods: Cross-sectional	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ Setting ▪ Deployment • 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)	○ participants were primarily males (89%) aged 33 ○ military breachers had approximately 10 years of exposure to explosives and seven years of breaching ○ breachers and controls had similar amounts of concussion and physical impacts to head ○ participants in both groups were age and sex matched • The authors state that it was difficult to report specific details of blast overpressure as they were variable and dependant on geographical position, functional role, and other factors ○ Breachers working near blasts could be exposed to a maximum of six blasts a week ○ Certain military roles (e.g., range safety officers) typically work further from blasts, which may mean less exposure, but they can be exposed to more than six blasts a day • The following outcomes differed between breachers with blast exposure and controls: ○ Individuals with blast exposure had lower energy scores (50) than controls (65), p=0.022 ○ Individuals with blast exposure had worse perceptions of functional musculoskeletal performance (40) than controls (34), p=0.016 ○ Individuals with blast exposure showed greater concussive symptoms including somatic p=0.004, cognitive p=0.004, and emotional p<0.001 ○ Individuals with blast exposure showed more attention and memory challenges, compared to controls p<0.001 • Participants with blast exposure showed worse performance on tasks requiring cognitive-motor integration, suggesting that it is more profoundly impacted by blast exposure ○ The authors state that existing neurocognitive assessments do not capture this integration and that multifaceted and comprehensive measures are needed to understand the impacts of blast exposure • Concussion history was associated with greater concussive scores (p=0.002) and musculoskeletal-related functional disturbances (p<0.001) • Military deployment was associated with greater concussive scores (p<0.001), lower energy levels (p=0.006), and greater PTSD symptoms (p<0.001)			
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) • Cognitive and mental health effects of mTBIs	High blast exposure, as defined by greater scores on the Generalized Blast Exposure Value Tool, was related to worse cognitive and somatic symptoms in current and former serving members of the Canadian Armed Forces and Royal Canadian Mounted Police (16) • This study explored the relationship with blast exposure, neurobehavioral problems, mental health, and brain function in servicing and former	High	Publication date: October 2024 Jurisdiction studied: Canada	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ Memory or concentration problems • 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)	members of the Canadian Armed Forces and Royal Canadian Mounted Police • Participants were categorized into two groups, high vs low blast exposure, based on their scores on the Generalized Blast Exposure Value Tool ○ The questionnaire quantified blasts using five categories of blast type and severity (not described in this study) • Participants were excluded if they had history of moderate or severe traumatic brain injury • Groups were similar in the number of concussions (mTBIs) and mental health conditions • Participants in the high-level blast exposure group showed worse somatic and cognitive scores compared to participants in the low-level group ○ In this analysis, the authors controlled for age, sex, psychological trauma, and blast exposure • Participants with high blast exposure showed greater Delta activity in the frontal and right temporal lobes and right subcortical regions, indicating slower neural activity in these regions • Participants with high blast exposure showed greater functional disconnectivity in the default mode network • Neither finding from the brain imaging assessments were significant when accounting for concussion history		Methods: Cross-sectional	
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Non-blast ▪ Impact injuries (i.e., non-blast related collision between head and a stationary or moving object) ○ Additional dimensions of exposure ▪ Number of exposures • Possible effect modifiers ○ Biological sex ▪ Male ○ Setting ▪ Operations ○ Co-morbid PTSD or mental health conditions • Causality criteria	Higher blast exposure was associated with changes in brain structure – in particular, increased cortical thickness in the left rostral anterior cingulate cortex – decreased function, neuroimmune markers, and lower quality of life among active-duty United States Special Operations Forces (5) • The primary aim of this study was to examine the impact of repeated blast exposure on the cognitive performance, psychological health, physical symptoms, blood proteomics, and neuroimaging measures of 30 active-duty United States Special Operations Forces • Special Operations Forces had extensive combat experience and blast exposure in Iraq, Afghanistan, Syria, and Libya, with the Combat Exposure Scale indicating 'moderate-heavy' or 'heavy' exposure in 28 of the 30 participants ○ All 30 participants had exposure to extensive blast overpressure for at least 10 years ▪ Blast exposure was measured through an interview-based version of the Generalized Blast Exposure Value; the range for cumulative blast exposure was 387,861 to 363,812,869, with small arms being between 67,200 to 224,640, 270 to 1,260,000 for large arms, 240 to 16,200 for artillery or missiles carried by vehicle,	High	Publication date: May 2024 Jurisdiction studied: United States Methods: Cross-sectional study	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ 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)	aircraft, or boat, 648 to 2,550 for small explosives, and 11 to 180 for large explosives ▪ The Generalized Blast Exposure Value is unitless, representing cumulative blast exposure that is weighted to the average frequency of exposure to different types of weapons ○ Lifetime exposure to traumatic brain injury was obtained through an interview-based Brain Injury Screening Questionnaire ▪ 21 participants were categorized in the "high incidence" blunt head trauma group as they had more blows to the head than they could recall, while nine participants were in the "low incidence" as they had between one and 13 blows to the head ○ Cortical thickness was obtained through T1-weighted MRI scans • Increased blast exposure was associated with increased cortical thickness in the left rostral anterior cingulate cortex; a finding with a standardized regression coefficient (β) of 0.67 (95% CI 0.33–1.02) ○ This structural change in the brain can have impacts in emotion regulation and cognitive control • The findings from this study add to the growing body of evidence to suggest that repetitive blast brain injury is a pathophysiologic entity that is distinct from single blast-related mTBI			
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Additional dimensions of exposure ▪ Number of exposures • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems ○ Dizziness, loss of balance, or proprioception issues ○ Mood changes • Possible effect modifiers ○ Stage in a military career ▪ Late ○ Biological sex ▪ Male ○ Setting ▪ Training ▪ Operations	Experienced breachers with a minimum of four years of experience or a history of 400+ low-level blast exposures presented balance problems with postural limits of stability, but not with sensory control of balance (2) • The primary aim of this study was to investigate the long-term effects of repetitive low-level blast exposure on balance among 20 experienced active-duty military or civilian law enforcement breachers • Participants were assessed using the Sensory Organization Test and Limits of Stability tests, with the aid of a NeuroCom Smart Balance Master ○ Experienced breachers reported an average of 4,628 blast exposures, with 18 participants having experienced a blast exposure in the past 12 months ○ Experienced breachers reported higher levels of cognitive and mental health effects, such as memory problems, ringing in ears, issues with concentration, and irritability ○ The Sensory Organization Test assessed for balance by measuring a participant's ability to maintain a quiet stance under six sensory conditions in 20 seconds trials: 1) eyes open, no sway reference; 2) eyes closed, no sway reference; 3) eyes open, visual/surround sway reference; 4) eyes open, support surface sway reference; 5) eyes	High	Publication date: November 2021 Jurisdiction studied: United States Methods: Cross-sectional study	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations

• Causality criteria
  ○ Strength of association (e.g., association should meet statistical significance to demonstrate that it was not simply a chance occurrence)
	closed, support sway reference; and 6) eyes open, support surface and visual/surround sway reference
	  ○ The Limits of Stability test measured postural control as participants adjusted their centre of gravity in eight different directions while keeping their feet planted; the test also noted reaction time to start movements and balance/stability limits
	• When compared with the control group, experienced breachers undertaking the limits of stability tests exhibited reduced reaction time (p=0.048) and movement velocity (p=0.039)
	  ○ This delayed reaction time may be attributed to auditory and cognitive issues, including concentration or hearing issues, and ringing in the ears
	• This study found that while acute effects of blasts on sensory control of balance may fade away, the chronic effects of posture limits of stability continue to persist over time			

• Type of exposure
  ○ Blast
    ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions)
• Cognitive and mental health effects of mTBIs
  ○ Memory or concentration problems
  ○ Mood change
• Causality criteria
  ○ Temporal relationship (e.g., exposure must precede the occurrence of the outcome)
  ○ Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)
	Neuroinflammations, differences in brain structure, and thickness of the medial and temporal brain regions were found in special operators with low-level primary blast exposures, as measured by the Generalized Blast Exposure Value (12)
	• This study explored the relationship between neuroinflammation and prior low-level primary blast exposure in special operators
	• Participants' injuries were assessed using the head injury questionnaire inquiring about cause of injury, age of injury, loss of consciousness, amnesia related to event, changes in mood, or sleep problems
	• Blast exposure was categorizing using: 1) the Naval Medical research Centre Blast Exposure Threshold Survey which asks about weapons, explosives, injury history, auditory symptoms, vestibular symptoms, mood issues, sleep disturbances, and cognitive symptoms; 2) the Blast Exposure Count asking about experience with weapons and numbers of blast per day; and 3) the Generalized Blast Exposure Value, a mathematical equation accounting for blast exposure count and frequency
	• Participants also completed blood samples, radiotracer synthesis, PET, and MRI scans
	• Participants were primarily male with an average age of 41
	• Participants in the blast exposed group had on average 21 years of service and controls had 13; they also had more concussions
	• Participants with blast exposure showed neuroinflammation and alterations in cerebellum and medio temporal brain regions, as well as reductions in volume and thickness of brain structures
	• No significant associations were seen between Naval Medical research Centre Blast Exposure and General Blast Exposure Value
		High	Publication date: April 2024
			
			Jurisdiction studied: United States
			
			Methods: Cross-sectional study
				• Occupation

<table>
<tr><th>Dimension of organizing framework</th><th>Declarative title and key findings</th><th>Relevance rating</th><th>Study characteristics</th><th>Equity considerations</th></tr>
<tr><td></td><td>These findings are consistent with pre-clinical models and studies examining similar brain regions in Veterans with blast exposure</td><td></td><td></td><td></td></tr>
<tr><td>Type of exposure
Blast
Primary (i.e., resulting from high pressure or overpressure created by explosions)
Possible effect modifiers
Setting
Training
Operations
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)</td><td>Military breachers with repetitive low-level primary blast exposures may show differences in brain anatomy and functional connectivity; however, additional research is needed to confirm hypotheses (6)
This study explored the relationship between repetitive low-level primary blast exposure, behavioural differences, and neuroimaging differences in military breachers
Breachers were required to have four years of experience and be actively involved in training or operations
All breachers reported an average of 4,628 blast exposures and controls reported 0–35 exposures
Breachers showed greater cortical thickness in the occipital lobes
Differences in fractional anisotropy ($p<0.0026$) and radial diffusivity ($p<0.0019$) were observed between groups
Fractional anisotropy and radial diffusivity measure the integrity of white matter tracts in the brain through the restriction or direction of water diffusion in the brain
Breachers showed higher default mode network activity and controls showed higher resting activity, for both findings
The neuropsychological and blood measurement results were not presented in this study
This study has a small sample size (20 cases) but shows that breachers' exposure to blasts may be related to differences in brain anatomy and functioning; these findings highlight potential hypotheses for future research</td><td>High</td><td>Publication date: December 2020

Jurisdiction studied: United States

Methods: Cross-sectional study</td><td>Occupation</td></tr>
<tr><td>Type of exposure
Blast
Primary (i.e., resulting from high pressure or overpressure created by explosions)
Additional dimensions of exposure
Number of exposures
Time between exposures
Cognitive and mental health effects of mTBIs
Possible effect modifiers
Stage in a military career
Mid
Late</td><td>Repetitive sub-concussive blast exposure, as experienced by military breachers with four or more years of operational history, is associated with elevated neuronal-derived extracellular vesicle (EV) concentrations of tau and greater self-reported neurobehavioral symptoms (11)
The objective of the study is to determine the concentrations of various biomarkers in experienced military and law enforcement breachers, and their associations with any neurobehavioural symptoms, to understand the cumulative effect of repetitive sub-concussive blast exposures over a military career
20 experienced breachers, with a mean age of 39, and 14 matched military/law enforcement controls without blast exposure participated in the study
Experienced breachers were exposed to 400 or more breaching blasts during their career, ranging from 456–34,800 blasts reported, compared to</td><td>High</td><td>Publication date: September 2021

Jurisdiction studied: United States

Methods: Cross-sectional study</td><td>Occupation</td></tr>
</table>

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ Setting ▪ Training ▪ Operations • 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) ○ Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)	controls who also had four or more years of military/law enforcement experience, but had zero to 40 career blast exposures ○ Time since the last exposure ranged from within the past week to more than one year ago for experienced breachers • Additionally, experienced breachers reported higher PTSD-related symptoms • Of the serum and neuronal-derived EV biomarkers measured, only neuronal-derived EV concentrations of tau were significantly changed (elevated) in experienced breachers (0.3301 ± 0.5225) compared to controls (−0.4279 ± 0.7557; F=10.43, p=0.003) and this was associated with increased Neurobehavioral Symptom Inventory (NSI) scores in experienced breachers (r=0.596, p=0.015) ○ Non-significant changes were observed for all serum biomarkers (NF-L, tau, and Aβ42) and for the EV levels of NF-L and Aβ42			
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Non-blast ▪ Impact injuries (i.e., non-blast related collision between head and a stationary or moving object) • Cognitive and mental health effects of mTBIs ○ Depression ○ Anxiety ○ Difficulty sleeping • Possible effect modifiers ○ Co-morbid PTSD or mental health 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	Blast-related concussions and occupational low-level blast exposure significantly increase the risk of persistent sleep problems in deployed U.S. Marines, especially when combined with psychological conditions such as PTSD and depression (20) • The objective of the study was to examine the effects of blast-related and impact-related mTBI (concussion), as well as occupational low-level blast exposure, on the risk of persistent sleep problems in deployed U.S. Marines • The study analyzed a large cohort of 64,464 active-duty enlisted U.S. Marines deployed between 2008 and 2012 • Exposure was categorized into blast-related mTBI (concussion) from blast overpressure (mbTBI), impact-related mild traumatic brain injury (miTBI), and occupational risk of low-level blast exposure based on military job classification ○ No pounds per square inch (psi) blast pressure measurements or thresholds were reported; low-level blast exposure was defined solely by occupational risk, without specific quantification of blast intensity or number of exposures ○ Repetitive exposure was inferred from military occupational specialty risk classification, but exact frequency, duration, or cumulative dose of blast were not reported • The temporal relationship was established by collecting exposure data at the first time point (post-deployment) and outcome data on persistent sleep problems at the second time point (approximately six months later)	High	Publication date: January 2025 Jurisdiction studied: United States Methods: Retrospective cohort	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
demonstrate that it was not simply a chance occurrence)	• Logistic regression analyses included blast concussion, impact concussion, occupational blast risk, probable PTSD, probable depression, probable alcohol misuse, baseline sleep problems, sex, and military pay grade as predictors • Interaction effects between concussion types and psychological conditions were modeled, revealing significant synergistic effects on persistent sleep problems • Prior sleep problems at the first assessment were the strongest predictor of persistent sleep problems six months later • Blast-related concussion (mbTBI) was the second strongest predictor and was associated with a higher risk of persistent sleep problems compared to impact concussion (miTBI) • Marines with both blast concussion and probable PTSD or depression had the highest risk of ongoing sleep problems, indicating significant interaction effects • Occupational low-level blast exposure was independently associated with increased risk of persistent sleep problems, even after accounting for concussion history and psychological conditions • Psychological comorbidities (PTSD, depression, alcohol misuse) were all significantly linked to increased risk of persistent sleep problems • The causal criteria of temporal relationship and partial dose-response were met: exposure preceded outcome, and higher occupational blast risk correlated with increased symptoms, but precise dose or frequency data were lacking • Overall, the study provided evidence that repetitive low-level blast exposure and blast concussion contribute to persistent post-deployment sleep problems, especially when combined with psychological conditions, but objective measures and detailed exposure quantification were absent			

• Type of exposure
  ○ Blast
    ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions)
  ○ Additional dimensions of exposure
    ▪ Number of exposures
    ▪ Intensity of exposures (psi)
• Sensory effects of mTBIs
  ○ Blurred vision, saccadic dysfunction, and vestibulo-ocular reflex challenges
  ○ Sensitivity to light
	Service members and Veterans with high lifetime blast exposure were found to have worse NSI (post-concussion symptom) scores and some TBI-quality of life (TBI-QOL) metrics after controlling for PTSD using the Blast Exposure Threshold Survey (BETS) metric (15)
	• The BETS measure is a more comprehensive interview of lifetime blast exposure that classifies the relative level of blast exposure through five weapon categories, and for each category the exposure to these weapons is quantified by number of years, months per years, days per month, and rounds per day
	  ○ The weapon categories include shotguns, Gustav rifles, missile weapon systems, and breaching explosives, among many others
		High	Publication date: December 2023
			
			Jurisdiction studied: United States
			
			Methods: Cross-sectional study
				• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ Changes in ability to taste or smell • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems ○ Dizziness, loss of balance, or proprioception issues ○ Mood changes ○ Difficulty sleeping ○ Fatigue • Possible effect modifiers ○ Resilience ○ Co-morbid PTSD or mental health conditions • Causality criteria ○ Temporal relationship (e.g., exposure must precede the occurrence of the outcome) ○ 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)	○ A Generalized Blast Exposure Value (GBEV) is calculated using a weighted formula, with a higher value representing greater lifetime blast exposure over a person's lifetime ▪ This GBEV score alongside an alternative PTSD score were used to create subcategories of high and low lifetime blast exposure cross-matched with high and low PTSD symptom reporting • Results were determined to be statistically significant if p<0.05 and/or the effect size was at least medium (d=0.50 or higher) ○ Despite conducting multiple statistical comparisons, an adjusted p value was not used due to the small sample sizes • When comparing high PTSD groups (high and low lifetime blast exposure), no differences were observed on the neurobehavioural measures between the groups, but when comparing low PTSD groups (high and low lifetime blast exposure), the high lifetime blast exposure group had significantly worse NSI total scores (p=0.013, d=0.79) and TBI-QOL measures of sleep disturbance (p=0.013, d=0.78), sleep impairment (p=0.058, d=0.58), fatigue (p=0.069, d=0.56), general cognitive concerns (p=0.028, d=0.68), and social participation (p=0.071, d=0.55) ○ Specific NSI measures of significance in low PTSD/high lifetime blast exposure (compared to low PTSD/low lifetime blast exposure) include loss of balance, poor coordination, nausea, vision problems, sensitivity to light, hearing difficulty, change in taste and/or smell, poor concentration, forgetfulness, fatigue/loss of energy, difficulty falling/staying asleep, and irritability • A relationship between high lifetime blast exposure and worse neurobehavioural functioning may not be statistically significant once PTSD is accounted for, and a larger cumulative effect may exist when there is both PTSD and high lifetime blast exposure ○ The relationship between PTSD and lifetime blast exposure could potentially be explained by increased exposure to combat stressors, since a higher CES score (p<0.001, d=1.34) and greater number of deployments (p<0.001, d=0.88) were observed in the demographics of the high lifetime blast exposure group compared to the low lifetime blast exposure group • An mTBI diagnosis was needed for inclusion in this study, including mTBIs with loss of consciousness, alteration of consciousness only (uncomplicated mTBI), and questionable but likely alteration consciousness (probably mTBI)			
• Type of exposure ○ Blast	Contrary to past studies, there was no evidence to suggest that there was an impact of blast exposure on neurocognitive functioning in military service members and Veterans with and without a history of TBI (15)	High	Publication date: March 2024	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Non-blast ▪ Recoil injuries (i.e., injuries sustained as a result of backward force produced during the use of medium to large calibre shoulder fired weapons) • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems • Possible effect modifiers ○ Biological sex ▪ Male ▪ Female ○ Setting ▪ Training ▪ Deployment ▪ Operations • 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)	• This study assessed the impact of lifetime blast exposure (LBE) on neuropsychological functioning of 282 US military service members and Veterans with and without a history of TBI ○ Participants with a history of significant neurological or psychiatric condition(s) unrelated to the injury event or deployment were excluded • LBE was based on Military Occupational Speciality (MOS) and service members and Veterans self-report; eight MOS were identified as High Risk for blast exposure (i.e., duties that require a high frequency of direct use of heavy weapons or explosives as well as higher rates of deployments to combat zones) ○ Participants were also asked to recall the number of times they had been close to an explosion in which they felt the blast wave ○ Participants who reported they were never exposed to such a blast were categorized as Blast Naïve (n=61) and those who reported blast exposure were placed in either the Blast + High Risk MOS group (n=125) or the Blast + Low Risk MOS group (n=96) • TBI history was based on a medical record review and a structured interview; TBI severity was categorized as uncomplicated mTBI, complicated mild, moderate and severe TBI, penetrating TBI, and no TBI ○ Cognitive assessments of attention/working memory, processing speed, executive function, memory and general cognition were also performed • Overall, there was no evidence to suggest that there was an impact of blast exposure on neurocognitive functioning in military service members with and without a history of TBI • Participants in the Blast + High Risk MOS group had more blast exposures and combat exposure, were less likely to be women, were more likely to be white, and differed in terms of TBI severity ○ Although there was evidence of a relationship between blast exposure and some aspects of psychological functioning, after consideration of relevant covariates (e.g., education, race, years of service, and/or combat exposure), the effect was attenuated and no longer statistically significant • These findings diverge from past studies that have suggested that blast exposure may be related to reaction time and attention		Jurisdiction studied: United States Methods: Cross-sectional study	
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions)	Military special operators exposed to long-term low-level blasts or high-calibre weapons usage displayed impaired oculomotor behaviour suggestive of TBI, and displayed higher symptom severity on a concussion assessment questionnaire compared to control (3)	High	Publication date: May 2022 Jurisdiction studied: United States	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ Non-blast ▪ Recoil • Sensory effects of mTBIs ○ Blurred vision, saccadic dysfunction, and vestibulo-ocular reflex challenges ○ Sensitivity to light • Cognitive and mental health effects of mTBIs ○ Dizziness, loss of balance, or proprioception issues • Possible effect modifiers ○ Stage in a military career ○ Biological sex ▪ Male ○ Setting ▪ Operations ○ Nature of protective equipment available (including the consistency with which it is worn and whether it fits correctly) (e.g., helmet; mouthguard; hearing protection) • 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) ○ Consistency of evidence (e.g., similar or the same results generated by studies using different methods in different settings) ○ Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)	• The purpose of this study was to determine whether long-term operators of low-level blast exposure or high-calibre weapons use displayed oculomotor behaviours that differed from controls • Oculomotor (eye motion) behaviour is a sensitive biomarker for TBI, with the ability to differentiate the diagnosis severity • Oculomotor assessments contain different components which can collectively reveal neurological abnormalities through comprehensive smooth pursuit eye movement testing • 25 military personnel participants (all male, and members of elite military units with lengths of service between 10 and 15 years) were sorted into a blast exposure groups (breachers, n=9; and gunners, n=9) and a control group (n=7) • History of blast exposure was established based on job description of participant as long-term operator of low-level blast exposure or high-calibre weapons use • Psi measurements were not included to measure blast or recoil • All participants did not wear additional protective headgear beyond the standard helmet • This is the first study using oculomotor assessment with a military population • An eye-tracking test was administered to participants to assess oculomotor skills across several established parameters (circular smooth pursuit test), and participants completed a concussion assessment questionnaire (The Sport Concussion Assessment Tool 2) • Results revealed significant differences in most measured oculomotor behaviours between the blast exposure group and control group ○ The blast exposure group's eye movements were slower, stopped at more frequent points when following a target, travelled further from the target in terms of both speed and direction, and showed higher rates of variation and inefficiency • The significant differences in oculomotor behaviours observed in the blast exposure group relative to the control group suggest TBI symptomology consistent with prior research • Poor oculomotor behaviour in the blast group also correlated with a higher symptom severity on the concussion assessment questionnaire ○ Blast-exposed participants reported increase in specific symptoms such as balance problems; blurred vision; headaches, nausea, and light sensitivity; neck pain, falling asleep, and eye strain ○ The final model accurately predicted 84.6% of the TBI status, with a sensitivity of 94% and specificity of 63%		Methods: Cross-sectional study	

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
	• Authors mention the difficulty in controlling for blast exposure as a variable, because despite control group participants not being trained as breachers or gunners, most military personnel will have some exposure to blasts throughout their career			
• Type of exposure ○ Recoil injuries (i.e., injuries sustained as a result of backward force produced during the use of medium to large calibre shoulder fired weapons) • Sensory effects of mTBIs ○ Blurred vision, saccadic dysfunction, and vestibulo-ocular reflex challenges ○ Tinnitus • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems • Causality criteria ○ Temporal relationship (e.g., exposure must precede the occurrence of the outcome) ○ Consistency of evidence (e.g., similar or the same results generated by studies using different methods in different settings) ○ Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)	Occupational exposure to repeated blast exposure, without diagnosed TBI, can lead to concussive-like symptoms, memory dysfunction, and altered biochemistry (21) • The study aimed to assess servicemen with at least a six-month history of testing and trialling heavy weapons (150 mm gun) for concussion-like symptoms, memory function, and blood-based protein and lipid molecules • The study included 21 servicemen with no prior history of illness, TBI, or concussion, as well as age, education, and geographically matched individuals • Participants were asked to report symptoms using the Rivermead Post-Concussion Symptoms Questionnaire, used a clinical memory battery using the PGI Battery of Brain Dysfunction and collected venous blood samples for biomarkers • Participants in the study showed impaired memory function when compared to controls, noting in particular delayed recall and challenges with immediate recall and visual retention • While the majority of participants were noted to have had symptoms within the ‘normal’ range, about 30% of participants exhibited headaches and hearing difficulties, about a quarter had coordination issues and tinnitus and about 15% reported vision problems and poor concentration • Significant elevation was identified in the neurofilament light chain, indicating neuroaxonal injury and elevated c-reactive protein levels, suggesting systematic inflammation • 23 lipid molecules exhibited clinically meaningful alterations after applying a cut off • The findings are in line with similar studies that have been conducted in the Canadian and U.S. contexts using similar tools to assess symptoms and memory dysfunction	High	Publication date: January 2025 Jurisdiction studied: India Methods: Matched cross-sectional study	• Occupation
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Additional dimensions of exposure ▪ Number of exposures	Repeated low-level blast exposure among military breachers is associated with significant neurovascular injury, evidenced by elevated blood biomarkers of inflammation, extracellular matrix degradation, and blood–brain barrier disruption, along with increased self-reported post-concussive symptoms and reduced energy, indicating a heightened risk for long-term neurological impairment (9)	High	Publication date: February 2025 Jurisdiction studied: Canada Methods: Cross-sectional study	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
▪ Time between exposures • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems ○ Mood changes ○ Difficulty sleeping ○ Fatigue • Possible effect modifiers ○ Stage in a military career ▪ Early ▪ Mid ▪ Late ○ Biological sex ▪ Male ○ Setting ▪ Training ○ 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) ○ Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)	• The study compared 18 blast-exposed military breachers to 19 unexposed matched controls, using self-reported exposure history, neuropsychological and blood-based biomarker to evaluate the impact of long-term repetitive low-level blast exposure on neurovascular health and post-concussive symptoms ○ The study defines repetitive low-level blast exposure as routine, occupational exposure to explosive breaching, with >6 blast events/day, one to two days per week, across seven to 10 years of breaching experience • Exposure was determined through self-reported military service history, including years of breaching (median: seven years) and blast exposure (median: 10 years). Blast exposure was universal among breachers (100%) versus 10.5% among controls (Cohen's D=6.3, p<0.001) • Plasma levels of myeloperoxidase were significantly elevated in breachers (median: 72.5 ng/mL) compared to controls (47.2 ng/mL, p < 0.01) • Matrix metalloproteinases (MMP)-3 (median: 19,402 vs. 13,718 pg/mL, p < 0.01), MMP-9 (27,781 vs. 16,694 pg/mL, p < 0.001), and MMP-10 (2431 vs. 1593 pg/mL, p < 0.01) were also higher; consequently, authors suggest it may indicate inflammatory and extracellular matrix-degrading activity • Breachers had elevated levels of occludin and syndecan-1; occludin was significantly higher (p < 0.05), and syndecan-1 was markedly elevated (p < 0.001); consistent with blood-brain barrier tight junction damage and endothelial glycocalyx degradation • The two groups were matched by age (median=32 years) and sex (89.5% male). However, breachers had longer military service (median=11.3 years vs. 5.0; Cohen's D=1.6, p < 0.001) and greater combat deployment (64.7% vs. 0%; Cohen's D=2.9, p < 0.001) • Several outcome differences met statistical significance with false discovery rate correction at p<0.05; biomarkers (e.g., MMP-9, p<0.001), symptom scores (p < 0.001) and exposure history (e.g., blast exposure, p<0.001) showed large effect sizes (Cohen's D>1.5) • The findings are biologically plausible, consistent with preclinical blast models showing blood brain barrier degradation via oxidative stress and MMP activation; the study aligns with prior human studies showing elevated MMP-9 and occludin in similarly exposed military cohorts • Although the study is cross-sectional, the exposure clearly preceded symptom and biomarker collection, and participants had no recent blast exposure within 48 hours, reducing short-term confounding			

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations

• Type of exposure
  ○ Blast
    ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions)
• Cognitive and mental health effects of mTBIs
  ○ Other – change in pathologic markers in the brain
• Possible effect modifiers
  ○ Biological sex
    ▪ Male
  ○ Setting
    ▪ Training
• Causality criteria
  ○ Temporal relationship (e.g., exposure must precede the occurrence of the outcome)
  ○ 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)
	Early brain amyloid β accumulation was identified in healthy military grenade and/or breacher instructors exposed to repeated sub-concussive blast events compared to individuals who were not exposed to blasts (4)
	• This study aimed to quantify early amyloid β accumulation in military personnel exposed to repeated blast events
	  ○ Note: Amyloid accumulation is the pathologic marker of Alzheimer's disease (AD), and head trauma is a known risk factor of AD
	• Study participants included nine male grenade and/or breacher instructors (median age, 33 years) at a U.S. military base routinely exposed to repeated blasts during their training duties; instructors' roles consisted of training recruits in the use of explosives, breaching charges, hand grenades, or other mechanical methods to force open doors and secure buildings during operations
	  ○ Participants with a history of concussions were excluded
	  ○ Control participants were nine age-matched civilians without a history of brain injury
	• Between January 2020 and December 2021, the 18 participants were evaluated at two points with visit 1 occurring before blast exposure from training and visit 2 occurring after blast exposure, approximately five months after visit 1
	  ○ The military instructors were required to keep a digital log of the number of breacher or demolition events and the total number of blasts
	  ○ PET examinations were also performed at visit 1 (baseline) and visit 2
	• The nine grenade and/or breacher instructors exposed to repeated blast episodes showed abnormal amyloid β accumulation at PET after injury when compared to the control participants; four of the six regions of the brain had increased amyloid deposition in the early phase after the blast events
	• Neither a statistically significant correlation nor a relationship between the reported number of blast events and the degree of amyloid accumulation could be identified
		High	Publication date: May 2023
			
			Jurisdiction studied: United States
			
			Methods: Prospective cohort study
				• Occupation

• Type of exposure
  ○ Non-blast
    ▪ Acceleration injuries (i.e., non-blast injuries resulting from the brain being suddenly forced to speed up and slow down within the skull)
  ○ Additional dimensions of exposure
    ▪ Number of exposures
	The results demonstrate that paratroopers exposed to repetitive sub-concussive impacts exhibit significant impairments in the alerting and executive control components of the attention network (23)
	• The study investigates repetitive sub-concussive exposure in military paratroopers, defined as mild brain impacts that do not meet clinical criteria for concussion or mTBI but involve mechanical forces transferred to the brain
		High	Publication date: November 2021
			
			Jurisdiction studied: Wuhan, China
			
			Methods: Cross-sectional study
				• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
▪ Time between exposures • Possible effect modifiers ○ Setting ▪ Training • 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)	• Exposure occurs through repetitive parachuting training and jumps, especially during the landing phase where deceleration forces transmit impact to the brain along the body axis and spine • Paratroopers completed at least six simulated parachuting trainings and a minimum of 500 platform jumps, with an average of 6.3 parachuting jumps • Exposure was determined retrospectively based on military training records and self-reporting of the number of jumps; no direct measurement tools such as accelerometers or blast gauges were used • No baseline pre-exposure data was collected; all testing was conducted at one point after exposure, with the time since last parachute jump averaging approximately 7.7 months • Outcomes focused on cognitive attention function, assessed behaviorally via the Attention Network Test (ANT) and neurophysiologically via event-related potentials (ERPs) recorded by EEG • Paratroopers showed significantly slower reaction times in the alerting network (both no-cue and double-cue conditions) compared to healthy controls; no significant reaction time differences were observed for orienting or executive control networks • ERP results revealed reduced cue-N1 amplitudes in the alerting network for the sub-concussion group during the double-cue condition, particularly at occipital electrode sites, indicating impaired ability to use cues efficiently and maintain alertness • No significant differences in cue-N1 amplitude or target-N1 amplitude were found between groups in the orienting network • The sub-concussion group exhibited reduced target-P3 amplitudes in the executive control network, especially for congruent target conditions, suggesting deficits in attentional resource allocation and inhibition control • Findings differ from mTBI studies likely due to milder injury severity and different injury mechanisms (acceleration-deceleration vs. direct impact)			
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Additional dimensions of exposure ▪ Number of exposures ▪ Time between exposures • Sensory effects of mTBIs	A generalized blast exposure estimator was created from military service member survey results and revealed differences in post-concussive syndrome-like symptoms between those with blast exposure values above and below a given threshold (17) • The purpose of this study was to utilize survey results about military service member lifetime blast exposure and behavioural health to develop and calculate a generalized blast exposure value that can be used to track ongoing exposure and identify those at risk for blast-related outcomes such as post-concussive syndrome-like symptoms	High	Publication date: May 2021 Jurisdiction studied: United States Methods: Cross-sectional study	• Occupation • Gender

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ 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 ○ Dizziness, loss of balance, or proprioception issues ○ Mood changes ○ Difficulty sleeping ○ Fatigue • Possible effect modifiers ○ Stage in a military career ○ Co-morbid PTSD or mental health conditions • Causality criteria ○ Temporal relationship (e.g., exposure must precede the occurrence of the outcome)	• The online self-reported survey contained demographics, blast exposure, health, behaviour (modified NSI), and stress (modified Four-Item abbreviated Post-Traumatic Stress Disorder Checklist) • Participants (n=984) were 88.3% male, 11.6% female, and 0.1% other with an average age of 36.6 years • Five weapons/explosives exposure categories were created: small arms, large arms (including shoulder-fired), artillery (or large weapons carried by vehicle), small explosives, and large explosives • Blast exposure tracking in the survey included questions about years over a lifetime, months per year, days per month, rounds or explosions per day, and frequency of back-to-back days of exposure • There was no definite blast exposure outcome and no measurement of pressure or blast or recoil ○ Authors instead created a composite of the strongest signals to predict from blast experience ○ This signal complex roughly representing outcomes of hearing loss, tinnitus, and change in taste/smell, was higher in heavy arms than light arms participants • The GBEV was created from a subset of exposure variables to represent the units of blast exposure over a lifetime and compare individuals with different levels of exposure in common GBEV units ○ GBEV, estimating weapons and explosives exposure, was also higher in heavy arms participants than for light arms • The general outcome threshold was determined to be 200,000 GBEV units ○ Participants with GBEV <200,000 (n=561) were compared with GBEV ≥200,000 (n=423) and all NSI symptoms were significantly different ○ The five highest ratios were change in taste/smell, numbness, sensitivity to noise, irritability, and vision problems			
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Additional dimensions of exposure ▪ Number of exposures ▪ Intensity of exposures ▪ Time between exposures • Sensory effects of mTBIs ○ Blurred vision, saccadic dysfunction, and vestibulo-ocular reflex challenges	Research indicates that measures of cumulative blast impulse have a predictive relationship to changes in neurobehavioral symptoms, and results further suggest that breaching instructors and former professional breachers display greater risk of persistent post-concussive symptoms than trainees (25) • Relationships between blast exposure and symptoms were first evaluated in mice and then tested in a military training environment • In the military training environment, 23 trainees enrolled in a six-week explosive breaching training course, 13 instructors, and ten service member controls without blast exposure participated in the study (n=46 total) • All participants provided weekly NSI surveys	Medium	Publication date: August 2024 Jurisdiction studied: United States Methods: Pre- and post-test	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ Sensitivity to light ○ Tinnitus ○ Changes in ability to taste or smell • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems ○ Dizziness, loss of balance, or proprioception issues ○ Mood changes ○ Difficulty sleeping ○ Fatigue • Possible effect modifiers ○ Stage in a military career ○ Setting ▪ Training ○ Co-morbid PTSD or mental health 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)	• Low-level blast measures were collected from trainees and instructors using Generation 7 Blast Gauges (BlackBox Biometrics) placed on the non-firing shoulder, the chest of the body armour, and the rear of the helmet • Blast exposure measurements for each participant included: peak blast overpressure (psi), impulse (psi times miliseconds), total number of blasts, time in low-level blast occupation, time in service • Repetitive blast exposure was found to induce lasting neurobehavioral change in mice and suggested that subjects with the highest exposure are at greatest risk • The mean number of blast exposures among trainees was 115.6 exposures (range 1–230), with mean peak pressure 1.256 (range 1.02–5.33) psi and mean impulse 1.406 (range 0.58–28.43) psi times miliseconds, as recorded by B3 Blast gauges • Flash bang grenades and single strand detonation cord door-breaching charges accounted for 63 (40.2%) and 109 (59.8%) events over 5 days of recorded charge counts • Cumulative blast impulse was found to predict changes in NSI score, with the most notable changes occurring during the most intense period of blast exposure • Breaching instructors had elevated baseline and post-training NSI scores for multiple persistent post-concussive symptoms including headaches, hearing difficulty, numbness or tingling, poor concentration, forgetfulness, slowed thinking, difficulty sleeping, and irritability • Authors cite a recent cross-sectional study suggesting that higher instructor scores for these persistent post-concussive symptoms may relate to either or both an aggravation of previous injuries or a loss of resiliency to the effects of blast exposure			
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Additional dimensions of exposure ▪ Number of exposures ▪ Intensity of exposures (psi) • Sensory effects of mTBIs ○ Tinnitus • Possible effect modifiers ○ Setting	While repeated occupational exposure to low-level blast among Canadian Armed Forces breachers was not significantly associated with measurable hearing loss, balance deficits, or ataxia compared to matched controls, it was significantly associated with a higher prevalence of self-reported tinnitus, and a notable proportion of blast events exceeded the recommended safety threshold of 3 psi (26) • The study compared 19 Canadian Armed Forces breaching instructors and range staff (exposed group) to 19 age- and sex-matched Canadian Armed Forces personnel with no breaching experience (control group), using a combination of blast overpressure measurements (via body-worn blast gauges recording peak overpressure during live breaching courses), standardized balance and ataxia tests, pure-tone audiometry for hearing	Medium	Publication date: January 2021 Jurisdiction studied: Canada Methods: Cross-sectional study	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
▪ Training ○ Nature of protective equipment available (including the consistency with which it is worn and whether it fits correctly) (e.g., helmet; mouthguard; hearing protection) ○ 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) ○ Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)	thresholds, and a self-reported health questionnaire to assess recent blast exposure, hearing history, and tinnitus symptoms ○ The study defines low-level blast as controlled, sub-concussive blast exposures (typically <4 psi) that occur during routine military training, particularly breaching exercises; repetitive exposure refers to long-term occupational exposure experienced by breaching instructors and range staff over months or years • For instructors, up to 32% of blast events exceeded the 3 psi threshold, with maximum recorded overpressure of 4.9 psi; for regular staff, fewer exposures exceeded 3 psi; maximum recorded pressure was 4.1 psi • There was no significant difference in measured hearing thresholds between breachers and controls; only four breachers (21%) met the hearing loss criteria (≥25 dB HL), and one control participant met the same threshold • Significantly more breachers (12 of 19) reported tinnitus compared to controls (4 of 19), with p=0.009; all breachers with hearing loss also reported tinnitus, and tinnitus was positively associated with years of military service (p=0.011), suggesting cumulative exposure effects • No statistically significant difference was found between groups on Sharpened Rombergor Walking on Floor Eyes Closed tests; however, both groups scored below normative civilian populations, indicating possible undetected vestibular effects • Some breachers had very recent exposure (e.g., within 24–72 hours), but the cross-sectional design limits definitive temporal or causal inferences • The findings, particularly tinnitus in the absence of measurable hearing loss, are consistent with other studies suggesting "hidden hearing loss" (e.g., cochlear synaptopathy) in blast-exposed populations • Most breachers used low-profile electronic earmuffs, which likely mitigated hearing damage; however, consistency and effectiveness of use were not systematically evaluated, limiting interpretation • Authors report that the small sample size (n=19 per group) limited the ability to draw strong causal conclusions			
• Type of exposure ○ Blast ○ Non-blast ▪ Recoil injuries (i.e., injuries sustained as a result of backward force produced during the use of medium to large calibre shoulder fired weapons)	Lifetime blast exposure has a negative impact on recovery from a TBI, with those reporting lifetime blast exposure (even when low, between one and nine) having almost twice as many affective, vestibular, cognitive, and somatic symptoms as well as greater symptoms of post-traumatic stress and lower quality of life (27) • The objective of the study was to examine the relationship between lifetime blast exposure and recovery from TBI	Medium	Publication date: March 2024 Jurisdiction studied: United States Methods: Cross-sectional	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ Additional dimension of exposures ▪ Number of exposures ▪ Intensity of exposures ▪ Time between exposures • Sensory effects of mTBIs ○ Blurred vision, saccadic dysfunction, and vestibulo-ocular reflex challenges ○ Sensitivity to light ○ Tinnitus • Cognitive ad mental health effects of mTBIs ○ Memory or concentration problems ○ Dizziness, loss of balance, or proprioception issues ○ Mood changes ○ Depression ○ Anxiety • Possible effect modifiers ○ Time to return to high-risk activities • Causality criteria ○ 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)	• Participants included 558 service members and Veterans and to participate individuals had to have experienced at least one TBI • Tools used in the study include the neurobehavioural symptom inventory, PTSD checklist (civilian version), and TBI quality of life survey • The average age of participant was 34.8 years with the majority of the sample being white (75%) men (92%) who had a history of no greater than one uncomplicated mild injury severity TBI ○ Though 20% of the sample had a history of either complicated mTBI or greater severity • On average participants were 80.6 months from their most recent injury • On average the participants had experienced 79.4 blasts in their lifetime but there was considerable variability (0–7,500) ○ Given high variability, the participants were separated into three groups: blast naïve (with no lifetime blast exposure), low blast exposure (1-9) and high blast exposure (10–1,256) • The study reported a small but statistically significant relationship between median lifetime blast exposure and total neurobehavioural symptom inventory scores (rho=0.188, $p<0.001$), while cluster scores revealed similar small effects on somatic, cognitive and affective symptoms, though a less pronounced relationship with vestibular symptoms was noted • The study found that the blast naïve group reported significant fewer neurobehavioral symptoms than both the low lifetime blast exposure and high lifetime blast exposure group, though the low and high groups did not differ • Further, the high lifetime blast exposure group was found to be more likely to have atypical symptoms on the neurobehavioural symptom index than the blast naïve group (OR 1.87, 95% CI 1.17–2.97), though the low lifetime blast exposure group was not found to be at greater risk • Similarly, for TBI quality of life, significantly worse scores were reported on 10 of 14 scales for the low lifetime blast exposure and high lifetime blast exposure groups than the blast naïve group ○ These scales included measures of anger, anxiety, emotional and behavioural dyscontrol, resilience, fatigue, headaches, pain interference, cognitive complaints-executive function and cognitive complaints generally			
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Additional dimensions of exposure	Altered neuromotor performance was observed among active-duty military personnel six hours after sub-concussive blast exposure, followed by a return to similar to baseline levels at 72 hours, two weeks, and the three-month mark post-tests (28) • The primary aim of this study was to examine the short- and long-term effects of repeated sub-concussive blast exposure from heavy weapons	Medium	Publication date: November 2024 Jurisdiction studied: United States	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
▪ Intensity of exposures (psi) • Possible effect modifiers ○ Setting ▪ Training • 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)	training on neuromotor performance among 214 active-duty military personnel ○ Of the 214 participants assessed, 137 had a history of repeated sub-concussive blasts, while 77 were part of the control group ○ Heavy weapons training included firing Carl Gustave recoilless refiles, light anti-armour weapons, and AT-4 anti-tank rockets • Participants were classified as exposed if they received blast exposure greater than or equal to 4 pounds per square inch (psi), which was measured through a wearable pressure sensor • Participants were assessed as they completed a stepping-in-place task while a smartphone app (AccWalker) recorded their movement kinematics at 100.84 Hz ○ The task included facing straight ahead with their eyes closed and stepping in place for 60 seconds; participants were instructed to synchronize their step to the app's metronome, which sounded for the first 10 seconds and then was turned off ○ Neuromotor performance was assessed by examining the thigh flexion angle • The effects of repeated sub-concussive blast exposure from heavy weapons training were observed to be acute and short-lived in nature ○ Measured symptoms returned to baseline in later follow-ups		Methods: Observational, longitudinal study	
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) • Possible effect modifiers ○ Stage in a military career ▪ Early ▪ Mid ▪ Late ○ Setting ▪ Training • Causality criteria ○ Strength of association (e.g., association should meet statistical significance to demonstrate that it was not simply a chance occurrence)	Canadian Special Operations service members (snipers and breachers) exposed to repetitive head injuries from training-related blast overpressure were older, self-reported more severe symptoms, and were associated with lower scores on the vestibular/ocular motor screening test than the healthy control group (29) • The cross-sectional study compared Canadian Special Operations Forces exposed to repetitive head injuries and health controls without blast-related exposure using vestibular/ocular motor screening (for headache, dizziness, nausea, and fogginess) and computerized eye-tracking system ○ The included population groups were breachers (n=9) and snipers (n=9), and healthy controls (n=7) ○ The type of exposure included training-related blast overpressure in the last 60 days ○ They included individuals who self-reported symptoms consistent with mTBI ○ They excluded those with any significant neurological, musculoskeletal, or mental health diagnoses, restricted range of motion, current severe vestibular symptoms with movement, and/or corrected visual acuity worse than 20/40	Medium	Publication date: December 2024 Jurisdiction studied: Canada Methods: Cross-sectional study	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
	○ The definition of the exposure and pressure measurements were not described in the study, in addition to no demographic information besides age • The authors reported significant group differences among snipers, breachers, and healthy controls in age (p= 0.01) and participant-reported total symptom severity (p=0.03) when they conducted an ANOVA analysis • Overall, the authors concluded that breachers and snipers who were older reported more severe symptoms and overall scored worse in their tests than healthy controls • The authors found that snipers performed better on the eye-tracking test and had higher vestibular/ocular motor screening scores than breachers, which they found to be surprising and suggested further research with a larger sample • The study had several limitations, including their inclusion criteria (i.e., did not define repetitive head injuries and quantifying the amount) and small sample size			
• 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) • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems ○ Depression • Possible effect modifiers ○ Setting ▪ Training ○ Co-morbid PTSD or mental health 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	Veterans with mTBI from blast exposure demonstrated slower cognitive processing, when controlling for PTSD and depression, than those with sub-concussive injuries and controls (30) • This study compared the effects of chronic blast related mild traumatic brain injuries and sub-concussive blast exposure on neuropsychological performance in Veterans • Participants were excluded from this study if they had a substance dependence disorder • Neuropsychological functioning was assessed using the National Institutes of Health Toolbox Cognition battery, specifically domains regarding intelligence, processing speed, executive function, attention, response inhibition, and working memory • The severity of blast exposures was assessed using the Quantification of Cumulative Blast Exposure • Combat blasts were categorized using the following diagnostic criteria: loss of consciousness, memory loss, confusion, or debris contact • Blasts were inconsistently reported, so the authors opted to organize the analysis by presence/absence of blast exposure • All participants were exposed to a non-combat blast exposure during their training • Veterans were primarily male, with an average age of 44 (25 to 62 years) • Veterans with blast mTBI showed greater PTSD symptom severity than those without (p=0.0005) and slower processing speed (0.016)	Medium	Publication date: June 2021 Jurisdiction studied: United States Methods: Cross-sectional	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
demonstrate that it was not simply a chance occurrence)	○ This difference did not persist when accounting for combat exposure as a covariate • No differences were found for PTSD symptom severity in the sub-concussive and control group (0.315) nor for processing speed (p=0.076) • Veterans with mTBI showed higher levels of combat exposure when compared to the sub-concussive and control group (p<0.001) • A difference between all three groups (mTBI, sub-concussive, and controls) in processing speed existed even when controlling for PTSD, depression, and prior injury (p=0.008), with Veterans with mTBI showing slower processing speeds			
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Additional dimensions of exposure ▪ Number of exposures ▪ Intensity of exposures (psi) • Sensory effects of mTBIs ○ Tinnitus • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems ○ Dizziness, loss of balance, or proprioception issues ○ Mood changes ○ Anxiety ○ Difficulty sleeping • Possible effect modifiers ○ Biological sex ▪ Male ○ Setting ▪ Training ○ Nature of protective equipment available (including the consistency with which it is worn and whether it fits correctly) • Causality criteria ○ Temporal relationship (e.g., exposure must precede the occurrence of the outcome)	DNA methylation, connected to symptoms of tinnitus and sleep changes, may capture cumulative lifetime blast exposure in military breacher trainees and instructors (31) • Significant changes to differentially methylated regions (DMRs) may be connected to self-reported symptoms of tinnitus (KCNE1 and CYP2E1) and changes to sleep duration (PAX8) in breachers with high exposure (40+ lifetime blasts) compared to low exposure (<40 lifetime blasts) ○ In other military and animal studies, KCNE1 and CYP2E1 genes have been associated with noise-related hearing loss ○ PAX8 has previously been associated with thyroid development and most recently with changes to sleep duration, and sleep dysregulation was a commonly reported symptom self-reported in this study ▪ However, the authors noted that abnormal sleep patterns may precede DNA methylation since this is a common symptom reported by most military service members • Significant changes to gene expression and inflammation cytokine changes were observed after acute exposure ○ At baseline, significant gene expression or inflammatory cytokine changes were not observed, supporting the authors' claim that gene expression changes are associated with acute exposure not cumulative lifetime exposure • Headaches, irritation, anxiety, dizziness, slow or long thinking, trouble concentrating, restlessness, frustration, numbness, and fatigue were self-reported by participants, but not significantly linked to biomarkers • The magnitude of the detonation, proximity to blast, and use of protective gear were highlighted as important dimensions of blast exposure; however, the data collection methods (e.g., blast gauges) were not identified • A blast of ~12 psi was experienced on one of the training days	Medium	Publication date: May 2020 Jurisdiction studied: United States Methods: Pre-post tests	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ Dose-response relationship (e.g., evidence that increasing exposure increases the risk of the outcome) ○ Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)				
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Non-blast ▪ Acceleration injuries (i.e., non-blast injuries resulting from the brain being suddenly forced to speed up and slow down within the skull) ○ Additional dimensions of exposure ▪ Number of exposures ▪ Intensity of exposures (psi) • Sensory effects of mTBIs ○ Tinnitus • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems ○ Dizziness, loss of balance, or proprioception issues • Possible effect modifiers ○ Setting ▪ Deployment ▪ Operations ○ Nature of protective equipment available (including the consistency with which it is worn and whether it fits correctly) (e.g., helmet; mouthguard; hearing protection)	Most service members interviewed, especially those with high exposure and high symptom burden, saw the value of body-worn blast/acceleration sensors to measure cumulative low-level exposure and support proactive decisions about brain health (32) • Interviews with 156 Army, Navy, and Marine Corps service members elicited feedback about the feasibility and acceptability of body-worn blast/acceleration sensors ○ Service members' specialties varied, including infantry, combat engineering, explosive ordnance disposal, artillery, mortar, and armor job specialties, with both trainers and operational force members included in these sub-categories ○ The Air Force and Navy were not represented ○ The types of exposures highlighted include blast (high calibre rifles, shoulder-launched rockets, recoilless rifles, grenades, artillery shells, mortar shells, demolition and breaching charges) and accelerative impact (static line parachute operations, accidents) exposures ○ The sensors would be worn in both 'garrison' (operations) and deployed settings (where more uncontrolled blasts take place) • Trainers (breaching, shoulder-mounted weapons, mortars, grenades) experienced high levels of overpressure and reported tinnitus, headaches, dizziness, nausea, and temporary memory loss • Artillery, M1 tank crewmembers, and explosive ordnance disposal specialists had relatively low levels of routine blast exposure due to small charges, infrequent use, and sufficient distancing from the blast, and these low exposure specialties generally reported a lack of physical symptoms • For accelerative impact, trainers in a basic airborne course reported TBI events, but generally denied experiencing milder/sub-concussive exposures • General consensus from the qualitative end-user interviews indicated that the gauges should be a single, unobtrusive, multi-directional sensor that is resistant to environmental stressors, mounted to the helmet, and convenient to use	Medium	Publication date: August 2024 Jurisdiction studied: United States Methods: Qualitative study	• Occupation

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The value of these sensors lies in the record of cumulative exposure for an individual, so the gauges must accurately measure ~1 psi blasts
Additionally, the need for immediate and actionable feedback was highlighted, allowing for this blast/impact data to provide real-time feedback about high-risk exposures and to be integrated with medical records

For medical use, additional test and subjective experience/symptom reports will need to accompany this data to inform decisions about fitness for duty and safety
Many participants believed that this objective, longitudinal data would be beneficial as prior evidence when they enter the Veterans Administration

Further details about implementation considerations (e.g., batteries, interface elements, training modules, convenience, cybersecurity, fiscal liability, career implications) can be found in the original study, but are outside the scope of this review's research question
A final recommendation from the study was to design dual blast overpressure and accelerative impact measurement devices in a singular sensor

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Type of exposure

Blast
Primary (i.e., resulting from high pressure or overpressure created by explosions)
Non-blast
Recoil injuries (i.e., injuries sustained as a result of backward force produced during the use of medium to large calibre shoulder fired weapons)

Sensory effects of mTBIs
Tinnitus
Possible effect modifiers
Setting
Training

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The study summarizes temporary threshold shift and noise exposure among U.S. service members exposed to breaching explosives, shoulder-mounted weapons, calibre weapons, or indirect fire weapons but any related information on the associations remains limited (33)

The observational study examined temporary threshold shift (temporary decrease in hearing sensitivity) and noise exposure on U.S. service members exposed to impulse noise/blast exposure and blast during tactical training

Impulse noise was defined as a 'fast, nearly instantaneous, rise in air pressure followed by a slower exponential decay back to baseline' and blast exposure is characterized as a sub-class of this
The source of exposure was the following: breaching explosives, shoulder-mounted weapons, 0.50 calibre weapons, and indirect fire weapons

The breaching group included training with explosive and shotgun breaching (two training events)
The shoulder-mounted group included a unit with 'M3A1 Multi-Role Anti-Armor Anti-Personnel Weapon System,' 'M136 Anti-Tank Weapon,' 'M3A1 Multi-Role, Anti-Armor, Anti-Personnel Weapon System,' and 'M141 Bunker Defeat Munition' rocket (number of trainings not reported)

</td><td>Medium</td><td>Publication date: March 2025

Jurisdiction studied: United States

Methods: Observational</td><td>
Occupation
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Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
	▪ The calibre group included a M2A1 machine gun, and GAU 17, GAU 21 in a flight environment (number of trainings not reported) ▪ The indirect fire group included training events with the M777 howitzer, 81- and 120-mm motors (four training events) o Pre-exposure testing was completed on arrival at the training site and within the same week of exposure, post-exposure testing took immediately following the exercise using the mNOISE doismeter o Auditory thresholds was assessed at 4000 and 6000 Hz, and a statistically significant shift was defined as an average threshold change of ≥5 dB • Noise exposure and hearing outcomes were collected from 214 individuals, including 209 males and five females, with an average age of 27.9 (+/– 6.9 years (range 19–60 years) • At baseline, there were only 10 participants with mild hearing loss or greater • Temporary threshold shift (temporary decrease in hearing sensitivity) was not pronounced across the training events, but roughly 13% of the participants had an acute shift in hearing due to noise exposure • The authors reported that each weapon system category resulted in A-weighted estimates well above the limit, indicating that it was hazardous for continuous noise without proper hearing protections • The authors concluded that measures based on cumulative energy exposure are more predictive of acute hearing injury than measures based on peak blast exposure • Details on the association between these events and demographic characteristics were not reported			
• Type of exposure o Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) o Non-blast ▪ Acceleration injuries (i.e., non-blast injuries resulting from the brain being suddenly forced to speed up and slow down within the skull) o Additional dimensions of exposure ▪ Number of exposures ▪ Intensity of exposures (psi) • Cognitive and mental health effects of mTBIs	Breaching instructors had greater cognitive and emotional impairment at baseline, compared to non-breacher special operation forces (SOF) controls (34) • The study collected data over four years, but with non-overlapping participants • During the breaching training exercise, participants were exposed to repetitive low-level blasts, where acute measurements were taken in the field after every 5 blast exposures; however, neuroimaging reported no significant changes, suggesting that brain structures are only impacted after cumulative blasts over a career rather than acute training sessions • Breachers (compared to controls) had greater impairments on cognitive ($t=3.66$, $p<0.01$, $d=1.38$) and emotional sub-scales ($t=2.81$, $p<0.01$, $d=1.06$), late (rather than acute) post-concussive symptoms (e.g., sleep disturbance) ($t=3.60$, $p<0.01$, $d=1.37$), and lower physical functioning ($t=-2.59$, $p<0.05$, $d=-0.89$), social functioning ($t=-2.29$, $p<0.05$, $d=-0.87$),	Medium	Publication date: February 2021 Jurisdiction studied: Canada Methods: Pre-post tests	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ Dizziness, loss of balance, or proprioception issues ○ Depression ○ Anxiety ○ Difficulty sleeping ○ Fatigue • Possible effect modifiers ○ Stage in a military career ○ Biological sex ▪ Male ○ Setting ▪ Training • 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)	energy/fatigue (t=–2.22, p<0.05, d=–0.84), and role limitation as a result of physical health (t=–2.59, p<0.05, d=–0.98) • There was not enough information collected to attribute the reduced gray matter volume observed in the prefrontal cortex of breachers to breaching • Years of service in the military was measured, as well as details about the blast exposure using blast gauges (e.g., cumulative overpressure levels across breachers) • Previous head injury exposures were documented, including acceleration-deceleration injuries and blast-induced mTBI, and may have a large impact on the results in addition to breaching history			
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ 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 when a gun or other weaponry is fired) ○ Additional dimensions of exposure ▪ Number of exposures ▪ Intensity of exposures (psi) ▪ Time between exposures	Breacher students/instructors and sniper students had significantly different subjective hearing survey scores and average delta high-low hearing thresholds compared to controls without blast exposure, suggesting that cumulative blast overpressure can impact hearing (35) • The setting of exposure was outside (not enclosed) using controlled explosives with blast gauges in a training course for explosive breaching and sniper exercises ○ To assess for the effects of cumulative blast overpressure, data was collected four weeks before training and three weeks post-training ▪ However, the delay between exposure and measurement means that temporal proximity and dose-response relationships could not be concretely determined, with specificity from the causality criteria eliminated completely • The delta values measured the difference between performance in the average high-frequency and average low-frequency hearing thresholds, for which there was a significant difference between the exposure and control groups (F-statistic=6.10, p<0.05), with a strong sensitivity specific to breachers (F-statistic=10.24, p<0.005) ○ Control participants had noise exposure, but no history of occupational breaching or heavy weapons blast exposure; controls were also age- and sex-matched to the exposure group	Medium	Publication date: March 2025 Jurisdiction studied: Canada Methods: Cohort study	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
• Sensory effects of mTBIs ○ Tinnitus • Possible effect modifiers ○ Stage in a military career ○ Setting ▪ Training ○ Nature of protective equipment available (including the consistency with which it is worn and whether it fits correctly) (e.g., helmet; mouthguard; hearing protection) • 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) ○ Consistency of evidence (e.g., similar or the same results generated by studies using different methods in different settings) ○ Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)	▪ The exposure group had far more blast exposure (lifetime and recently) and deployment/war zone experience compared to the control group ▪ Military experience and history of head trauma were also evaluated, with demographic data modelling indicating that differences in hearing categories between participants were influenced by previous lifetime exposures to blast or munitions and motor vehicle accidents ○ Hearing thresholds were sensitive to cumulative (p=0.0016) and more acute (training course; p=0.0142) blast exposure ○ Low frequency hearing threshold averages were defined as 2-4 kHz, and high frequency as 4-8 kHz ○ High-frequency hearing thresholds had greater variance, potentially due to individual variation related to energy exposure and/or variation in protective equipment compliance or exposure sources • The subjective hearing survey evaluated exposure to lifetime blast overpressure and supported the finding that cumulative blast exposure accounts for symptom differences between the exposure and control groups (p=0.034) ○ Blast symptoms may better predict measurable changes in hearing category compared to blast exposure reports • Some participants (seven) had multiple blasts (two to 16) experienced over 4 psi • Mechanisms of hearing injury and injury progression could not be established from this study • Biological plausibility was supported through animal model studies			
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Additional dimensions of exposure ▪ Number of exposures ▪ Intensity of exposures (psi) ▪ Time between exposures • Sensory effects of mTBIs ○ Sensitivity to light ○ Tinnitus • Cognitive and mental health effects of mTBIs	Mortarmen with high cumulative low-level blast exposures (even if the incident blasts are below 4 psi) reported a high prevalence of headaches, tinnitus, memory problems, sleep disturbance, and irritability (36) • Mortars are weapon systems operated by three to four people (sometimes with additional supervisors) that elicit low-level blasts ○ The operating positions include assistant gunner, gunner, squad leader, an ammo bearer (for the 120mm system only), and fire direction centers (supervisors) ○ Assistant gunners and gunners experienced blast overpressure significantly higher than the 4psi safety threshold in 91% and 74% of the blasts during training, incident pressures peaking at 5.33 psi and 5.84 psi, respectively, which has raised concerns about the cumulative overpressure experienced over a career	Medium	Publication date: September 2021 Jurisdiction studied: United States Methods: Prospective cross-sectional observational cohort study	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
○ Memory or concentration problems ○ Mood changes ○ Difficulty sleeping • Possible effect modifiers ○ Stage in a military career ▪ Early ▪ Mid ○ Biological sex ▪ Male ○ Setting ▪ Training ○ Nature of protective equipment available (including the consistency with which it is worn and whether it fits correctly) • Causality criteria ○ Temporal relationship (e.g., exposure must precede the occurrence of the outcome) ○ Consistency of evidence (e.g., similar or the same results generated by studies using different methods in different settings) ○ Dose-response relationship (e.g., evidence that increasing exposure increases the risk of the outcome) ○ Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)	○ During three firing days, 7/11 of the mortarmen experience cumulative blast overpressure similar to what shoulder-mounted artillery instructors experience over three years (from another study) ▪ One mortarmen was cumulatively exposed to 1,361 psi during the training period ○ The average cumulative impulse experienced by mortarmen in training is significantly more than breacher students and trainers in training settings (51 psi-ms for students, 43.3 psi-ms for instructors, and a range of 115 psi-ms to 1,033 psi-ms for mortarmen) • Self-reported symptoms and pupillary light reflex responses were measured before the six-day training exercise occurred (where there are three live firing days with rest days in between), on each rest day (to measure acute exposure), and 17 days after the end of training (to investigate prolonged effects) • mTBI symptoms were observed among all mortarmen, not just those with blast overpressure exposures over 4psi ○ 10/11 reported headaches, 9/11 reported ringing in the ears and forgetfulness/poor memory, 8/11 reported taking longer to think, and 7/11 reported sleep disturbance and being irritable or easily angered ▪ Forgetfulness/poor memory was reported in none of the controls, a unique symptom to mortarmen ▪ Sleep disturbance and ringing in the ears were highly prevalent among control participants, which could be explained by altered sleep schedules during training and tinnitus being a common symptom among all military service members ○ Symptom severity was highest in more experienced mortarmen, suggesting there is a cumulative effect of repetitive, sub-concussive exposures over a career, potentially with delayed onset neurodegeneration • The pupillary light reflexes of mortarmen were similar to those with mTBI or depressed autonomic neurological function (as reported in other studies), specifically mortarmen's dilation velocity and constriction velocity were significantly slower than ranger controls • The authors recommend that daily firing limits and safety thresholds be urgently established ○ Two approaches were highlighted: daily cumulative impulse thresholds for the entire mortar crew and each mortarmen wearing a blast gauge during training to record individual cumulative exposure ○ Usage of mortar simulators offer hands-on practice for certain elements of the mortar process without any blast exposure			

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
	• Standard protective equipment was worn (ear protection, helmets, ballistic body armor), plus ducking and a blast attenuation device (added to mortar opening) were trialled during the study, resulting in lower blast overpressures but insignificant impacts on health outcomes, signalling the need for additional protections (e.g., daily limits) • All mortarmen were male and did not have a mTBI • The 4 psi hearing safety threshold was discussed in this study; however, an alternative for brain/organ safety was not presented			

• Type of exposure
  ○ Blast
    ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions)
  ○ Non-blast
    ▪ Impact injuries (i.e., non-blast related collision between head and a stationary or moving object)
    ▪ Recoil injuries (i.e., injuries sustained as a result of backward force produced when a gun or other weaponry is fired)
  ○ Additional dimensions of exposure
    ▪ Number of exposures
    ▪ Intensity of exposures (psi)
    ▪ Time between exposures
• Cognitive and mental health effects of mTBIs
  ○ Depression
  ○ Anxiety
  ○ Difficulty sleeping
• Possible effect modifiers
  ○ Biological sex
    ▪ Male
    ▪ Female
  ○ Setting
    ▪ Training
    ▪ Deployment
    ▪ Operations
  ○ Time to return to high-risk activities
  ○ Co-morbid PTSD or mental health conditions
	Within an active-duty military population, a lifetime history of 3+ mTBIs is associated with increased self-reported PTS symptoms, mTBI symptoms, and depressive symptoms (37)
	• In this study investigating the associations between mTBI, blast exposure history and post-traumatic stress (PTS) symptoms, data was collected from active-duty service members (18 years or older; predominantly men) with combat exposure who had been referred to an outpatient program for persistent symptoms related to TBI or behavioral health conditions
	  ○ Participants were excluded if they had a history of moderate or severe TBI, incomplete TBI history, or incomplete self-assessments
	  ○ mTBI was defined using Department of Veterans Affairs (VA)/DoD guidelines: loss of consciousness (LOC) less than 30 minutes and/or post-traumatic amnesia/alteration of consciousness (AOC) less than 24 hours; LOC had to be witnessed by an additional person at the time of the event, and AOC needed to be substantiated by a clear disruption in cognitive functioning
	• Data collection consisted of semi-structured interviews that collected the total lifetime number of blast exposures of all magnitudes, including all operational and training events (but excluding breaching charges)
	  ○ Blast exposures ranged from small overpressures experienced firing small arms (e.g., pistols and rifles) to large overpressures experienced from Improvised Explosive Devices (IEDs)
	  ○ Additional exploratory variables collected were the total number of parachute jumps and breaching exposures during operational and training events
	• The primary outcome measured was PTS symptoms severity using the PTSD Checklist – Civilian version (PCL-C); secondary outcomes measured were depressive symptoms (assessed by the Patient Health Questionnaire 9 (PHQ-9)), anxiety symptoms (assessed by the Generalized Anxiety Disorder 7-item (GAD-7)), chronic mTBI symptoms (assessed by the NSI), and sleep symptoms (assessed by the Epworth Sleepiness Scale (ESS))
		Low	Publication date: May 2022
			
			Jurisdiction studied: United States
			
			Methods: Case control study
				• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
• 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)	• The number of mTBIs were positively associated with the total PCL-C, whereas the number of blast and breach exposures were each negatively correlated with the total PCL-C ○ The number of lifetime mTBIs of the participants ranged from 0 to 7 (mean=1.59), while reported blast exposures ranged from 0 to 13,170 (mean = 1,070) ○ Among participants with at least one mTBI, the time since most severe injury ranged from 22 days to 46.7 years (mean 16.9 years ○ Post-hoc tests identified significantly higher total PCL-C scores in the 3+ mTBI group relative to the 0 mTBI group (p=0.010) and 1 mTBI group (p=0.010) ○ Only PHQ-9 and NSI were significantly different between mTBI groups			
• Type of exposure ○ Blast ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) • Cognitive and mental health effects of mTBIs ○ Depression • Possible effect modifiers ○ Co-morbid PTSD or mental health conditions • Causality criteria ○ Temporal relationship (e.g., exposure must precede the occurrence of the outcome) ○ Dose-response relationship (e.g., evidence that increasing exposure increases the risk of the outcome)	Higher blast severity was associated with higher chronic mental health symptoms (post-traumatic stress, depression, and neurobehavioral), beyond PTSD diagnosis and deployment mild TBI history in combat Veterans (38) • The purpose of this study was to evaluate the effects of primary blast exposure on the brain and behaviour for combat Veterans with at least one deployment • Lifetime blasts were evaluated using the Salisbury Blast Interview, and maximum pressure ratings were used to represent blast severity on a behaviourally anchored scale of 0 through 5 (pressure measurements were not used to measure blast severity) • Deployment mTBI (mild TBI sustained during deployment) was chosen as the independent variable • The PTSD checklist for DSM-5, the NSI, and the Quality of Life after Brain Injury scale (QOLIBRI) were used • Of 275 total participants 71.27% (n=196) had blast exposure history, defined as experiencing any noticeable pressure wave resulting from an explosion ○ 29.82% (n=82) had a current diagnosis of PTSD, and 45.45% (n=125) had deployment mTBI; of those with mTBI history, 76% (n=95) had at least one TBI involving blast • This is the first study to demonstrate the increased severity of psychiatric symptoms in the chronic phase (greater than one year) following blast exposure • Deployment mTBI was significantly related to PTSD symptoms, depressive symptoms, and neurobehavioral symptoms beyond the effects of combat exposure and PTSD diagnosis • Without adjusting for blast severity, deployment mTBI significantly contributed to symptom presentation, but when blast severity was	Low	Publication date: November 2021 Jurisdiction studied: United States Methods: Interviews, modelling	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
	included in the model, deployment mTBI history was no longer a significant predictor of any outcome • Results demonstrating the associations between chronic mental health symptoms increasing proportionately to blast severity were independent from PTSD diagnosis and deployment mTBI history, but findings did not extend to sleep quality, pain interference, or quality of life			

• Type of exposure
  ○ Blast
    ▪ Primary (i.e., resulting from high pressure or overpressure created by explosions)
• Possible effect modifiers
  ○ Co-morbid PTSD or mental health conditions
• Causality criteria
  ○ Temporal relationship (e.g., exposure must precede the occurrence of the outcome)
	Self-reported lifetime blast exposure is not related to white matter integrity in service members and Veterans with and without uncomplicated mTBI (39)
	• The purpose of this study was to examine the impact of lifetime blast exposure on white matter integrity in service members and Veterans, with the relationship between PTSD and white matter integrity in models accounting for mTBI and blast exposure being a secondary objective
	• 227 U.S. service members and Veterans were recruited and classified based on self-reported lifetime blast exposure:
	  ○ no blast exposure (n=53); low blast exposure (i.e., 1–9 blasts; n=81); or high blast exposure (i.e., ≥10 blasts; n=93)
	• A comprehensive lifetime TBI history was conducted alongside interviews and (n=124) participants were determined as having uncomplicated mTBI (no trauma related abnormalities in MRI)
	  ○ 58% of these participants (n=72) had a history of mTBI that involved blast exposure
	• Lifetime blast exposure was assessed with a single interview question: "In your life, how many times have you been close enough to an explosion in which you felt the blast wave?"
	• PTSD symptoms were assessed using the PTSD Checklist-Civilian version and given a score to represent symptom burden
	• Participants underwent neuroimaging via MRI to measure cerebral white matter
	• Authors found no evidence to suggest an impact of blast exposure on white matter integrity in service members with and without a history of mTBI, which contrasts with past work suggesting otherwise
	  ○ Findings echo two previous smaller studies which also did not find relationships between blast exposure and white matter integrity
	• Findings did not support a relationship between remote mTBI history or current PTSD and white matter integrity
	• Authors recommend future research incorporate blast exposure metrics
		Low	Publication date: December 2023
			
			Jurisdiction studied: United States
			
			Methods: Interview, clinical trial, modelling
				• Occupation

• Type of exposure ○ Blast	Primary blast exposure, particularly the intensity of perceived pressure and proximity to the blast, is the strongest predictor of TBI among Iraq and Afghanistan war Veterans, and higher blast characteristic ratings (pressure,	Low	Publication date: February 2020	• Occupation

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristics	Equity considerations
▪ Primary (i.e., resulting from high pressure or overpressure created by explosions) ○ Additional dimensions of exposure ▪ Number of exposures • Cognitive and mental health effects of mTBIs ○ Memory or concentration problems ○ Mood changes • Possible effect modifiers ○ Setting ▪ Training ○ 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 • 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)	temperature, wind) are significantly associated with greater PTSD and post-concussive symptom severity, independent of TBI history (40) • The study used a prospective cohort study design with 287 post-deployment U.S. service members and Veterans who completed the Salisbury Blast Interview to report lifetime blast exposures (including number, distance, and subjective ratings of pressure, wind, debris, temperature, and sound), along with structured clinical interviews and self-report measures to assess TBI history, PTSD, and post-concussive symptoms • The study defines blast exposure broadly as any lifetime experience of blasts or explosions (combat, training, or civilian) and evaluates them using the Salisbury Blast Interview, which records details such as distance, subjective intensity (pressure, wind, debris, temperature, sound), and protective factors ○ The study primarily investigates primary blast exposure (overpressure) but also notes secondary or tertiary events (e.g., being hit by objects) occurred in a small minority of cases (6–10%) • Exposure intensity is determined by self-reported ratings (0–5 scale) for pressure, wind, ground shaking, debris, temperature, and sound • 4.4% of participants (n=287) reported at least one blast event during their lifetime, with a mean of 337.7 blast events (SD=984.0; range 0–11,555); about 64.8% of blasts occurred during combat, and 19.7% of participants experienced a TBI during a blast event • Pressure rating and distance were the strongest predictors of TBI ○ Logistic regression indicated that pressure ($\chi^2=16.92$, $p<0.001$) and distance ($\chi^2=21.69$, $p<0.001$) significantly predicted TBI, with pressure showing the highest AUC=0.75 for predicting blast-related TB • Higher maximum blast characteristic ratings correlate with greater PTSD symptom severity and neurobehavioral symptoms, independent of TBI history, suggesting blast effects can contribute to mental health outcomes even without diagnosed TBI • Being behind cover significantly reduced subjective ratings of blast severity (e.g., wind, pressure, sound), highlighting the modifying effect of environmental and protective measures (helmet worn in 65.6% of events)		Jurisdiction studied: United States Methods: Prospective, cohort study	

Appendix 5: Key findings from Five Eyes countries and NATO documents on Clinical Practice Guidelines and benefits reimbursement policies for occupational exposure to sources of repetitive sub-concussive head injuries

Jurisdiction	Declarative title and key findings about clinical practice guidelines	Declarative title and key findings about reimbursement policies
Australia	• No clinical practice guidelines on the assessment or management of repetitive sub-concussive exposures were identified • A clinical practice guideline for the care of people living with traumatic brain injury (TBI) in the community that was funded by the Motor Accidents Authority was identified but this pertains to severe traumatic brain injuries • A clinical practice guideline for physical activity for people with moderate to severe traumatic brain injury developed by the Australia Physiotherapy Association was identified	• Within the Department of Veterans Affairs, a Statement of Principle relevant to injuries from blast explosions was established and is used to connect military services to compensation and treatment coverage • The explosive blast injury statement of principle covers any physical injury resulting from explosive blasts including direct effects of the overpressure waves, flying debris, or being thrown against an object by force of blast ○ It should be noted that within the standard, relevant service means operational service, peacekeeping, hazardous service, war-like service, or non-war-like service, but would not include training • A separate Statement of Principle is established for concussion, acute mild traumatic brain injury (but claims for ongoing/persisting effects beyond three months are not covered), and moderate to severe traumatic brain injury

Canada	• Veterans Affairs diagnostic criteria for mTBI allow for various diagnostic definitions, including:
	  ○ 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
	• Clinical features include a range of physical symptoms (e.g., loss of consciousness, headache, nausea, vomiting), cognitive symptoms (e.g., memory problems, confusion and disorientation, slowed thinking) and emotional and behavioural symptoms (e.g., mood swings, anxiety and depression, impulsivity)
	• The guideline notes that recovery may differ and though for many it is improved within 7–10 days about 13% of people with mild traumatic brain injuries (mTBIs) have lasting problems with memory and thinking
		• For Veterans Affairs, the following factors are accepted to cause or aggravate mTBI and can be considered alongside evidence to assist in establishing a relationship to service; these include:
		  ○ 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
		  ○ inability to obtain appropriate clinical management
		• Additionally, other medical conditions that are included in the entitlement and assessment of mTBI include post-traumatic headaches, post-traumatic migraines, and non-specific dizziness

New Zealand	• No relevant clinical practice guidelines for repetitive sub-concussive exposures were identified	• No reimbursement policies for Veterans for repetitive sub-concussive exposures were identified
United Kingdom	• No military or Veteran guidelines specific to sub-concussive injury were identified	• No reimbursement policies for Veterans for repetitive sub-concussive exposures were identified

Jurisdiction	Declarative title and key findings about clinical practice guidelines	Declarative title and key findings about reimbursement policies

	• A National Institute for Health and Care Excellence (NICE) guideline on head injury including assessment and early management was identified
	• The guideline broadly covers:
	  ○ decision-making and mental capacity
	  ○ pre-hospital assessment, advice, and referral to hospital
	  ○ immediate management at the scene and transport to hospital
	  ○ assessment in the emergency department
	  ○ investigating clinically important TBIs
	  ○ investigating injuries to the cervical spine
	  ○ information and support for families and carers
	  ○ transfer from hospital to a neuroscience unit
	  ○ admission and observation
	  ○ discharge and follow-up
	• For diagnosis of an acute clinically important TBI the guideline recommends the use of CT scanning and notes that while MRI should not be the primary means of diagnosis it may provide additional information on prognosis
	  ○ This is recommended for those with a Glasgow Coma Score of 15 and under
	• In addition, two related evidence reviews underpinning the National Health Service (NHS) guidance were identified:
	  ○ The first of which covers the use of biomarkers and MRI for post-concussive syndrome and concludes that the committee is unable to make recommendations for the use of biomarkers and/or MRI in the prediction of post-concussion syndrome in those with mTBI as the evidence included in the review is too limited
	    ▪ Further, the evidence review notes that while evidence did show some signs that certain biomarkers and MRI features could be useful, including thresholds used for biomarkers or features measured on MRI, populations and outcomes differed too much across studies
	  ○ The second covers admission and observation of people with concussion symptoms, which notes that there remains uncertainty regarding whether those presenting with concussion symptoms but no abnormalities in brain imaging should be admitted
	    ▪ The evidence review notes that concussion symptoms could include: headache, dizziness, nausea, amnesia, clumsiness or trouble with balance, altered cognition, feeling stunned, dazed or confused, and changes in vision – all of which would qualify someone for a Glasgow Coma score of 15 or under, but these symptoms are all noted as being in the acute term rather than medium or long-term	

United States	• In 2019, Veterans Affairs and the Department of Defense recommended an updating of the clinical guidelines for management and rehabilitation of patients with symptoms attributed to mTBI
	  ○ The clinical guideline uses the terms for mTBI and concussion interchangeably
	• The guidelines define a TBI as a new onset or worsening of any of the following clinical signs:
	  ○ any period of loss of or a decreased level of consciousness
		• Veterans are eligible for medical care and health services needed to provide the standard of care supported by the 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.

Jurisdiction	Declarative title and key findings about clinical practice guidelines	Declarative title and key findings about reimbursement policies
	◦ 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, and forces generated from events such as blasts or explosions • No recommendations within the clinical practice guidelines had strong evidence (based on GRADE profile) to support their use; those with weak evidence include: ◦ for setting of care, should use a primary care (as opposed to specialty care) symptoms-focused approach in the evaluation and management of the majority of patients with symptoms attributed to mTBI ◦ for diagnosis and assessment of patients with new symptoms that develop more than 30 days after mTBI, should use a symptom-specific evaluation non-mTBI etiologies ◦ for treatment of cognitive symptoms including memory, attention, or executive function problems despite appropriate management of other contributing factors, should be referred for a short trial of clinician directed cognitive rehabilitation services ◦ for treatment of behavioural symptoms attributed by mTBI, including PTSD, substance use disorder, and mood disorders, should be evaluated and managed the same whether they have had mTBI or not, according to the relevant existing VA/DoD clinical practice guidelines ◦ for treatment of vestibular ad proprioceptive symptoms, should be offered a trial of specific vestibular rehabilitation and proprioceptive therapeutic exercise • In addition, the use of hyperbaric oxygen therapy for the treatment of patients with symptoms attributable to mTBIs was found to have strong evidence against. • In addition, the American College of Radiology has clinical decision rules for determining appropriate procedures for head trauma	
North Atlantic Treaty Organization (NATO) – Science and Technology Organization	• A technical report from 2015 from the North Atlantic Treaty Organization's Science and Technology Organization provides an overview of available clinical guidelines from NATO countries, including Canada, the Netherlands, U.K., and U.S., as well as an overview of the state of the evidence base, proposed white papers for the organization to push forward, and a literature review about the prevention of mTBIs in military service members • In addition, NATO's Science and Technology Organization is in the process of developing two related guidelines: ◦ guidelines to mitigate military occupational brain health risks from repetitive blast exposure (due in 2025) ◦ guidelines for evaluation of personal protective material and systems against blasts (due in 2027)	• No reimbursement policies for Veterans for repetitive sub-concussive exposures were identified

Appendix 6: Documents excluded at the final stages of reviewing

Document type	Hyperlinked title
Single studies	Neuroinflammatory biomarkers associated with mild traumatic brain injury history in special operations forces combat soldiers
	Can mild traumatic brain injury alter cognition chronically? A LIMBIC-CENC multicenter study
	Electrophysiological analysis of traumatic optic neuropathy and traumatic brain injury among active military
	Self-reported concussion symptomology during deployment: Differences as a function of injury mechanism and low-level blast exposure

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This rapid evidence synthesis was funded by the Chronic Pain Centre of Excellence for Canadian Veterans and the Atlas Institute for Veterans and Families, which in turn are funded by Veterans Affairs Canada. The McMaster Health Forum received both financial and in-kind support from McMaster University. The views expressed in the rapid evidence profile are the views of the authors and should not be taking to represent the views of the Chronic Pain Centre of Excellence for Canadian Veterans and the Atlas Institute for Veterans and Families or McMaster University.

ISSN 2819-5639 (online)