APPENDIX A. SEARCH STRATEGIES

Ovid MEDLINE(R) ALL 1946 to March 04, 2020
Date searched: March 5, 2020

1	Brain Concussion/ or Brain Contusion/ or Brain Hemorrhage, Traumatic/ or Brain Injuries, Traumatic/ or Brain Stem Hemorrhage, Traumatic/ or Cerebral Hemorrhage, Traumatic/ or Chronic Traumatic Encephalopathy/ or Contrecoup Injury/ or Craniocerebral Trauma/ or Head Injuries, Closed/ or Intracranial Hemorrhage, Traumatic/ or Post-concussion Syndrome/ or Blast Injuries/
2	(TBI or mTBI or bTBI or ((trauma or traumas or traumatic or posttraumatic or post-traumatic) adj2 (brain or crania* or cranio* or cerebr* or cortex or cortical or head*)) or concussion or concussions or concussive or contrecoup or coup-contrecoup or "minor brain" or "minor head" or postconcussion or postconcussive or post-concussion or post-concussive).ti,ab,kf.
3	or/1-2
4	Arthritis/ or Arthritis, Psoriatic/ or exp Arthritis, Rheumatoid/ or Back Pain/ or Chronic Pain/ or exp Chondrocalcinosis/ or Complex Regional Pain Syndromes/ or exp Facial Neuralgia/ or Fatigue Syndrome, Chronic/ or Femoral Neuropathy/ or Fibromyalgia/ or exp Gout/ or Headache/ or Headache Disorders/ or Headache Disorders, Primary/ or Headache Disorders, Secondary/ or Low Back Pain/ or exp Migraine Disorders/ or Musculoskeletal Pain/ or Myalgia/ or Myofascial Pain Syndromes/ or Neck Pain/ or exp Neuralgia/ or exp Osteoarthritis/ or Pain, Intractable/ or Phantom Limb/ or Post-Traumatic Headache/ or Radial Neuropathy/ or exp Spondylosis/ or Tension-type Headache/ or exp Trigeminal Autonomic Cephalalgias/ or Vascular Headaches/
5	(exp Pain/ or pain.hw.) and (arthrit* or "complex regional pain" or CRPS or fibromyalgia or gout or headache* or "low back" or migrain* or myalgia or neuralgia or neuropath* or nocicept* or osteoarthrit* or osteo-arthrit* or "phantom limb" or "reflex sympathetic dystrophy" or spondylosis or (central* adj2 (pain* or sensit*))).ti,ab,kf.
6	(arthrit* or "chronic fatigue" or "complex regional pain" or CRPS or fibromyalgia or gout or headache* or migrain* or myalgia or neuralgia or neuropath* or nocicept* or osteoarthrit* or osteo-arthrit* or "phantom limb" or “polytrauma clinical triad” or "reflex sympathetic dystrophy" or spondylosis or (central* adj2 (pain* or sensit*)) or pain).ti,ab,kf.
7	or/4-6
8	and/3,7
9	8 not ((exp Animals/ not Humans/) or ("animal model*" or cat or cats or dog or dogs or mice or mouse or rat or rats or rodent).ti.)
10	9 not (((Adolescent/ or exp Child/ or exp Infant/) not exp Adult/) or (adolescent or adolescents or adolescence or child or children or childhood or juvenile or pediatric or paediatric or preschool or pre-school or school-age or teen or teens or teenager or teenagers or youth or youths).ti.)
11	10 not case reports.pt.

12 limit 11 to english language

Veteran/ Servicemember filter terms used:

13 exp Veterans/ or exp "United States Department of Veterans Affairs"/ or exp Veterans Disability Claims/ or exp Veterans Health/ or Veterans Health Services/ or exp Hospitals, Veterans/ or Aerospace Medicine/ or Armed Conflicts/ or Hospitals, Military/ or Military Health/ or Military Personnel/ or Military Medicine/ or Military Nursing/ or Military Psychiatry/ or exp Naval Medicine/ or Psychology, Military/ or Gulf War/ or Vietnam Conflict/ or World War ii/ or Afghan Campaign 2001-/ or Iraq War, 2003-2011/ or War/ or exp "Warfare and Armed Conflicts"/ or War-Related Injuries/ or War Exposure/ or Warfare/ or Biological Warfare/ or Chemical Warfare/ or Nuclear Warfare/ or Psychological Warfare/

14 ("active duty" or "armed forces" or "armed service*" or "coast guard*" or military or "air force" or army or "defense force*" or "marine corps" or marines or "national guard*" or (navy not bean) or naval or "security force*" or air-men or air-man or airmen or airman or corpsman or corpsmen or guardsman or guardsmen or infantry* or medic or medics or reservist* or sailor* or soldier* or servicemember* or service-member* or "special forces" or submariner* or troops or battle* or combat or deployed or deployment* or post-deployment* or postdeployment* or veteran* or VAMC or Veterans Administration Medical Center* or VHA or Veterans* Health Administration or war or wars or warfare or war-fighter* or warfighter* or war-related).tw,kf.

15 (((VA or Veteran Affairs or Veterans' Affairs or Veterans Affairs or Veterans Administration) adj4 (health care system or healthcare system or medical center or hospital)) or VAMC or Veteran Affairs or Veterans' Affairs or Veterans Affairs or Veterans Administration Medical Center or Veterans' Affairs Medical Center or Veterans Affairs Medical Center or Veterans Health Administration or QUERI or "Mental Health Quality Enhancement Research Initiative" or HSR&D or "Center of Innovation for Veteran-Centered Value-Driven Care" or "Evidence-based Synthesis Program" or ((Veteran* or VA) adj5 (Office of Research and Development)) or "Center for Health Equity Research and Promotion" or "Women's Health Research Network" or "Cooperative Studies Program" or "Million Veteran Program").in.

16 (military or army or soldier* or navy* or veteran or veterans).jw.

17 or/13-16

18 and/12,17

CINAHL Plus with Full Text (EBSCOHost)

Date searched: February 10, 2020

S1 MH Brain Concussion OR Brain Contusions OR Brain Injuries OR Chronic Traumatic Encephalopathy OR Head Injuries (32,064)

S2 TI (TBI OR mTBI OR bTBI OR ((trauma OR traumas OR traumatic OR posttraumatic OR post-traumatic) N2 (brain OR crania* OR cranio* OR cerebr* OR cortex OR cortical OR head*)) OR concussion OR concussions OR concussive OR contrecoup OR coup-contrecoup OR "minor brain" OR "minor head" OR postconcussion OR postconcussive OR post-concussion OR post-concussive) OR AB (TBI OR mTBI OR bTBI OR ((trauma OR traumas OR traumatic OR

posttraumatic OR post-traumatic) N2 (brain OR crania* OR cranio* OR cerebr* OR cortex OR cortical OR head*)) OR concussion OR concussions OR concussive OR contrecoup OR coup-contrecoup OR "minor brain" OR "minor head" OR postconcussion OR postconcussive OR post-concussion OR post-concussive) (22,788)
S3 S1 OR S2 (38,328)
S4 MH Arthritis OR Arthritis, Psoriatic OR Arthritis, Rheumatoid OR Back Pain OR Chondrocalcinosis OR Chronic Pain OR Cluster Headache OR Complex Regional Pain Syndromes OR Facial Pain OR Fatigue Syndrome, Chronic OR Gout OR Headache OR Headache, Primary OR Headache, Secondary OR Low Back Pain OR Migraine OR Muscle Pain OR Myofascial Pain Syndromes OR Neck Pain OR Neuralgia OR Osteoarthritis OR Phantom Limb OR Phantom Pain OR Spondylosis OR Tension Headache OR Trigeminal Autonomic Cephalalgias OR Vascular Headache (127,543)
S5 TI (arthrit* OR chondrocalcinosis OR "chronic fatigue" OR "complex regional pain" OR CRPS OR fibromyalgia OR gout OR headache* OR "low back" OR migrain* OR musculoskeletal OR musculo-skeletal OR myalgia OR neuralgia OR neuropath* OR nocicept* OR osteoarthrit* OR osteo-arthrit* OR "phantom limb" OR "reflex sympathetic dystrophy" OR spondylosis OR (central* N2 (pain* OR sensit*)) OR ((chronic OR intractable OR long-term OR longer-term OR noncancer OR non-cancer OR nonmalignant OR non-malignant OR persistent* OR refractory) N3 pain)) OR AB (arthrit* OR chondrocalcinosis OR "chronic fatigue" OR "complex regional pain" OR CRPS OR fibromyalgia OR gout OR headache* OR "low back" OR migrain* OR musculoskeletal OR musculo-skeletal OR myalgia OR neuralgia OR neuropath* OR nocicept* OR osteoarthrit* OR osteo-arthrit* OR "phantom limb" OR "reflex sympathetic dystrophy" OR spondylosis OR (central* N2 (pain* OR sensit*)) OR ((chronic OR intractable OR long-term OR longer-term OR noncancer OR non-cancer OR nonmalignant OR non-malignant OR persistent* OR refractory) N3 pain)) (198,244)
S6 S4 OR S5 (239,755)
S7 S3 AND S6 Limiters - English Language; Human; Age Groups: Adult: 19-44 years, Middle Aged: 45-64 years, Aged: 65+ years, Aged, 80 and over, All Adult (435)

PsycINFO (Ovid) 1806 to February Week 1 2020
Date searched: February 7, 2020
1 Traumatic Brain Injury/ or Brain Concussion/ (19109)
2 (TBI or mTBI or bTBI or ((trauma or traumas or traumatic or posttraumatic or post-traumatic) adj2 (brain or crania* or cranio* or cerebr* or cortex or cortical or head*)) or concussion or concussions or concussive or contrecoup or coup-contrecoup or "minor brain" or "minor head" or postconcussion or postconcussive or post-concussion or post-concussive).ti,ab. (21754)
3 or/1-2 (25224)
4 Arthritis/ or Rheumatoid Arthritis/ or Back Pain/ or Chronic Pain/ or "Complex Regional Pain Syndrome (Type I)"/ or Chronic Fatigue Syndrome/ or Fibromyalgia/ or Headache/ or Migraine Headache/ or Myofascial Pain/ or Muscle Contraction Headache/ or Neuropathy/ or Neuropathic Pain/ or Phantom Limbs/ or Trigeminal Neuralgia/ (43617)
5 (arthrit* or chondrocalcinosis or "chronic fatigue" or "complex regional pain" or CRPS or fibromyalgia or gout or headache* or "low back" or migrain* or musculoskeletal or musculo-skeletal or myalgia or neuralgia or neuropath* or nocicept* or osteoarthrit* or osteo-arthrit* or "phantom limb" or "reflex sympathetic dystrophy" or spondylosis or (central* adj2 (pain* or

sensit*)) or ((chronic or intractable or long-term or longer-term or noncancer or non-cancer or nonmalignant or non-malignant or persist?nt* or refractory) adj3 pain)).ti,ab. (86759)
6 or/4-5 (89596)
7 and/3,6 (1680)
8 limit 7 to animal (246)
9 7 not 8 (1434)
10 limit 9 to ("300 adulthood<age 18 yrs and older>" or 320 young adulthood<age 18 to 29 yrs>or 340 thirties<age 30 to 39 yrs>or 360 middle age<age 40 to 64 yrs>or "380 aged<age 65 yrs and older>" or "390 very old<age 85 yrs and older>") (711)
11 9 not (adolescent or adolescents or adolescence or child or children or childhood or juvenile or pediatric or paediatric or preschool or pre-school or school-age or teen or teens or teenager or teenagers or youth or youths).ti. (1327)
12 or/10-11 (1355)
13 limit 12 to ("0200 clinical case study" or 1400 nonclinical case study) (127)
14 12 not 13 (1228)
15 limit 14 to english language (1180)

EBM Reviews (Ovid) - Cochrane Central Register of Controlled Trials (December 2019) and Cochrane Database of Systematic Reviews (2005 to February 4, 2020)
Date searched: February 7, 2020
1 (TBI or mTBI or bTBI or ((trauma or traumas or traumatic or posttraumatic or post-traumatic) adj2 (brain or crania* or cranio* or cerebr* or cortex or cortical or head*)) or concussion or concussions or concussive or contrecoup or coup-contrecoup or "minor brain" or "minor head" or postconcussion or postconcussive or post-concussion or post-concussive).ti,ab. (5149)
2 (arthrit* or "chronic fatigue" or "complex regional pain" or CRPS or fibromyalgia or gout or headache* or "low back" or migrain* or myalgia or neuralgia or neuropath* or nocicept* or osteoarthrit* or osteo-arthrit* or "phantom limb" or "reflex sympathetic dystrophy" or spondylosis or (central* adj2 (pain* or sensit*)) or ((chronic or intractable or long-term or longer-term or noncancer or non-cancer or nonmalignant or non-malignant or persist?nt* or refractory) adj3 pain)).ti,ab. (87910)
3 and/1-2 (297)
4 3 not ("animal model*" or cat or cats or dog or dogs or mice or mouse or rat or rats or rodent).ti. (297)
5 4 not (adolescent or adolescents or adolescence or child or children or childhood or juvenile or pediatric or paediatric or preschool or pre-school or school-age or teen or teens or teenager or teenagers or youth or youths).ti. (273)

Scopus
Date searched: February 10, 2020
(TITLE-ABS-KEY (tbi OR mtbi OR btbi OR ((trauma* OR posttraumatic OR post-traumatic) W/2 (brain OR crania* OR cranio* OR cerebr* OR cortex OR cortical OR head*)) OR concussion* OR concussive OR contrecoup OR coup-contrecoup OR "minor brain" OR "minor head" OR postconcuss*)) AND ((TITLE-ABS-KEY (arthrit* OR "chronic fatigue" OR "complex regional pain" OR crps OR fibromyalgia OR gout OR headache* OR migrain* OR myalgia OR neuralgia OR neuropath* OR nocicept* OR osteoarthrit* OR osteo-arthrit* OR "phantom limb") OR TITLE-ABS-KEY ("reflex sympathetic dystrophy" OR spondylosis OR (

central* W/2 (pain* OR sensit*)) OR ((chronic OR intractable OR long-term OR longer-term OR noncancer OR non-cancer OR nonmalignant OR non-malignant OR persist?nt* OR refractory) W/3 pain)))) AND (LIMIT-TO (DOCTYPE , "cp")) AND (LIMIT-TO (LANGUAGE , "English")) (155)

Epistemonikos
Date searched: February 10, 2020
advanced_title_en:(TBI OR mTBI OR bTBI OR (trauma OR traumatic OR posttraumatic OR post-traumatic) AND (brain OR crania* OR cranio* OR cerebr* OR cortex OR cortical OR head*) OR concussion* OR concussive OR "minor brain" OR "minor head" OR postconcuss*) AND advanced_title_en:(arthritis OR chronic OR "complex regional" OR crps OR fibromyalgia OR gout OR headache OR migraine OR myalgia OR neuralgia OR neuropathy OR nociceptive OR osteoarthritis OR osteo-arthritis OR phantom limb OR spondylosis OR centralized pain OR central sensitization OR intractable OR long-term OR longer-term OR noncancer OR non-cancer OR nonmalignant OR non-malignant OR persistent OR refractory) NOT advanced_title_en:(adolescent OR adolescents OR adolescence OR child OR children OR childhood OR juvenile OR pediatric OR paediatric OR preschool OR pre-school OR school-age OR teen OR teens OR teenager OR teenagers OR youth OR youths) [Filters: classification=systematic-review, protocol=no, cochrane=missing, pmc=without] (109)

ClinicalTrials.gov
Date searched: February 10, 2020
(arthritis OR chronic fatigue OR complex regional pain OR crps OR fibromyalgia OR gout OR headache OR migraine OR myalgia OR neuralgia OR neuropathy OR nociceptive OR osteoarthrits OR osteo-arthritis OR phantom limb OR post-traumatic headache OR reflex sympathetic dystrophy OR spondylosis OR central pain OR centralized pain OR centralized sensitivity OR chronic pain OR intractable pain OR long-term pain OR longer-term pain OR noncancer pain OR non-cancer pain OR nonmalignant pain OR non-malignant pain OR persistent pain OR refractory pain) | TBI OR mTBI OR bTBI OR (trauma* OR posttraumatic OR post-traumatic) AND (brain OR crania* OR cranio* OR cerebr* OR cortex OR cortical OR head*) OR concussion* OR concussive OR contrecoup OR coup-contrecoup OR EXPAND[Concept] "minor brain" OR EXPAND[Concept] "minor head" OR postconcuss* | Adult, Older Adult (210)

WHO ICTRP
Date searched: February 10, 2020
Title=TBI OR mTBI OR bTBI OR (trauma OR traumatic OR posttraumatic OR post-traumatic) AND (brain OR crania* OR cranio* OR cerebr* OR cortex OR cortical OR head*) OR concussion* OR concussive OR "minor brain" OR "minor head" OR postconcuss*
Condition=arthritis OR chronic OR "complex regional" OR crps OR fibromyalgia OR gout OR headache OR migraine OR myalgia OR neuralgia OR neuropathy OR nociceptive OR osteoarthritis OR osteo-arthritis OR phantom limb OR reflex sympathetic dystrophy OR spondylosis OR centralized pain OR central sensitization OR intractable OR long-term OR longer-term OR noncancer OR non-cancer OR nonmalignant OR non-malignant OR persistent OR refractory (without synonyms checked)
Recruitment status=ALL (140)

Google Scholar
Date searched: February 10, 2020
2 separate searches were conducted, reviewed first 10 pages of results for each
(TBI OR mTBI OR "traumatic brain" OR concussion OR "minor brain" OR "minor head" OR postconcuss*) AND (pain OR central sensitization OR intractable OR long-term OR noncancer OR non-cancer OR nonmalignant OR non-malignant OR persistent OR refractory)
(TBI OR mTBI OR "traumatic brain" OR concussion OR "minor brain" OR "minor head" OR postconcussion) AND (chronic OR intractable OR long-term OR persistent OR refractory) AND (treatment OR management OR intervention)
(10)

APPENDIX B. STUDY SELECTION

Inclusion/Exclusion Criteria for Full Text Review

VA-ESP Chronic Pain in Veterans and Servicemembers with a History of Mild Traumatic Brain Injury

1. **Language**: Is the full text of the article in English?
   Yes → Proceed to #2
   No → Code **X1**. STOP

2. **Publication type:** Is this a published study (exclude: dissertations, conference abstracts, protocols, unpublished results, letters, reviews, *etc*)?
   Yes → Proceed to #3
   No → Code **X2**. Add code **B** (example: X2 – B) if retaining for background/discussion. STOP

3. **Population**: Does the study include adult Veterans or Servicemembers with chronic pain and a history of mTBI?
   Definitions: ***Pain****: Include headaches/migraines. Chronic>3 months. Assume chronic unless explicitly says acute.* ***mTBI****: If mixed TBI population (eg mild, mod, and or severe), only include if mTBI results are reported separately. Include concussion. "Post-concussive symptoms" okay only if there's confirmation of mTBI or concussion that caused the symptoms (eg, a sample of recently returned Vets who complete the NSI and score 20 or higher does NOT qualify unless the study specifies that they all had a concussion or mTBI).*

   Yes → Proceed to #4
   No → **Code X3**. Add code **B** if retaining for background/discussion. STOP

4. **Population**: Is this a U.S. population?
   Yes → Proceed to #5
   No, they're international → Does it appear to address benefits and harms of interventions to treat chronic pain in Veterans or Servicemembers with a history of mTBI (KQ3)?
   Yes → Proceed to #5
   No → **Code X3.** STOP

5. **Intervention:** Is the study examining pharmacologic, nonpharmacologic, or complementary and integrative health interventions to treat chronic pain in Veterans or Servicemembers with a history of mTBI (KQ3)?
   Yes → Proceed to **#8**
   No, not a treatment/intervention study → Proceed to **#6**.
   No, not treating chronic pain → **Code X5**

6. **Study design**: Does the study report prevalence of chronic pain in the population of interest?
   Yes, reports prevalence → Proceed to #7
   No → Code **X6**

7. **KQ2**: Does this study report the prevalence of suicide-related outcomes (including suicide, suicidal ideation/intent/plan, and suicidal self-directed harm) in Veterans or Servicemembers with chronic pain and a history of mTBI?
   Yes → **Code 1 for KQ2**. Proceed to #8
   No → Proceed to #8

8. **Study design**: Is this an RCT, NRCT, cohort, prospective, or retrospective study (Exclude: Case studies/reports, cross-sectional, modeling studies)?
   Yes → Proceed to #9
   No → but it does have at least 1 KQ coded. STOP.
   No → and it has no previous code. **Code X6**

9. **Comparators**: Is the comparator population 1 of the following: Placebo, active comparator, usual care, wait-list control, pre-post? *Note: KQ1 and 1c do not require comparator, proceed to #11.*
   Yes → Proceed to #10
   No → **Code X4**

10. **Outcomes**: does the study report benefits (*eg* reduced pain, mental health diagnosis/symptoms, opioid use; better QOL, functioning, treatment adherence) or harms (*eg* AEs, SAEs, withdrawals due to AEs) outcomes for chronic pain in Veterans/Servicemembers with history of mTBI measured by a validated tool?
    Yes → **Code 1 for KQ3**. STOP
    No → **Code X5**. STOP

Codes Key:
X1: Not English-language
X2: Excluded publication type
X3: Excluded population
X4: Excluded comparator
X5: No outcomes of interest
X6: Excluded study design

APPENDIX C. QUALITY ASSESSMENT

Table 10. Criteria used in quality assessment of randomized controlled trials

Cochrane RoB 2.0:[33] Five domains through which bias may be introduced	
1. Risk of bias arising from the randomization process: 1.1. Was the allocation sequence random? 1.2. Was the allocation sequence concealed until participants were enrolled and assigned to interventions? 1.3. Did baseline differences between intervention groups suggest a problem with the randomization process?	
2. Risk of bias due to deviations from the intended interventions (effect of assignment to intervention): 2.1. Were participants aware of their assigned intervention during the trial? 2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial? 2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context? 2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups? 2.5. If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome? 2.6. Was an appropriate analysis used to estimate the effect of assignment to intervention? 2.7. If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	
3. Risk of bias due to missing outcome data: 3.1. Were data for this outcome available for all, or nearly all, participants randomized? 3.2. If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data? 3.3. If N/PN to 3.2: Could missingness in the outcome depend on its true value? 3.4. If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	
4. Risk of bias in measurement of the outcome: 4.1. Was the method of measuring the outcome inappropriate? 4.2. Could measurement or ascertainment of the outcome have differed between intervention groups? 4.3. If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants ? 4.4. If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received? 4.5. If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	
5. Risk of bias in selection of the reported result: 5.1. 5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis? Is the numerical result being assessed likely to have been selected, on the basis of the results, from... 5.2. ...multiple outcome measurements (*eg* scales, definitions, time points) within the outcome domain? 5.3. ...multiple analyses of the data?	
Overall risk-of-bias judgement	
Low ROB	The study is judged to be at **low risk of bias for all domains** for this result.
Some Concerns	The study is judged to raise **some concerns** in at least 1 domain for this result, but not to be at high risk of bias for any domain.
High ROB	The study is judged to be at **high risk of bias** in at least 1 domain for this result. OR The study is judged to have **some concerns** for **multiple domains** in a way that substantially lowers confidence in the result.

Abbreviations: NI=not indicated; N=no; PN=probably not; PY=probably yes; ROB=risk of bias; Y=yes

Table 11. Quality ratings for studies reporting prevalence of chronic pain in Veterans/Servicemembers with history of mild traumatic brain injury

Study *Author, year*	#1	#2	#3	#4	Overall study quality/Quality concerns	Applicability
Beswick-Escanlar, 2016[45]	1	NA	0	0	Entire population of SMs and focused on incident mTBI with incident headache or migraine pain (no diagnosis codes prior to study start date) during 1-year follow-up period. Both mTBI and pain were defined as ≥1 diagnosis code.	Post-9/11 SMs receiving military health care between 2006 and 2015.
Brickell, 2014[42]	1	0	0	0	Small sample size, and different patients at each follow-up. High attrition; no report of non-responder characteristics. mTBI definition inconsistent with VA-DoD common definition (required LOC<15 minutes and allowed intracranial abnormality). Non-standard pain measure (based on open-ended telephone interview questions).	Post-9/11 SMs with mTBI and polytrauma.
Couch, 2016[46]	0	0	1	0	Small sample size; highly selective patient group treated in 1 reintegration clinic. mTBI assessed clinically according to VA/DoD common definition. Headache or migraine pain self-reported based on clinical assessment questionnaire.	Male, Post-9/11 Veterans at 1 site, between ages of 20 and 60, enrolled in reintegration clinic.
Farrell-Carnahan, 2015[47]	1	0	1	1	Small study of Post-9/11 Veterans admitted to inpatient rehabilitation at 1 of 4 VA polytrauma rehabilitation centers and enrolled in TBI Model Systems. mTBI assessed using TBI Model Systems form. Headache intensity assessed using single item from NSI. Differences between participants (80% of those recruited) and non-participants (20% of recruited) are unclear.	Post-9/11 Veterans requiring inpatient rehabilitation for TBI and who enroll in VA TBI Model Systems.
Hoge, 2008[15]	1	0	0	1	Survey with 59% response rate, no information on non-respondents. mTBI assessed using screening questions; mTBI group included n=4 with LOC>30 mins. Pain measures assessed using validated instrument.	Post-9/11 Army SMs shortly after return from combat deployment.
Hoot, 2018[41†]	1	0	1	1	Fairly selective study sample from 4 sites (no information on Veterans/SMs who were recruited but did not enroll). Standardized and validated measures of mTBI and pain were used.	Post-9/11 Veterans/SMs with combat exposure enrolled in a comprehensive longitudinal study.
Jackson, 2016[48]	1	0	1	0	Veterans sampled nationally. mTBI assessed using VA 4-item screen plus	Post-9/11 Veterans who received mental health

Study *Author, year*	#1	#2	#3	#4	Overall study quality/Quality concerns	Applicability
					clinical interview. Headache pain assessed using post-concussive symptom indicators on VA 4-item screen.	evaluation in VA; oversampled females and Veterans with PTSD.
King, 2014[40]	1	NA	0	0	Entire population of VA users across region. mTBI defined using ≥1 ICD diagnosis code for post-concussion syndrome. Pain conditions also based on ICD diagnosis codes.	Post-9/11 Veterans who used VA primary care in VISN 2.
Kulas, 2016[39]	1	NA	0	0	Large study that included full population of patients from VA for 1 year. Both mTBI and pain conditions based on presence of ≥1 ICD diagnosis code during study period.	Post-9/11 Veterans receiving VA care in fiscal year 2012.
Lew, 2009[25]*	0	NA	1	1	Single site; chart review of all patients assessed for 22 months. No demographics provided. mTBI and general chronic pain defined as clinician documentation in CTBIE chart note but making assumption that post-concussive symptoms associated only with mTBI and not TBI of greater severity.	Post-9/11 Veterans treated at single Level 2 polytrauma clinic.
MacGregor, 2013[49]	1	NA	0	0	Fairly small multi-site sample but representative of population described. mTBI measurement based on ICD codes and include 1 that would be categorized as 'moderate' using VA/DoD common definition. Pain assessment not validated but standard.	Post-9/11 SMs that incur minor-to-moderate deployment injuries as recorded in deployment healthcare database and complete both PDHA and PDHRA within 1-year post-deployment.
Patil, 2011[50]*	0	NA	1	0	Consecutive patients from a single VA polytrauma site. mTBI assessed using CTBIE. Headache pain assessed using question on CTBIE and referral/follow-up at Neurology clinic.	Post-9/11 Veterans receiving care in a single VA (polytrauma network site).
Powell, 2015[43]	1	0	1	0	Fairly selective study sample from 1 site (no information on Veterans/SMs who were recruited but did not enroll). mTBI based on clinical interview and consensus among PhD-level psychologists. General pain assessment non-standard.	Post-9/11 Veterans receiving VA care in Boston that would enroll in TRACTS longitudinal study.
Pugh, 2019[7]	1	NA	1	0	Entire population of VA users. mTBI defined using complex algorithm taking many data sources into account. Pain conditions based on ICD diagnosis codes.	Post-9/11 Veterans who enrolled in and used VA healthcare.
Romesser, 2012[44]	0	NA	1	0	Fairly selective study sample from 2 polytrauma sites. mTBI and pain assessed from patient self-reported	Post-9/11 Veterans assessed in 2 VA polytrauma clinics.

Study *Author, year*	#1	#2	#3	#4	Overall study quality/Quality concerns	Applicability
					clinical questionnaire; unclear if standardized or validated.	
Ruff, 2008[6]	1	NA	1	0	Fairly small sample of consecutive patients at VA polytrauma clinic. mTBI assessed clinically and defined using VA-DoD standard definition. Headache pain measures were self-reported; focused on deployment-related headaches.	Post-9/11 Veterans seeking care for TBI at VA with blast-related mTBI.
Schwab, 2017[51]	1	1	1	1	Sampled from among SMs with positive mTBI screen at 2 sites; used structured interview to confirm mTBI history. Headache intensity assessed using NSI. Excluded participants with potential symptom exaggeration. Loss to follow-up of 34%; compared responders to non-responders and reported few differences.	Post-9/11 Army soldiers with Iraq/Afghanistan deployment history from 2 military sites.
Seal, 2017[4]*	1	NA	1	1	Large study of entire patient population; mTBI assessed using CTBIE; General chronic pain assessed using ICD diagnosis codes, but pain interference assessed using standardized measure from CTBIE.	Post-9/11 Veterans who use VA and completed CTBIE.
Suri, 2017[53]*	1	0	1	1	Large multi-site sample of VA users that completed CTBIE, considered gold standard assessment for mTBI. Pain measures standard and/or validated (pain interference question from NSI).	Post-9/11 Veterans who use VA and completed CTBIE.
Suri, 2019[52]*	1	NA	1	0	Large multi-site population of VA users that completed CTBIE, considered gold standard assessment for mTBI; pain assessed using “pain location” measure on CTBIE. Large proportion of Veterans excluded because of missing data.	Post-9/11 Veterans who use VA and completed CTBIE.
Theeler, 2012[54]	0	0	1	0	Participants from 1 site; enrolled based on positive mTBI screen but presumed confirmed in TBI clinic. Demographics not reported. Unknown if pain measure was standardized or validated.	Post-9/11 SMs who had a deployment-related concussion in Iraq or Afghanistan.
Tsao, 2017[55]	1	0	0	0	Sample of post-deployment SMs from 3 sites; unclear what proportion of recruited SMs participated and how responders differed from non-responders. mTBI assessed using screening questions (VA-DoD common definition). Headache pain assessed using non-	Post-9/11 male Marines returning from Iraq/Afghanistan deployments at 1 of 3 sites in the US.

Study *Author, year*	#1	#2	#3	#4	Overall study quality/Quality concerns	Applicability
					standardized/validated item(s) on questionnaire.	
Vanderploeg, 2009[56]	1	0	0	0	Random-sample and in-person assessments. No description of non-respondents. Non-standard measures of mTBI and pain.	Male Vietnam-era Army Veterans.
Walker, 2018[57†]	1	0	1	1	Fairly selective study sample from 4 sites (no information on Veterans/SMs who were recruited but did not enroll). Standardized and validated measures of mTBI and pain were used.	Post-9/11 Veterans/SMs with combat exposure enrolled in a comprehensive longitudinal study.
Webb, 2015[58]	1	NA	0	0	Entire population of Military Health System users across multiple sites. mTBI defined using CDC-recommended series of ICD diagnosis codes. Headache and migraine pain based on ICD diagnosis codes.	Post-9/11 Air Force SMs who used Military Health System between 2001 and 2008.
Wilk, 2010[60]	1	0	0	1	Survey from single-site with 57% response rate, no information on non-respondents. mTBI assessed using screening questions. Pain measures assessed using validated instrument (PHQ-15). Bivariable analyses only in blast/non-blast comparisons.	Post-9/11 Army SMs shortly after return from high-combat deployment.
Wilk, 2012[59]	1	0	0	1	Survey from single site with 73% response rate, no information on non-respondents. mTBI assessed using screening questions. Pain measures assessed using validated instrument (PHQ-15).	Post-9/11 Army SMs shortly after return from combat deployment.

*Study based on VA Comprehensive TBI Evaluation (CTBIE) data. †Chronic Effects of Neurotrauma Consortium (CENC) longitudinal cohort study.
Abbreviations: CDC=Centers for Disease Control and Prevention; CTBIE=Clinical TBI Evaluation; DoD=Department of Defense; ICD=International Classification of Diseases; mTBI=Mild Traumatic Brain Injury; SMs=Servicemembers; VA=Veterans Affairs; VISN=Veterans Integrated Services Network; PTSD=Posttraumatic stress disorder; NA=Not applicable

Quality Assessment Criteria

1. **Representativeness of the sample:**
   1=Truly representative of the target population
   1=Somewhat representative of the target population
   0=Selected subset of Veterans/SMs
   0=No
2. **Non-respondents/non-enrolled:**
   Enter 0 or 1:
   1=Comparability between respondent and non-respondent characteristics is established; response rate is satisfactory
   0=Comparability between respondents and non-respondents is unsatisfactory; response

rate is unsatisfactory
0=No description of the characteristics of the responders versus non-responders; no description of response rate
NA=EHR studies (patient does not opt in versus opt out)

3. **Were objective, standard criteria used for measurement of mTBI?**
   Enter 0 or 1:
   1=Validated measures (*eg* any that uses VA/DoD common definition with clinical interview)
   0=Administrative codes
   0=Non-validated (*eg*, reported concussion, self-report, initial screen)
4. **Were standard, validated criteria used for measurement of chronic pain?**
   Enter 0 or 1:
   a) All measures standard and/or validated? (if some are validated and some are not, note which get 1 or 0)
   1=yes
   0=no, self-report measure; not validated for chronic pain measurement
   0=no, proxy measure used (*eg*, opioid medication use)

APPENDIX D. STUDIES EXCLUDED AT FULL TEXT LEVEL

Excluded publication type

Barrett RS. Post-traumatic headache. Combat soldiers are suffering. Adv NPs PAs. 2012;3(1):33-34.

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No outcome of interest

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Theeler BJ, Flynn FG, Erickson JC. Headaches after concussion in US soldiers returning from Iraq or Afghanistan. Headache. 2010;50(8):1262-1272.

Walker WC, Franke LM, Sima AP, Cifu DX. Symptom Trajectories After Military Blast Exposure and the Influence of Mild Traumatic Brain Injury. J Head Trauma Rehabil. 2017;32(3):E16-E26.

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Wu E, Graham DP. Association of Chronic Pain and Community Integration of Returning Veterans with and Without Traumatic Brain Injury. J Head Trauma Rehabil. 2016;31(1):E1-12.

Excluded study design

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Erickson JC. Treatment outcomes of chronic post-traumatic headaches after mild head trauma in US soldiers: an observational study. Headache. 2011;51(6):932-944.

Hoot MR, Khokhar B, Walker WC. Self-report Pain Scale Reliability in Veterans and Service Members with Traumatic Brain Injuries Undergoing Inpatient Rehabilitation. Mil Med. 2019;09:09.

Janak JC, Cooper DB, Bowles AO, et al. Completion of Multidisciplinary Treatment for Persistent Postconcussive Symptoms Is Associated with Reduced Symptom Burden. J Head Trauma Rehabil. 2017;32(1):1-15.

Leung A, Fallah A, Shukla S, et al. rTMS in Alleviating Mild TBI Related Headaches--A Case Series. Pain physician. 2016;19(2):E347-E354.

Ruff RL, Riechers RG, 2nd, Wang XF, Piero T, Ruff SS. For veterans with mild traumatic brain injury, improved posttraumatic stress disorder severity and sleep correlated with symptomatic improvement. J Rehabil Res Dev. 2012;49(9):1305-1320.

Ruff RL, Ruff SS, Wang XF. Improving sleep: initial headache treatment in OIF/OEF veterans with blast-induced mild traumatic brain injury. J Rehabil Res Dev. 2009;46(9):1071-1084.

Yerry JA, Kuehn D, Finkel AG. Onabotulinum Toxin A for the Treatment of Headache in Service Members with a History of Mild Traumatic Brain Injury: A Cohort Study. Headache: The Journal of Head & Face Pain. 2015;55(3):395-406.

Duplicate publication of included study

Ferdosi H, Schwab KA, Metti A, et al. Trajectory of Postconcussive Symptoms 12 Months After Deployment in Soldiers with and Without Mild Traumatic Brain Injury: Warrior Strong Study. Am J Epidemiol. 2019;188(1):77-86.

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APPENDIX E. PEER REVIEW COMMENTS/AUTHOR RESPONSES

Reviewer Number	Comment	Author Response
Are the objectives, scope, and methods for this review clearly described?		
1	Yes	
2	Yes	
3	Yes	
4	Yes	
5	Yes	
6	Yes	
7	Yes	
8	Yes	
9	Yes	
10	Yes	
Is there any indication of bias in our synthesis of the evidence?		
1	No	
2	No	
3	No	
4	No	
5	No	
6	No	
7	Yes - This review had tremendous amount rejection of articles. Would like to see a list of articles that were rejected by a third reviewer, as opposed to those that had 2 reviewers that agreed.	We understand this point. Our search terms were purposely broad to identify all possible papers with data on TBI and pain. This resulted in a large number of irrelevant studies that were excluded upon review of abstracts or full text for reasons such as focusing on moderate/severe rather than mild TBI, or being conducted in civilian samples (i.e., outside of the scope of this review). Inclusion/exclusion determinations were based on dual review and consensus. We now include a table of studies that were excluded after the full text review (Appendix D).
8	No	
9	No	
10	No	
Are there any published or unpublished studies that we may have overlooked?		
1	No	
2	No	
3	Yes - For awareness and potential mention- study of VHA cohort just published: Amy L. Byers, Yixia Li, Deborah E. Barnes, Karen H. Seal, W. John Boscardin & Kristine Yaffe (2020) A national study of TBI and risk of suicide and unintended death by overdose and	Thank you. We have cited this new publication in the Introduction and Discussion sections of the report.

	firearms, Brain Injury, 34:3, 328-334, DOI: 10.1080/02699052.2019.1701708	
4	No	
5	No	
6	No	
7	No	
8	No	
9	No	
10	No	
Additional suggestions or comments can be provided below. If applicable, please indicate the page and line numbers from the draft report		
1	This is a well-conducted and well-described review. I have only a few minor suggestions.	We appreciate the feedback.
	Page 16: The authors have been appropriately inclusive in their selection criteria for studies of chronic pain and have not applied a strict definition of chronic pain; however, I think it would be helpful to provide a standard definition of chronic pain (e.g., IASP, National Pain Strategy) in the introduction.	Thank you for this suggestion. We have added a definition of chronic pain to the Introduction section of the report.
	Page 58, lines 23-34: I think it is misleading to describe use of ICD-9/10 codes as "comprehensive diagnostic assessment." ICD-9/10 do not include a systematic approach to chronic pain, so studies using these codes typically infer the presence of chronic pain from codes that indicate the presence of a symptom (e.g., low back pain), imaging finding (e.g., disc degeneration), or disease (e.g., osteoarthritis) that may or may not be associated with chronic pain. Perhaps the best way to think about most of these codes is as "diagnoses potentially related to chronic pain." Clinicians often do not code comprehensively, but typically chose codes for reasons related to billing. This could lead to under or over coding. In most cases when chronic pain is present, clinicians have little incentive to add codes for pain-related diagnoses because they add little to the overall complexity of the visit. In some cases, such as when patients have a service-connected condition potentially related to chronic pain, clinicians may code a pain-related diagnosis to spare a patient a copay, even if the condition was briefly discussed and determined not to be bothersome.	Thank you for this information. We agree that ICD diagnosis codes do not necessarily equate to chronic pain and there are circumstances when the use of these codes may increase false positive or false negative rates. We have edited the report to include this as a limitation to the conclusions drawn from studies using ICD codes. Additionally, we have reviewed and edited the report for use of appropriate language, including the suggested "diagnoses potentially related to chronic pain."
2	This reviewer appreciates the efforts put forth to produce this review. Methods are clearly articulated and implemented.	We appreciate this feedback.
	*May be helpful to clarify that the most robust study - Key Question 1 - CTBIE - findings - are for that specific cohort. The fact that those in this group also had the most comprehensive	We agree. We have added additional information about the CTBIE to the Results section, including potential caveats when interpreting findings from these studies.

	eval creates further challenges in terms of interpretation.	
	*The role of co-occurring MH sx could be further integrated throughout. If this is not possible - may be helpful to identify as a limitation.	Though this was outside the scope of Key Question 1, Key Question 2 examined suicide-related outcomes (evidence from 1 study). Key Question 3 examined whether benefits or harms of treatment differed by mental health comorbidities, though due to the small number of studies and participants relevant to this key question, we were unable to generalize about potential impacts of mental health comorbidities. We have noted this as a limitation of our review and recommended it as a future research area in the discussion. We have also included a discussion section highlighting differences in prevalence estimates for individuals with PTSD: “Although we did not find strong evidence suggesting that pain prevalence varied by mTBI etiology, it was clear across studies that, when examined, pain prevalence levels were substantially higher among those with comorbid PTSD. Although the assessment of pain prevalence by comorbid PTSD was not a specified focus of KQ1, the consistency of this finding across studies is noteworthy, particularly given the high prevalence of diagnoses PTSD among those with a history of mTBI. This finding lends further evidence to prior discourse about the “polytrauma clinical triad”[25] and has implications for the ongoing clinical management of Veterans and SMs with mTBI.”
	*In addition, further discussion of multiple pain types and clinical implications would be useful.	We have included a description of pain definitions in the evidence tables to facilitate comparisons across different definitions of pain used in the included studies. Few studies reported the prevalence of participants with multiple pain types; however, where possible, we have added this information to the Results section as well as a description of the clinical implications in the Discussion section.
3	1. P4 (line 46) Consider reporting the higher rates of suicide in Veterans with history of mTBI (beyond non-TBI or all Veterans). Given that suicide is VA's clinician priority, it may be prudent to briefly summarize findings from published, peer-reviewed studies on the prevalence of suicide following TBI. This may serve to highlight it's importance for this	We have added text and references to the Executive Summary identifying the higher rates of mortality, and suicide mortality, among Veterans with a history of mTBI. In the full Introduction section, we have added a paragraph describing the findings from past peer-reviewed studies.

	population in light of the lack of studies that met the ESR's criteria.	
	2. The ESR on mTBI and pain could be stronger by mentioning the contributions of other factors, including prevalent medical/mental health comorbidities to pain/symptom chronicity. Along the same lines, the conclusion could be more compelling from a clinical, research and VHA policy perspective if there was brief mention of the impact of co-existing mTBI and pain on (for example) long-term healthcare utilization, functional outcomes and quality of life.	We agree with this recommendation and have added more information on the consideration of comorbidities in the included studies and the potential interplay of comorbidities with chronic pain among those with mTBI. Similarly, we have included a brief reference to likely healthcare utilization, functional outcomes, and quality of life in this patient population.
	Very interesting to read and informative ESR. Thank you.	We appreciate this feedback.
4	This is a very nice review and summary of the literature. I appreciate the authors grouping of the studies and the fact that the summary results were not overstated. I would like to recommend a paragraph in the executive summary that provides a high level overview of the noted gaps in the literature as this would be helpful for future grant applications to reference. There body of the report could include a short discussion of the gaps in the literature and challenges (lack of consistent use of similar outcome measures, impact of co-morbid MH diagnosis and pain prevalence which is already described on page 64, recommendations to include suicide risk assessment in future studies, and need for treatment studies). Overall very nicely done.	Thank you for this suggestion. We have added a paragraph to the executive summary identifying the gaps and challenges and have now better highlighted this throughout the report, including additional text in the Discussion section.
5	P 2 line 49 figure 2 Insert comment/analytics about the reasons for the wide range of reported prevalence's and how this affects report utility.	We have added text describing the likely reasons for heterogeneity in prevalence estimates as well as the effect on report utility.
6	As expected, this is a critical, comprehensive, unbiased, and important review of the scientific literature regarding co-occurring TBI and pain that identifies both the limited available high quality literature and the lack of clinically important associations. I have no significant recommended edits or additions.	Thank you. We agree this review highlights gaps in the current literature and important next-steps for addressing chronic pain among Veteran and military populations with a history of mTBI.
7	Would like a list of publications that required a tie-breaker vote.	We now include an appendix (Appendix D) with the list of studies excluded after full text review. We used dual review and team consensus to determine study eligibility.
8	This Evidence Synthesis Program review is both timely and significant in light of growing attention to chronic pain as a significant public health and clinical problem, particularly for Veterans and Military Service Members (SMs).	We appreciate this feedback.

	Overall, the report is very well done. Prespecified key questions were addressed appropriately via strong and well-supported review and thoughtful and comprehensive discussion of the findings. Although there are numerous concerns about the reliability and reproducibility of the findings, the authors have generally acknowledged serious limitations of the existing literature and the approach to answering the questions. The methods employed in the search process are state-of-the-art and encourage confidence that the literature relevant to addressing key questions was identified and considered. The description of individual studies identified in the search is a strength of the report. Tables are particularly valuable in capturing key features of individual studies. While the authors' efforts to draw conclusions based on a summary of these findings given the heterogeneity of the studies and their approaches is admirable, summary statements and conclusions based on this review are likely to be less than optimally useful in informing operational partner interests in identifying actionable recommendations for improving the care of Veterans and SMs with co-occurring mTBI and chronic pain.	
	Numerous concerns and recommendations for improving the quality of the report, most of which already acknowledged by the authors, can be cited. In the Executive Summary, care is taken to explicate how "chronic pain" was ascertained. However, the examples don't provide confidence since standard definitions of chronic pain abound, and none would consider pain lasting 30 days as "chronic." I think that inclusion of studies that explicitly including persons with pain for only the past month is a mistake. Surely, most people experiencing a significant TBI will experience acute head pain, and since TBI in this population commonly is associated with polytrauma, that is, injury to other sites, as well, acute pain may occur in sites other than the head and face, as well. Multiple other caveats should be noted, even in the Executive Summary. For example, arthritis can be painful, but for many who have a diagnoses of osteoarthritis, for example, pain may be rare (people with the disease can go long periods without any pain, and even then,	We agree that there are limitations related to broadly defining chronic pain in this manner. Though we include more studies, it is not as clear that all participants met a more conservative definition of chronic pain when the definitions are allowed to vary so greatly. We have attempted to mitigate this concern by providing definitions of chronic pain used in each of the primary studies in the evidence tables. We can also assume that in many cases, when a participant responds that they have had pain for at least 30 days, that the pain lasted longer than that period of time in many cases (i.e., many positive endorsements of this item likely indicate chronic pain, though some cases might possibly reference acute pain lasting just over 30 days). This is particularly likely because many pain assessments were reflective of routine follow-up assessment of pain, not assessments completed at the time of injury (i.e., one can assume that the pain lasted longer than 30 days). Other assumptions such as that a diagnosis of osteoarthritis is associated with chronic

most “flares” are short in duration) and it can certainly not be assumed that people with a diagnosis of arthritis experience chronic pain. Also, the currently accepted nomenclature increasing distinguishes “chronic pain” and “high impact chronic pain.” A note about this potentially important distinction would be helpful.	pain are well supported in the literature, though our description of the chronic pain measures and definitions in each included study enables readers to select and examine only those with a more narrow and specific definition if they so choose. Finally, we mention the distinction between chronic pain and high impact chronic pain in the revised discussion section, though note that most included studies were published prior to this terminology being commonly used.
Realizing that many studies reported on prevalence of headache or migraine as a single group, I’m not sure of the value of this approach given that migraine is understood to be a specific condition that is quite distinct from other headache conditions. In the context of mTBI, this difference may be particularly important.	We agree that these are distinct conditions and have now made edits throughout the report to help distinguish these two types of pain conditions. We have reported data for headache and migraine prevalence separately when the distinct data were reported separately in the primary studies. Of the 23 included studies for Key Question 1, only 1 combined headaches and migraines; 4 reported both outcomes separately, and the remaining 18 reported only headaches with no mention of migraines.
Also, as important is the definition used to define mTBI, so I think this should be added. This is not a minor point, since it could have been expected that an answer to key questions hinges on the operational definition of both mTBI and chronic pain that is applied in the search.	We agree and have added a standard definition of mTBI to the report. We chose to include studies with a range of approaches for operationalizing “mTBI” in order to include all available and relevant data for the Key Questions of interest. Though this means that some studies were included that may have used a broader definition of mTBI than that we cited, we have described these approaches in the evidence tables and considered the definitions and operationalizations in the data synthesis. Readers who are interested in a more specific definition or operationalization of “mTBI” can utilize the evidence tables to examine only the studies using definitions relevant to their questions of interest.
Bottom of page 1 (page 9/94) - Reference to “pain medication” includes “non-analgesics” as example; it is unclear what is meant by a non-analgesic pain medication. The authors probably intended to refer to “non-opioids” such as NSAIDS and/or “co-analgesics” such or anti-depressants or gabapentinoids.” This is not a minor point, since many medications have analgesic properties and are commonly used for purposes other than pain management (even NSAIDs).	We appreciate this point. The original publication provides no additional detail about this category of data and the two publications that reported data from the same parent study did not include a category with this label. We have therefore removed “non-analgesic pain medication” from the findings section of the report.

Be more careful in use of terms such as "directly related to mTBI." (Page 2) How is this term defined? For example, does it mean that the onset was at the same time? Or that there was evidence of trauma to the specific site? Although one might conclude that "headache" could be associated with TBI, that's not necessarily the case, since headache is known to be common in younger persons including an unknown proportion of SMs prior to their military service. And, of course, TBI is often associated with traumatic injury to other body sites, including painful traumatic injuries. Or pain may emerge in the context of prolonged bed rest and/or activity restrictions and other factors, even other treatments, in the context of acute treatment for TBI.	Thank you for bringing this to our attention. We have revised the language in the report to better represent the variety of circumstances in which individuals with mTBI may experience chronic pain (and, in most cases, our inability to distinguish between them).
I'm not sure how valuable Figure ii is. It seems likely that there are many factors that affect prevalence estimates of chronic pain across studies reporting on specific sites, so it doesn't seem helpful to know how estimates vary within pain site and to try to compare them across sites, as implied by presenting the estimates in a single figure.	We have included Figure ii to summarize findings from Key Question 1 and not necessarily to compare prevalence levels across pain conditions. We have retained this Figure because we believe it helps depict the state of the science on pain condition prevalence in Veterans and Servicemembers with mTBI.
The first sentence on page 3 should be referenced and information about the methodology, and a critique of the weaknesses of the study, should be provided. The CTBIE should be described. Is it a clinical exam or self-report measure?	Thank you. We have added a citation to this sentence and provided more context about the study, including the CTBIE.
I note that later in the Summary, a point is made that this measure is completed by treatment-seeking patients. Of course, this fact suggests that the estimates of prevalence of chronic pain in such samples will be highly inflated (if one is interested in true population level estimates). The following sentence about an observational study using VA health record data seems at least as relevant; I'm not sure why the estimates reported in this study are questioned whereas the estimates from the former "best" study are not.	We concur that estimates will be greatly influenced based on whether participants are seeking treatment or part of a general, non-treatment seeking sample. We have edited this section to provide better consistency in our evaluation of study samples. Additionally, we have included this consideration in our risk of bias assessment of the included studies and provided detailed information regarding the samples and inclusion criteria to transparently provide readers with information pertaining to potential sources of bias.
On page 3, the term "pain interference" is introduced and should be defined. How was 'moderate to severe pain" defined? Note that the concept of having pain on half the days in a specific time frame is an accepted way to operationalize "chronic pain" although a minimum three-month period (or six-month) is usually required.	Thank you. We have now defined "pain interference" as well as pain severity levels.
Again, headache and migraine should not be considered as a single "pain type." They are	As noted above, we have now been more careful to distinguish between these two

quite distinct and should not be considered together. Also, note that these diagnoses are known to be poorly identified by clinicians and particularly poorly captured in the electronic record.	distinct conditions in the report. We reported prevalence data for the conditions separately when the data were reported separately in the primary studies. Of the 23 included studies for Key Question 1, only one combined headaches and migraines; 4 reported both outcomes separately, and the remaining 18 reported only headaches with no mention of migraines.
The paragraph beginning with “Five studies” on page 3 is not useful without explication of how medication use was employed to define presence of chronic pain.	Thank you. We have clarified this paragraph and revised other locations in the report where pain medication use is used as a proxy measure for chronic pain.
With regard to KQ1b, etiology is apparently solely defined in terms of history of blast-injury and LOC. Another important factor studied in the literature is whether pain is at the site of traumatic injury, so since TBI often occurs in the context of multiple sites of injury, and since sites of pain other than the face or head are being examined, then whether the onset of pain co-occurred with the mTBI may also be important.	This is an interesting point and one that we would like to include in the report. However, the included studies do not report details on polytraumatic sites of injury or timing of pain onset. We have included this point as a potential limitation of the review findings and a gap in the current literature.
With regard to KQ1c, the issue of pain measurement is critical. As already noted, inferring the presence of chronic pain from ICD or medication use data is fraught with problems. In addition, the population from which study samples were derived is also a critical variable. Prevalence estimates from samples of treatment seeking persons will clearly result in inflated estimates. And although some ICD codes specifically include the word “chronic” in the name of the diagnosis, most potentially painful conditions do not. The report from Goulet et al., 2016 noted that a large proportion of Veterans with musculoskeletal diagnoses such as osteoarthritis reported no pain on the date of the diagnosis. Even more problematic is inferring the presence of chronic pain from health record data on medication fills. Greater clarity in the description of the approaches employed both in the studies and during the review is important to encourage confidence in the results of the review.	We agree with the reviewer on each of these assessments. Per our prior responses, we have added text to the report to clarify the pain assessment methods used in each of the studies and to acknowledge the limitations inherent to these methods. We have also now cited the Goulet et al. 2016 paper in the Discussion section of the report.
The bottom line is that the detailed reporting of the prevalence rates reported in the literature is not particularly relevant given all the apparent differences in the methods across studies from which these estimates were derived. It seems to me that it would be more important to summarize the variations and limitations of the literature rather than presenting estimates that are almost certainly unreliable and not	We understand this recommendation. In the revised report, we have taken care to specify the variations and limitations of the literature and to not make inferences based on disparate study types. Additionally, the referenced conclusion statement has now been moved to an earlier section of the Executive Summary to help highlight this point.

	meaningful. The conclusion in the paragraph on the top of page 4 should be moved to the front of the summary.	
	Although I was a member of the Technical Expert Panel that helped develop the key questions and approach, in retrospect, it seems that the review was likely misguided. Rates of chronic pain are known to be high among Veterans and SMs. A CDC MMWR published in 2017 reported that Veteran status was specifically and uniquely associated with the presence of chronic pain. Other data on Veterans and SMs also encourage similar conclusions. The key question is not whether prevalence rates are high among Veterans and SMs with histories of mTBI, it's whether the rates of chronic pain are higher in this subpopulation than among the general population of Veterans and SMs.	We agree with this sentiment. Although the Key Questions and approach remain the same, we have taken this opportunity to revise the results section for Key Question 1 so that, where available, prevalence estimates of chronic pain are included for those with, versus without, a history of mTBI. We have also added a summary of these findings to the Executive Summary and to the Discussion section.
	Similarly, KQ3 might have been more appropriately specified as whether there is evidence that Veterans and SMs with mTBI are less likely to accrue benefit from commonly delivered interventions for chronic pain. In the absence of answers to these questions, it seems that current policies for universal screening for the presence and intensity of pain, and for suicide risk assessment, should continue, and that Veterans and SMs with histories of mTBI should continue to be offered evidence-based treatments for chronic pain.	Thank you for this feedback. We have added additional information about this important consideration to the discussion of Key Question 3.
9	Line 17 P1: Helpful to include databases searched in the summary as described on P10 Search Strategy.	Thank you. This has been added to the summary.
	Huge variability in the incidence of headaches - 3 - 98%. What could this be attributed to?	We agree. The wide range is likely due to variation in study design, particularly in samples, pain definitions, and pain ascertainment periods. This has been added to the report.
	It is extremely interesting that the analysis started with >2000 pubs but only 31 made the "cut". Are your inclusion/exclusion criteria too stringent? Can you use some of the studies or parts of studies not meeting criteria? There is a paucity of studies in the area and most of these studies are of poor quality.	Our search terms were purposely broad to identify all possible papers with data on mTBI and pain. This resulted in a large number that were excluded upon review of abstracts or full text. Inclusion and exclusion determinations were based on dual review and consensus. We now include an appendix (Appendix D) table of studies that were excluded after the full text review.
10	Page 25 line 22-23 has an incomplete sentence.	Thank you. We have edited this sentence.
	Table 2: Reference 4 also provided prevalence of "other pain". This is other musculoskeletal pain including arthritis. If the mixed definition is	We agree and have added the data from this reference to the "other pain" section.

	the reason for exclusion of this, that makes sense. If the authors think this should be included it could be added to the other pain aspect of Table 5	
	For the study examining suicide, it may be worthwhile to also note that the phenotype that transitioned from relatively healthy to Polytrauma phenotype where chronic pain emerged between year 1 and 5 also had significantly higher odds of suicidal ideation/attempt after the phenotype development period.	Thank you. We have added the Moderately Healthy + Decline phenotype to these findings.