CLINICAL PRACTICE GUIDELINE: HEADACHE (8A)

SYSTEMATIC REVIEW FOR IMAGING OF HEADACHE

CPG 8A Abstract (Updated December 2019)

Headache (HA) is one of the most common symptoms evaluated by primary care, emergency room, and general neurology providers (Goldstein et al., 2006). The decision whether to perform neuroimaging in such patients represents a frequent diagnostic challenge. To facilitate assessment and management of these patients, it is helpful to categorize headaches as '**primary**' or '**secondary**.' The differentiation between primary and secondary HA disorders is based upon pattern recognition with clinical assessment involving a thorough history and neurologic exam. **Primary** headaches, such as migraine, tension, are best understood as not possessing warning signs/symptoms with their pattern stable and history longstanding (greater than 6-12 months, unless younger child). Neuroimaging is not indicated as the underlying cause is physiological, i.e. HA itself is the disorder. Conversely, **secondary** headaches such as those related to infection, bleeding, or mass lesions warrant radiographic imaging to further elucidate the underlying process causing pain. Along these lines, several 'warning' signs/symptoms have been identified that signify an increased likelihood of brain pathology (that is headache 'secondary' to another pathology). These include the "SNOOP" or "S2NOOP4" mnemonic (Do et al., 2019; Dodick, 2003; Micieli & Kingston, 2019):

- Systemic symptoms (fever, weight loss) or secondary risk factors (HIV+, cancer, autoimmune disorder)
- Neurological symptoms or signs
- Onset: sudden, abrupt, peak within minutes
- Older: new onset and progressive headache, age >50 years
- Papilledema (increased pressure causing optic nerve to swell)
- Chronic headache that has changed in nature/intensity
- Precipitated by Valsalva (moderately forceful attempt at exhaling against a closed airway), exertion, etc.
- Postural, positional (headache changes with different positions)
- Pregnancy (Robbins et al., 2015)

The importance of a thorough neurologic exam in differentiating primary from secondary HA cannot be overemphasized. This approach is supported by extensive literature which has demonstrated that patients with abnormal neurologic findings are more likely to have significant brain pathology compared to those with normal exams—that is neuroimaging yields very little in the

absence of risk factors/’warning’ symptoms if the neurologic examination is normal (Evans, 1996; Mitchell et al., 1993; Sempere et al., 2005). Nonetheless, the decision to image or not to image in the setting of HA remains one of clinical judgment as there are no randomized, controlled trials that specifically indicate when neuroimaging is indicated (or when it is not). Further, it is unlikely that such data will be available in the future as blinding and randomization to conduct such studies pose ethical issues.

In the evaluation of patients with HA, different imaging modalities have different strengths and thus different indications. Magnetic resonance (MR) imaging, for example, provides excellent soft tissue detail and is generally more sensitive than computed tomography (CT) imaging for detecting edema, vascular lesions, tumors, and other types of intracranial pathology, particularly in the posterior fossa (brainstem and cerebellum). CT imaging, on the other hand, is very accessible, less costly, and generally more expeditious in urgent care settings when concern for infection, traumatic injury, or hemorrhage is high. Although CT is preferred for suspected subarachnoid hemorrhage (SAH), it is important to note that timing of the scan is critical--when performed within 6 hours of HA onset, the sensitivity of CT for SAH is 100%. This falls to 93%, however, after 6 hours, and continues to drop as time progresses (Perry et al., 2011). As such, MR becomes the more sensitive test for “late” identification of SAH (Mitchell et al., 2001). Lumbar puncture (LP) for cerebrospinal fluid analysis is indicated in HA patients when clinical suspicion of SAH persists despite normal imaging and when suspicion of an infectious or inflammatory etiology for HA is present.

Diagnostic strategies also vary with suspected etiologies for secondary HA. Giant cell arteritis (GCA), also known as temporal arteritis, is an inflammatory vasculopathy and in suspected cases initiating immediate treatment is recommended. Clinical assessment that utilizes the American College of Rheumatology criteria is the reference standard for the diagnosis of GCA (Hunder, 1990). In pregnancy, HA symptoms should prompt neuroimaging (MR or CT) especially when abnormal neurologic exam findings are present as a high incidence of cerebral venous thrombosis, pituitary adenoma and pituitary apoplexy, and posterior reversible encephalopathy syndrome (PRES) has been reported in this population (Ramchandren et al., 2007; Robbins et al., 2015).

Once SAH has been determined, advanced imaging modalities may be used to determine the etiology of the SAH using any of the methods (Westerlaan et al., 2011). The advanced imaging modalities to evaluate the lumen of cerebral arteries include computed tomography angiography (CTA), magnetic resonance angiography (MRA), and digital subtraction angiography (DSA). All three methods can also evaluate vein patency, however CT venography (CTV) and MR venography (MRV) are traditionally done independently of CTA and MRA. Currently, gadolinium enhanced MRV is the “gold standard” for evaluation of the cerebral venous system (Agid et al., 2008).

Multiple factors affect the decision-making process when evaluating the appropriateness of ordering imaging studies. These include cost (both initial and 'downstream'), availability, patient preference and expectations, radiation exposure concerns, prior imaging results, and presence of contraindications for a specific modality. Further, such factors are not always quantifiable and frequently vary across therapeutic settings. Panelists review available literature to recommend appropriate imaging studies in specific clinical scenarios but acknowledge that these other variables impact the decision-making process and are not necessarily addressed by published literature. In the recommendation justifications, these issues would be part of the consideration, especially when the resulting "grade" is judged to be "Consensus" rather than based upon strong clinical evidence.

Database Sources: PubMed, Google Scholar, Cochrane Central Registry of Controlled Trials, the Cochrane Database of Systematic Reviews

Search Strategy: For the annual update a systematic search and thorough review of the medical literature focused on headache in adults and appropriate diagnostic imaging techniques, published in the last five years through December 2019, was conducted. The advanced search option in PubMed/Medline was used, incorporating the search strategy utilizing Population, Intervention, Comparator, Outcome (PICO) framework.

Keywords: The following keywords (using MeSH and full-text search strings) were used individually or in combination with one another in different permutations and/or combinations using Boolean Operators: Headache, migraine, tension headache, migraine headache, head trauma, mild head trauma, moderate head trauma, thunderclap headache, head CT, MRI brain, lumbar puncture, neuroimaging, brain imaging, primary headache imaging, sinus headache, traumatic brain injury, concussion, post-concussion syndrome, meningitis, sensitivity, specificity, and diagnostic accuracy.

Methods: A total of 2694 articles resulted from the general search for the role of neuroimaging in adults with headaches. References of relevant articles were scanned for potentially missing studies. Titles and abstracts were scanned, and then full articles were reviewed. The articles were evaluated and considered from the following groups: Clinical predictors warranting conservative care versus initial imaging care (80 articles), imaging adults with suspected giant cell arteritis (43 articles), role of CT in adults with self-reported sinus headache (82 articles), CT in headache with sudden and severe onset (31 articles), role of CT in mild traumatic brain injury (23 articles), role of CT in identification of potential surgery candidates in adults with moderate to severe head injury (21 articles), relevance of neuroimaging in adults with persistent headache with suspicions of post-concussive syndrome (47 articles), clinical predictors of MR imaging in adults with headache (30 articles) and clinical predictors of CT prior to LP (lumbar puncture) for adults with suspected meningitis (18 articles). Some articles were considered for more than one group. Finally, these articles were evaluated, based, in part, upon study design, sample size, and public availability. They were further reviewed to see if they answered the respective PICO questions.

Based on 2019 literature review, the following changes have been made to the Headache Clinical Practice Guideline: 1) All PICO's have been revised, relevant literature has been added, and the conclusions & recommendations have been updated based on current evidence. 2) The role of imaging (PET, MR and US) in GCA (Giant cell arteritis) and its impact on management has been discussed in detail and from the literature it was unclear as what should be the preferred imaging modality for diagnosing GCA. Biopsy remains the standard. 3) Ottawa SAH rules were studied along with the role of MR imaging modalities for detecting Sub arachnoid hemorrhage (SAH). Based on literature, CT remains the imaging modality of choice for emergent headache and suspected SAH.

Clinical Focus Questions

PICO #1: In adults with headache (HA), is neuroimaging warranted as part of a "new" headache evaluation for optimal patient assessment?

PICO #2: In adults with new headache and suspected giant cell (temporal) arteritis (GCA), based on ACRh classification, is imaging recommended for optimal patient management?

PICO #3: In adults with self-reported "sinus headache," when should sinus CT be performed as a part of the initial diagnostic evaluation?

PICO #4: In adults with sudden onset and severe headache, does CT offer adequate sensitivity to identify subarachnoid hemorrhage (SAH)?

PICO #5: In adults with headache and minimal to mild traumatic brain injury (Glasgow coma scale 13, 14 or 15) should CT of the head be used to identify significant pathology for optimal patient management?

PICO #6: In adults with moderate to severe head injury should initial evaluation include CT of the head for optimal patient management?

PICO#7: In adults with persistent headache and suspected post-concussive syndrome should neuroimaging be used for optimal patient management?

PICO #8: In adults with headache what clinical predictors warrant MR imaging of the brain for optimal patient management?

PICO #9: In adults with headache and suspected meningitis, is CT of the head warranted prior to LP (lumbar puncture) for optimal patient management?

PICO #1: In adults with headache (HA), is neuroimaging warranted as part of a "new" headache evaluation for optimal patient assessment?

SEMPI Grading QOE—Table 8A.1a—Summary of Findings						
PICO #1: In adults with headache (HA), is neuroimaging warranted as part of a "new" headache evaluation for optimal patient assessment?						
Author/Year/Title	Design	Population	Intervention Vs Comparator	Results	Conclusion Summary	SEMPI QOE Rating
Do et al., 2019 Red and Orange flags for secondary headaches in clinical practice	Review article	N/A	N/A	"Red flags" for secondary headaches: 1) systemic symptoms including fever; (2) neoplasm history; (3) neurologic deficit (including decreased consciousness); (4) sudden or abrupt onset; (5) older age (onset after 65 years); (6) pattern change or recent onset of new headache; (7) positional headache; (8) precipitated by sneezing, coughing, or exercise; (9) papilledema; (10) progressive headache and atypical presentations; (11) pregnancy or puerperium; (12) painful eye with autonomic features; (13) posttraumatic onset of headache; (14) pathology of the immune system such as HIV; (15) painkiller overuse or new drug at onset of headache	New headache patients should be screened for "red flag" signs/symptoms to increase the likelihood of detecting a secondary headache and its etiology	Very Low
Young et al., 2018 Neuroimaging utilization and findings in headache outpatients: Significance of red and yellow flags	Retrospective, cross-sectional study in 1 US community clinic All outpatients with headache (HA) who had neuroimaging in 2015	N=190 outpatients, had 304 neuroimaging studies	N/A	Median age=46.5 years Female gender=65% No prior HA=51% Prior Neuroimaging=15% Imaging post-neurology consult=7% Red-flag Sign/Symptom in 77% Abnormal imaging in Red-flag pts=3% (5/161) • Carotid dissection (n=3) • Reversible cerebral vasoconstrictive syndrome (n=2) Imaging against guidelines=35% (e.g. primary HA disorder, normal neuro exam, absence of red-flag symptom/sign)	The prevalence of serious pathology causing headache symptoms in outpatient settings is low despite the presence of 'documented' red-flag symptoms	Low

				Imaging ordered by: PCP: 66% APPP: 18% Neurologist: 16% MRI: 54.7% MRA brain: 32.6% MRA neck: 16.3% MRV: 2.1% CTA head: 1.6% CTV brain: 1.1% CTA neck: 1.1% Only 5 studies (2.6%) revealed acute abnormality explaining symptoms		
Ifediora, 2018 Insights into radiographic investigations for headaches in general practice	Retrospective chart review 7-year period; Primary care setting HA=headache	N=517 adults with HA N=109 patients had an image obtained	N/A	57%--"recurrent" HA 62%--"severe" 78%--"red flag" symptoms present 109/517 (21%) had imaging (CT or MR) Scan 1 was CT in 83.5% 12/109 (11%)—"likely cause" identified per imaging; no difference between CT vs MR imaging (p=0.41) Patients with psycho-morbidities—less likely to have imaging identify HA cause (OR=0.22, CI, 0.06-0.88; p=0.03) Repeat imaging offered no increased rate of identifying cause of HA	Significant intracranial findings are uncommon in patients undergoing diagnostic imaging for headache	Very Low
Miller et al., 2018 Reduced computed tomography use in the emergency department evaluation of headache was not followed by increased death or missed diagnosis	Retrospective study Assess if 10% decrease in head CT use in ER for headache (HA) eval is followed by increase in mortality or missed intracranial diagnoses	N=582 ER visits following period of 9.6% reduction in head CT for HA; included neuro, ER, primary care providers, 2-yr follow-up	Pre- vs Post-reduction in head CT imaging Death rate and/or missed intracranial diagnoses	After a 9.6% reduction in head CT imaging for HA that resulted from a quality improvement effort, there was no increase in death or missed diagnoses compared to the pre-reduction period: (p=0.337 and p=0.312, respectively) No deaths had a missed intracranial diagnosis	A reduction in diagnostic imaging for assessment of headache can be undertaken without an increase in death or missed diagnoses of significant pathology	Low

Clarke et al., 2010 Imaging results in a consecutive series of 530 new patients in the Birmingham Headache Service	Prospective, 5-year period	N=3655 'new HA' clinic—530 imaged (14.5%) 2 hospitals—UK, "non-acute" Mean age=42 69% female	CT or MR	11 Significant findings (2%) in 530 that got imaged: (6 tumors, 2 AVMs, 1 vasculitis/stroke, 1 neurosarcoidosis; 1 blocked shunt) CT in 226 71.2% normal 27.9% insignificant abnormality 0.9% significant abnormality MRI in 304 51.0% normal 46.1% insignificant abnormality 3.0% significant abnormality **2/167** w migraine - 1.2% **2/212** w tension-0.9% **3/55 (5.5%)** with 'high likelihood' of intracranial disease **3400/3655** (93%) had primary HA diagnosis— migraine, tension, cluster, other **250/3655** (7%) had secondary HA	In patients presenting with headache, the practice of selecting patients with 'suspicious' ('warning', 'red flag') findings for imaging is supported by clinical data, **rather than imaging all patients**	Very Low
Edlow et al., 2008 Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute headache	Clinical Policy/Expert Opinion (American College of Emergency Physicians)	Emergency settings (ED) (43 studies)	CT and MR	Level B Recommendations (Rec) (moderate certainty, Class II, III evidence) 1. Patients presenting to the ED with **HA and new abnormal findings on neurologic exam** (e.g., focal deficit, altered mental status, altered cognitive function) should **undergo** emergent non-contrast head CT. (ED) 2. Patients presenting with **new sudden- onset severe HA** should **undergo an** emergent* head CT. (ED) 3. HIV-positive patients with a **new type of HA** should be considered for emergent neuroimaging (on site) Level C Rec (panel consensus) Patients older than 50 yrs. with new type of HA but with a normal neurologic examination should be considered for urgent neuroimaging	**In the absence of 'warning'/'red flag' symptoms, neuroimaging is not recommended for initial evaluation in patients presenting with headache (HA).** Patients with HA in ED settings with abnormal exam findings ('warning' or 'red flag' signs/symptoms) warrant immediate neuroimaging. Patients in ED setting with new, severe, sudden-onset HA warrant immediate neuroimaging	Moderate

Sempere at al., 2005 [Neuroimaging in the evaluation of patients with non-acute headache]	Prospective, consecutive	N=1876 patients (2012 images) Age=15-95 yr. seen by Primary Care then referred to neurologist Non-acute HA (4 weeks+) New < 1 yr. (1/3 patients) Chronic > 1 yr. (2/3 patients)	CT (1432) or MR (580) (CT+MR=136)	Significant Findings in 22 Patients. (1.2%) 5/22--Abnormal Neuro exam: Likelihood ratio (42, 95%CI of 16-113) Neuro Exam only clinical variable significantly increased the likelihood of finding a significant intracranial lesion 85% of all Patients. had 'primary HA' diagnosis— migraine, tension, cluster	A low rate of significant intracranial lesions on neuroimaging is found in patients with "chronic" headache; an abnormal neurologic exam is the only clinical variable that significantly increases the likelihood of identifying an intracranial lesion in such patients	Moderate
Sobri et al., 2003 [Red flags in patients presenting with headache: clinical indications for neuroimaging]	Retrospective study	N=111 adults with headache	Clinical evaluation versus neuroimaging	Three red flag features proved to be statistically significant (p-value < 0.05) on both univariate and multivariate analysis for the prediction of abnormal neuroimaging. These were: paralysis; papilledema; and "drowsiness, confusion, memory impairment and loss of consciousness".	The presence of three or more "red flags" is highly predictive of abnormal neuroimaging in patients with headache	Very Low
Mitchell et al., 1993 [Computed tomography in the headache patient: is routine evaluation really necessary?]	Prospective, consecutive enrollment at a US military tertiary care hospital (mixed population of referrals from neurology, ED, primary care, and other)	N=350 Excluded if etiology known (History of CA, trauma, seizures) 55%-M 45%-F Age=2-81 yrs. Mean=33 yrs.	CT vs clinical exam (Referral from: 36%--Neuro 27%%--ED 36%--Primary care/other)	7 (**2%**) of 350 had CT findings that were clinically significant 25 (7%) had CT findings deemed clinically insignificant ('false positive') All 7 with significant findings had an abnormal neurologic exam and/or unusual clinical symptoms	In patients being evaluated for headache, only those with an abnormal neurologic exam and/or unusual ("red flag") clinical symptoms demonstrate significant abnormalities on CT neuroimaging	Moderate
Initial QOE Score Across Studies for PICO #1: **Moderate (2)**						

SEMPI Grading QOE—Table 8A.1b—Risk of Bias		
PICO #1: In adults with headache (HA), is neuroimaging warranted as part of a "new" headache evaluation for optimal patient assessment?		
Evaluate Outcome for Risk of Bias Across Studies		
Initial QOE Score Across Studies for PICO: **MODERATE**		
Criteria	**Assessment**	**Reason for Assessment**
Negative Bias		
Risk of Bias	Not Serious	No blinding, incidental findings often categorized as 'significant intracranial lesions', mixed populations of "HA" Patients.
Inconsistency	Not Serious	
Indirectness	Serious	Definition of HA onset varied; chronic HA greater representation than acute HA; 'referral' role of neurologist unclear; some 'pre-screened'
Imprecision	Serious	Incidental vs significant pathology (mixed in some studies—adenoma or pineal cyst not same as malignant brain tumor)
Positive Bias		
Strength of Association	Moderate	Overall low incidence of significant imaging findings in all HA populations (<2%) in literature; consistent agreement across studies that abnormal neuro exam/warming symptoms were predictive of intracranial disease
Other Considerations	No	
Overall Effect of Bias on Initial QOE Grade: Downgraded to LOW		
Final QOE Grade for Outcome Across Studies: **LOW**		

High – Very confident the true effect lies close to that of the estimate of the effect
Moderate – Moderately confident in the effect estimate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different)
Low – Confidence in the effect estimate is limited (the true effect may be substantially different from the estimate of effect)
Very Low – Very little confidence in the effect estimate (the true effect is likely to be substantially different from the estimate of effect)

SEMPI Grading QOE – Table 8A.1c—Evidence to Recommendations				
PICO #1: In adults with headache (HA), is neuroimaging warranted as part of a "new" headache evaluation for optimal patient assessment?				
SEMPI Quality of Evidence (QOE) & Recommendation Strength				
Author/Year/Title	Highlights	SEMPI QOE Rating	Final QOE Category	Recommendation Strength
Do et al., 2019 Red and Orange flags for secondary headaches in clinical practice	A reduction in diagnostic imaging for assessment of headache can be undertaken without an increase in death or missed diagnoses of significant pathology	Very Low	Low (3)	Strong (A)
Young et al., 2018 Neuroimaging utilization and findings in headache outpatients: Significance of red and yellow flags	In patients presenting with headache, the practice of selecting patients with 'suspicious' ('warning', 'red flag') findings for imaging is supported by clinical data, **rather than imaging all patients**	Low		
Ifediora, 2018 Insights into radiographic investigations for headaches in general practice	**In the absence of 'warning'/'red flag' symptoms, neuroimaging is not recommended for initial evaluation in patients presenting with headache (HA).** Patients with HA in ED settings with abnormal exam findings ('warning' or 'red flag' signs/symptoms) warrant immediate neuroimaging. Patients in ED setting with new, severe, sudden-onset HA warrant immediate neuroimaging	Very Low		
Miller et al., 2018 Reduced computed tomography use in the emergency department evaluation of headache was not followed by increased death or missed diagnosis	A low rate of significant intracranial lesions on neuroimaging is found in patients with "chronic" headache; an abnormal neurologic exam is the only clinical variable that significantly increases the likelihood of identifying an intracranial lesion in such patients	Low		
Clarke et al., 2010 Imaging results in a consecutive series of 530 new patients in the Birmingham Headache Service	The presence of three or more "red flags" is highly predictive of abnormal neuroimaging in patients with headache	Very Low		
Edlow et al., 2008 Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute headache	In patients being evaluated for headache, only those with an abnormal neurologic exam and/or unusual ("red flag") clinical symptoms demonstrate significant abnormalities on CT neuroimaging	Moderate		

Sempere et al., 2005 Neuroimaging in the evaluation of patients with non-acute headache	A reduction in diagnostic imaging for assessment of headache can be undertaken without an increase in death or missed diagnoses of significant pathology	Moderate		
Sobri et al., 2003 Red flags in patients presenting with headache: clinical indications for neuroimaging	In patients presenting with headache, the practice of selecting patients with 'suspicious' ('warning', 'red flag') findings for imaging is supported by clinical data, **rather than imaging all patients**	Very Low		
Mitchell et al., 1993 Computed tomography in the headache patient: is routine evaluation really necessary?	**In the absence of 'warning'/'red flag' symptoms, neuroimaging is not recommended for initial evaluation in patients presenting with headache (HA).** Patients with HA in ED settings with abnormal exam findings ('warning' or 'red flag' signs/symptoms) warrant immediate neuroimaging. Patients in ED setting with new, severe, sudden-onset HA warrant immediate neuroimaging	Moderate		

Recommendation Rating: 3A—Strong recommendation for the intervention based on low quality evidence
Justification: Risk of bias sufficient to downgrade quality of evidence

Rating Definitions:

Quality of Evidence: High quality = **1**; Moderate quality = **2**; Low quality = **3**; Very low quality = **4**
Strength of Recommendation: A = Strength of Recommendation from Consistent Evidence; **B** = Strength of Recommendation from Panel Consensus

Conclusion: Most patients presenting with "primary" headache (migraine, tension), do not need neuroimaging. The importance of a thorough neurologic exam and careful history is critical to define the need for neuroimaging based upon extensive literature that demonstrates a high likelihood of significant intracranial pathology in those with an abnormal neurologic exam/presence of "warning" or "red flag" signs/symptoms compared to those without such findings (Dodick, 2003; Starling, 2018). The yield of neuroimaging is very low (generally less than 1-2%) in the absence of "red-flag" signs/symptoms or when the neurologic examination is normal (Evans, 1996; Wang et al., 2019; Mitchell et al., 1993; Sempere, 2005).

Although it has been proposed that "pregnancy" should be added to the list of indications warranting neuroimaging to identify secondary headache disorders, this is not without serious issues and the proper alternatives are not supported by strong evidence (Micieli & Kingston, 2019; Ramchandren et al., 2007; Robbins et al., 2015; Sandoe & Lay, 2019). Depending on urgency/availability/clinical findings, unenhanced CT imaging with adequate shielding to minimize fetal radiation exposure, can be performed as an alternative to MR imaging in pregnant patients presenting with a new headache or one that has changed in severity or symptomatology. Therefore, pregnancy represents a clinical scenario in which consultation between radiologist, ordering provider, and, if possible, obstetrician is required to optimize imaging accuracy while ensuring maximal safety.

Final Recommendation: 3A—In adults presenting with headache, neuroimaging is not recommended in the absence of warning or red flag signs/symptoms, particularly when primary headache conditions (e.g. tension, migraine) are present.

PICO #2: In adults with new headache and suspected giant cell (temporal) arteritis (GCA), based on ACRh classification, is imaging recommended for optimal patient management?

SEMPI Grading QOE—Table 8A.2a—Summary of Findings						
PICO #2: In adults with new headache and suspected giant cell (temporal) arteritis (GCA), based on ACRh classification, is imaging recommended for optimal patient management?						
Author/Year/Title	Design	Population	Intervention Vs Comparator	Results	Conclusion Summary	SEMPI QOE Rating
Sammel et al., 2019 Diagnostic Accuracy of PET/CT Scan of the Head, Neck and Chest for Giant Cell Arteritis: The Double-Blinded Giant Cell Arteritis and PET Scan (GAPS) Study	Prospective, double-blind, cross-sectional study Giant Cell Arteritis and PET Scan (GAPS study)	N=64 with suspected giant cell arteritis (GCA) Clinical diagnosis made at 6-months by consensus between the PET-CT blinded treating clinician and blinded external reviewers	All had PET-CT from vertex to diaphragm within 72 hours of starting corticosteroids and pre-temporal artery biopsy (TAB) PET-CT versus TAB, clinical diagnosis	58/64 (91%) underwent TAB and 12/58 (21%) biopsies +++ for GCA 21/64 (33%) had a clinical Dx GCA and 42 (66%) met 1990 ACR GCA criteria **PET-CT** performance compared to **TAB** (95% CI): Sensitivity: 92% (CI, 62-100) Specificity: 85% (CI, 71-94) NPV: 98% (CI, 87-100 **PET-CT** compared to **clinical diagnosis** (95% CI): Sensitivity: 71% (48-89) Specificity: 91% (78-97) NPV: 87% (73-95) 5/12 TAB +++ patients had aortitis **incidentals** 20% had clinically relevant finding -7 pts with infection -5 pts with malignancy	PET-CT imaging can be used to exclude the diagnosis of giant cell arteritis (GCA) based on a high negative predictive value (98%). PET-CT may be a superior first-line diagnostic test compared to temporal artery biopsy for GCA	Moderate
Dejaco et al., 2018 EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice	Systematic literature review for EULAR guidelines	12 recommendations	US, MR, CT and PET for large vessel vasculitis	In patients with suspected GCA, an early imaging test is recommended to complement the clinical criteria for diagnosing GCA, assuming high expertise and prompt availability of the imaging technique. However, imaging should not delay initiation of treatment. Treatment should never be delayed in patients with a strong suspicion of GCA due to outstanding imaging or other diagnostic tests, because ischemic complications such as blindness occur almost exclusively before initiation of therapy.	Ultrasound of temporal ± axillary arteries is recommended as a first-line imaging modality in patients with suspected cranial giant cell arteritis	Moderate

Luqmani et al., 2016 The role of ultrasound compared to biopsy of temporal arteries in the diagnosis and treatment of giant cell arteritis (TABUL): a diagnostic accuracy and cost effectiveness study	Prospective, multicenter cohort study	N=381 With newly suspected GCA and within 10 days of starting Rx Secondary care setting Mean age=71, 72% Female	US and Biopsy Reference standard ACRh criteria- based Sensitivity/ specificity of US vs Biopsy; or US and Biopsy for diagnosing GCA and interobserver reliability in interpreting US or biopsy results	**Biopsy Sensitivity: 39%** 95% CI, 33% to 46% **US Sensitivity: 54%** 95% CI, 48% to 60% **Biopsy Specificity: 100%** 95% CI, 97% to 100% **US Specificity: 81%** 95% CI, 73% to 88% **US and Biopsy of –US**: Sensitivity up to 65%, Specificity same-81% Reduced Biopsy by 43% **Clinical exam with US: Sens/Spec—93/77% Clinical exam with Biopsy: Sens/Spec—91/81%** Moderate agreement among sonographers (R coefficient-0.6195% CI 0.48 to 0.75; pathology--0.62, 95% CI 0.49 to 0.76)	When clinical assessment is combined with temporal artery US or biopsy, diagnostic accuracy of each improves. The moderate inter-observer agreement for both US and biopsy indicates a need for improved assessment techniques	Moderate
Klink et al., 2014 Giant cell arteritis: diagnostic accuracy of MR imaging of superficial cranial arteries in initial diagnosis-results from a multicenter trial	Prospective, multicenter, referral population	N=185 GCA suspected 98/185—TA Biopsy	MR in all (TA biopsy in half) 2 'gold standards': Clinical diagnosis Or TA biopsy	Clinical Diagnosis as gold standard compared to MR Sensitivity--78.4% Specificity—90.4% Positive TA Biopsy as gold standard: Sensitivity: 88.7% Specificity: 75% "Diagnostic accuracy higher when Corticosteroid Rx <5 days"	Magnetic resonance (MR) imaging of cranial arteries is accurate for early diagnosis of giant cell arteritis (GCA) when biopsy-proven temporal artery involvement is concurrent; MR diagnostic accuracy decreases with time and treatment	Moderate
Diamantopoulos et al., 2014 Diagnostic value of color Doppler ultrasonography of temporal arteries and large vessels in giant cell arteritis: a consecutive case series	Prospective, referral population	N=88 (46 GCA by clinical exam) 39/46 GCA Patients. had TA biopsy CDUS=Color-Doppler US	US temporal artery (TA) vs Biopsy of TA GCA clinical evaluation by Rheumatologist (American College of Rheumatology) Considered 'gold standard'	44/46 GCA (clinical diagnosis) had a positive US of TA Sens./Spec. of TA US: 96%/94% Only 26/39 GCA positive patients had a positive TA biopsy--Sens./Spec.: 67%/95% All positive TA Biopsy =positive US	Ultrasound (US) of temporal arteries demonstrates high sensitivity for giant cell arteritis compared to temporal artery biopsy	Low

Bley et al., 2008 Comparison of duplex sonography and high-resolution magnetic resonance imaging in the diagnosis of giant cell (Temporal) arteritis	Retrospective	N=59 (41 had TA biopsy; 24/41 + GCA) GCA "final diagnosis" at 6-mo follow-up	MR vs US ACRh-criteria based diagnosis as one 'gold standard' TA Biopsy as another 'gold standard'	36/59-GCA by clinical diagnosis 24/41-GCA by +Temporal Artery biopsy Clinical Diagnosis as gold standard: Sensitivity—MR/US: 69% / 67% Specificity—MR/US: 91% / 91% PPV-93%/92% NPV-66%/64% +TA Biopsy as gold standard: Sens: 83%/79% Spec: 71%/59% PPV- 80% /73% NPV-75% / 67%	Magnetic resonance (MR) is comparable to ultrasound (US) imaging in detecting giant cell arteritis but both modalities offer low to moderate sensitivity	Low
Karassa et al., 2005 Meta-analysis: test performance of ultrasonography for giant-cell arteritis	Meta-analysis	23 Studies (N=2036) Patients with suspected or confirmed GCA (some PMR) Age: 67-76 F=40-76%	US compared to Temporal artery biopsy (biopsy) as reference standard	Sensitivity/Specificity: "Halo"—69%/82% Stenosis/Occlusion-68%/77% All 3 findings-88%/78% Post-test probability of GCA positive US vs –US when pre-test: Low—71%/2% Mod—96%/12% High—99%/55%	When pre-test probability is low (<10%) for giant cell arteritis (GCA), a negative US of the temporal artery practically excludes GCA and obviates the need for temporal artery biopsy	Moderate
Initial QOE Score Across Studies for PICO #2: **Moderate (2)**						

SEMPI Grading QOE—Table 8A.2b—Risk of Bias		
PICO #2: In adults with new headache and suspected giant cell (temporal) arteritis (GCA), based on ACRh classification, is imaging recommended for optimal patient management?		
Evaluate Outcome for Risk of Bias Across Studies		
Initial QOE Score Across Studies for PICO: **MODERATE**		
Criteria	**Assessment**	**Reason for Assessment**
Negative Bias		
Risk of Bias	Serious	Selection bias, decision to biopsy/not biopsy missing, all had steroid treatment but for varying durations, 'high dose' steroid treatment not defined, secondary/tertiary settings; wide confidence interval for PET-CT
Inconsistency	Not Serious	
Indirectness	Not Serious	
Imprecision	Serious	Clinical diagnosis used as reference standard, and/or TA biopsy used as reference standard or combination, overall lack of definitive 'gold standard'
Positive Bias		
Strength of Association	Low	
Other Considerations	No	
Overall Effect of Bias on Initial QOE Grade: Downgraded to Low		
Final QOE Grade for Outcome Across Studies: **LOW**		
High – Very confident the true effect lies close to that of the estimate of the effect **Moderate** – Moderately confident in the effect estimate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different) **Low** – Confidence in the effect estimate is limited (the true effect may be substantially different from the estimate of effect) **Very Low** – Very little confidence in the effect estimate (the true effect is likely to be substantially different from the estimate of effect)		

SEMPI Grading QOE—Table 8A.2c—Evidence to Recommendations				
PICO #2: In adults with new headache and suspected giant cell (temporal) arteritis (GCA), based on ACRh classification, is imaging recommended for optimal patient management?				
SEMPI Quality of Evidence (QOE) & Recommendation Strength				
Author/Year/Title	Highlights	SEMPI QOE Rating	Final QOE Category	Recommendation Strength
Sammel et al., 2019 Diagnostic Accuracy of PET/CT Scan of the Head, Neck and Chest for Giant Cell Arteritis: The Double-Blinded Giant Cell Arteritis and PET Scan (GAPS) Study	PET-CT imaging can be used to exclude the diagnosis of giant cell arteritis (GCA) based on a high negative predictive value (98%). PET-CT may be a superior first-line diagnostic test compared to temporal artery biopsy for GCA	Moderate	Low (3)	Strong (A)
Dejaco et al., 2018 EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice	Ultrasound of temporal ± axillary arteries is recommended as a first-line imaging modality in patients with suspected cranial giant cell arteritis	Moderate		
Luqmani et al., 2016 The role of ultrasound compared to biopsy of temporal arteries in the diagnosis and treatment of giant cell arteritis (TABUL): a diagnostic accuracy and cost effectiveness study	When clinical assessment is combined with temporal artery US or biopsy, diagnostic accuracy of each improves. The moderate inter-observer agreement for both US and biopsy indicates a need for improved assessment techniques	Moderate		
Klink et al., 2014 Giant cell arteritis: diagnostic accuracy of MR imaging of superficial cranial arteries in initial diagnosis-results from a multicenter trial	Magnetic resonance (MR) imaging of cranial arteries is accurate for early diagnosis of giant cell arteritis (GCA) when biopsy-proven temporal artery involvement is concurrent; MR diagnostic accuracy decreases with time and treatment	Moderate		
Diamantopoulos et al., 2014 Diagnostic value of color Doppler ultrasonography of temporal arteries and large vessels in giant cell arteritis: a consecutive case series	Ultrasound (US) of temporal arteries demonstrates high sensitivity for giant cell arteritis compared to temporal artery biopsy	Low		
Bley et al., 2008 Comparison of duplex sonography and high-resolution magnetic resonance imaging in the diagnosis of giant cell (temporal) arteritis	Magnetic resonance (MR) is comparable to ultrasound (US) imaging in detecting giant cell arteritis but both modalities offer low to moderate sensitivity	Low		

Karassa et al., 2005 Meta-analysis: test performance of ultrasonography for giant-cell arteritis	When pre-test probability is low (<10%) for giant cell arteritis (GCA), a negative US of the temporal artery practically excludes GCA and obviates the need for temporal artery biopsy	Moderate		
Recommendation Rating: 3A—Strong recommendation for the intervention based on low quality evidence **Justification:** Bias in studies (no definitive standard, treatment ongoing at start of study) is sufficient to downgrade QOE				
Rating Definitions: **Quality of Evidence:** High quality = **1**; Moderate quality = **2**; Low quality = **3**; Very low quality = **4** **Strength of Recommendation: A** = Strength of Recommendation from Consistent Evidence; **B** = Strength of Recommendation from Panel Consensus				
Conclusion: Giant cell arteritis (GCA) or "temporal arteritis," is an inflammatory vasculopathy and a medical emergency. A delay in diagnosis and treatment can lead to serious complications including irreversible loss of visual function. Several imaging modalities have been evaluated for clinical use in GCA including ultrasound (US) of the temporal artery and contrast-enhanced magnetic resonance (MR) imaging. US is highly operator-dependent and the data on usefulness of US has been mixed. MR has shown accuracy in delineation of large and superficial temporal arteries for diagnosis of cranial GCA, but it does not have an established precision for the identification of temporal artery histologic abnormalities (Duftner et al., 2018; Dejaco et al., 2018). Additionally, the sensitivity of MR decreases after the initiation of corticosteroid therapy. Given the high negative predictive value (NPV) of PET-CT for GCA, it can be used to exclude the diagnosis (Sammel et al., 2019). As such, there is no imaging modality that represents an independent diagnostic reference standard for giant cell (temporal) arteritis. Rather, clinical assessment that utilizes the American College of Rheumatology criteria for giant cell (temporal) arteritis maintains consistent results as a reference standard (Hunder et al., 1990; Sait et al., 2016).				
Final Recommendation: 3A—In adults with new headache symptoms and suspected giant cell (temporal) arteritis (GCA), clinical classification based upon American College of Rheumatology criteria (may include biopsy) for GCA, is recommended to diagnose and begin treatment. Imaging does not offer an advantage in guiding patient management.				

For purposes of classification, a patient shall be said to have giant cell (temporal) arteritis if at least 3 of these 5 criteria are present. The presence of any three (3) or more criteria yields a sensitivity of 93.5% and a specificity of 91.2% (Hunder et al., 1990):

1. Age at disease: Signs/Symptoms beginning at age 50 or older
2. New headache: New onset or new type of localized headache pain
3. Temporal artery abnormalities: Tenderness on palpation or decreased pulsation of temporal artery
4. Elevated erythrocyte sedimentation rate: ESR >/= 50 mm/hour by the Westergren method
5. Abnormal artery biopsy: Temporal artery showing vasculitis with mononuclear infiltration or granulomatous inflammation with multinucleated giant cells.

PICO #3: In adults with self-reported "sinus headache," when should sinus imaging be performed as a part of the initial diagnostic evaluation?

SEMPI Grading QOE—Table 8A.3a—Summary of Findings						
PICO #3: In adults with self-reported "sinus headache," when should sinus imaging be performed as a part of the initial diagnostic evaluation?						
Author/Year/Title	Design	Population	Intervention Vs Comparator	Results	Conclusion Summary	SEMPI QOE Rating
Jayawardena & Chandra, 2018 Headaches and facial pain in rhinology	Review: What is best diagnostic approach for possible "**sinus headache**"	N/A	N/A	"Sinus headache" often misunderstood, self- or mis-diagnosed by non-ENT providers Wide differential diagnosis for "sinusitis headache"—migraine, cluster, trigger/contact point headaches, allergic sinusitis, trigeminal neuralgia	With improved technology (reduced radiation risk) and lower cost, CT imaging of the sinuses as an initial assessment tool offers advantages over empiric antibiotic therapy/nasal endoscopy for patients presenting with "sinus headache." Lower microbial resistance and more appropriate non-ENT treatment/referrals can result	Very Low
Pedram et al., 2016 Sinus Headache in Chronic Rhinosinusitis (CRS): An Analysis of Otolaryngology Initiated Treatment Efficacy of Migraine in the CRS Patient	Retrospective review **CRS-chronic rhinosinusitis** International Headache Society (IHS)	N=29 CRS patients with 10 m follow-up N=45 Migraine patients (controls) Control group: Met IHS criteria for migraine headaches and eval for CRS was negative based on CRS task force criteria, sinus CT and nasal endoscopy	Treatment outcomes in Migraine ("sinus HA") patients with or without CRS symptoms	No significant difference in treatment success of migraine headaches in patients with CRS compared to those without (p=0.95)	In "sinus headache" patients with or without chronic rhinosinusitis symptoms, **anti-migraine therapy** improves patient quality of life, eliminates symptom that cloud further rhinosinusitis-directed treatment, and avoids unnecessary sinus surgery	Low

Lohiya et al., 2016 Comparative study of diagnostic nasal endoscopy and CT paranasal sinuses in diagnosing chronic rhinosinusitis	Comparative analysis	N = 100	CT scan paranasal sinuses versus Nasal endoscopy	Compared to CT scan which is the gold standard: Sensitivity (88.04 %), Specificity (28.57 %), PPV (94.19 %), NPV (15.38 %), PLR (1.23), NLR (0.42) p value (0.10565)	Nasal endoscopy can be used as an early diagnostic tool in the evaluation of chronic rhinosinusitis but should be followed by CT imaging if sinuses are not visualized. CT imaging is also useful in patients with refractory symptoms unresponsive to therapy and for patients in whom surgery is planned.	Low
El-Shehally & Sobh, 2014 Is it rhinogenic headache or migraine? The role of sino-nasal endoscope and sinus CT	Prospective Cohort	N= 63 patients enrolled, 50 patients completed study. Divided into two groups based on CT and endoscopy evaluations each was given appropriate treatment for diagnosis and effectiveness of treatment was evaluated	N/A	Group A- Normal sino-nasal endoscopic examination and CT (35 patients) **Migraine diagnosis**- 28 total, 27 with complete remission one with partial remission. **Tension headache**-5 total treatment results not reported **Cluster headache**-2 total- results of treatment not reported Group B- Abnormal sino-nasal endoscopic examination and/or CT (15 patients) **Contact point abnormalities**- 13 total; 10- full remission after treatment; 2- partial remission after treatment; 1-no response to treatment **Unilateral isolated fungal sinusitis** 1- full remission Unilateral ethmoidal fibrous dysplasia;1- refused treatment	Diagnosis of sinus headache that is based only on sino-nasal symptoms leads to misdiagnosis and inappropriate treatment. Consideration of vascular event-derived headaches (especially migraine), and detailed examination of this group of patients using endoscopy and CT imaging, can minimize the rate of misdiagnosis between rhinogenic and migraine headache	Moderate
Patel et al., 2013 "Sinus headache": rhinogenic headache or migraine? An evidence-based guide to diagnosis and treatment	Systematic review of literature	Review focused on adults with self- diagnosed or physician diagnosed sinus headache	N/A	N/A	Patients presenting with " sinus" headache require thorough assessment for both sino-nasal diagnoses with nasal endoscopy/CT imaging as well as neurologic diagnoses. A majority of patients will have a primary headache disorder (migraine, tension)	Low

Mehle & Kremer, 2008 Sinus CT scan findings in "sinus headache" migraineurs	Prospective cohort study	N=35 adult patients with physician (clinical) diagnosed "sinus headache"	CT used to confirm or refute diagnosis of sinus headache	Twenty-six "sinus headache" patients (74.3%) were diagnosed with migraine via IHS criteria. The mean CT scan score (Lund-McKay-LM) did not differ significantly between the 'new' migraine (2.07) and non-migraine cohort (2.66). 5 of the 26 patients with migraine were found to have sinus disease on CT	A clinical diagnosis of sinus headache or positive migraine history may not exclude the need for a complete ear, nose, and throat (ENT) workup, including head/sinus CT imaging	Moderate
Eross et al., 2007 The Sinus, Allergy and Migraine Study (SAMS)	Prospective study	N=100 consecutive patients with self-diagnosed sinus headache	Classify headache types	IHS diagnoses mistaken as sinus headache: • migraine with or without aura (52%) • chronic migraine associated with medication overuse versus probable medication overuse headache (11%) probable migraine (23%) • cluster headache (1%) • hemicrania continua (1%) • headache secondary to rhinosinusitis (3%) and headaches non- classifiable (9%). Weather changes (83%), seasonal variation (73%), exposure to allergens (62%), and changes in altitude (38%) were frequent migraine triggers. 76% of migraine subjects reported pain in the distribution of the second division of the trigeminal nerve (either unilateral or bilateral), and 62% experienced bilateral forehead and maxillary pain. The most common associated features included nasal congestion (56%), eyelid edema (37%), rhinorrhea (25%), conjunctival injection (22%), lacrimation (19%), and ptosis (3%).	A majority of patients with self-diagnosed "sinus headache" have migraine or probable migraine conditions. In those patients with migraine, the most common reasons for misdiagnosis include headache triggers, pain location, and associated features ("guilt by provocation, location, and association") commonly attributed to sinus headache	Moderate

Cady et al., 2005 Sinus Headache: A neurology, Otolaryngology, Allergy and Primary Care Consensus on Diagnosis and Treatment	Consensus Statement	N/A	N/A	N/A	Prominent rhinogenic symptoms with headache as one of several symptoms should be evaluated carefully for otolaryngolic conditions, especially those with signs of infection	Low
Initial QOE Score Across Studies for PICO #3: **Moderate (2)**						

SEMPI Grading QOE—Table 8A.3b—Risk of Bias		
PICO #3: In adults with self-reported "sinus headache," when should sinus imaging be performed as a part of the initial diagnostic evaluation?		
Evaluate Outcome for Risk of Bias Across Studies		
Initial QOE Score Across Studies for PICO: **MODERATE**		
Criteria	**Assessment**	**Reason for Assessment**
Negative Bias		
Risk of Bias	Serious	Review of patients selected using ICD-codes, Loss to follow-up; Small sample size and comparator (CT) as the reference standard; Small sample size, incomplete reporting, lack of control group; Bias possible in assembly of working group
Inconsistency	Not Serious	
Indirectness	Serious	No evidence that CT sinus abnormality equates to treatable sinus disease; Studies do not specifically address symptoms that support the use of CT imaging
Imprecision	Not Serious	
Positive Bias		
Strength of Association	Low	
Other Considerations	No	
Overall Effect of Bias on Initial QOE Grade: Downgraded to LOW		
Final QOE Grade for Outcome Across Studies: **LOW**		
High – Very confident the true effect lies close to that of the estimate of the effect **Moderate** – Moderately confident in the effect estimate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different) **Low** – Confidence in the effect estimate is limited (the true effect may be substantially different from the estimate of effect) **Very Low** – Very little confidence in the effect estimate (the true effect is likely to be substantially different from the estimate of effect)		

SEMPI Grading QOE—Table 8A.3c—Evidence to Recommendations				
PICO #3: In adults with self-reported "sinus headache," when should sinus imaging be performed as a part of the initial diagnostic evaluation?				
SEMPI Quality of Evidence (QOE) & Recommendation Strength				
Author/Year/Title	Highlights	SEMPI QOE Rating	Final QOE Category	Recommendation Strength
Jayawardena & Chandra, 2018 Headaches and facial pain in rhinology	With improved technology (reduced radiation risk) and lower cost, CT imaging of the sinuses as an initial assessment tool offers advantages over empiric antibiotic therapy/nasal endoscopy for patients presenting with "sinus headache." Lower microbial resistance and more appropriate non-ENT treatment/referrals can result	Very Low	Low (3)	Consensus (B)
Pedram et al., 2016 Sinus Headache in Chronic Rhinosinusitis (CRS): An Analysis of Otolaryngology Initiated Treatment Efficacy of Migraine in the CRS Patient	In "sinus headache" patients with or without chronic rhinosinusitis symptoms, **anti-migraine therapy** improves patient quality of life, eliminates symptom that cloud further rhinosinusitis-directed treatment, and avoids unnecessary sinus surgery	Low		
Lohiya et al., 2016 Comparative study of diagnostic nasal endoscopy and CT paranasal sinuses in diagnosing chronic rhinosinusitis	Nasal endoscopy can be used as an early diagnostic tool in the evaluation of chronic rhinosinusitis but should be followed by CT imaging if sinuses are not visualized. CT imaging is also useful in patients with refractory symptoms unresponsive to therapy and for patients in whom surgery is planned.	Low		
El-Shehally & Sobh, 2014 Is it rhinogenic headache or migraine? The role of sino-nasal endoscope and sinus CT	Diagnosis of sinus headache that is based only on sino-nasal symptoms leads to misdiagnosis and inappropriate treatment. Consideration of vascular event-derived headaches (especially migraine), and detailed examination of this group of patients using endoscopy and CT imaging, can minimize the rate of misdiagnosis between rhinogenic and migraine headache	Moderate		
Patel et al., 2013 "Sinus headache": Rhinogenic headache or migraine? An evidence-based guide to diagnosis and treatment	Patients presenting with "sinus" headache require thorough assessment for both sino-nasal diagnoses with nasal endoscopy/CT imaging as well as neurologic diagnoses. A majority of these patients will have a primary headache disorder (migraine, tension)	Low		

Mehle & Kremer, 2008 Sinus CT scan findings in "sinus headache" migraineurs	A clinical diagnosis of sinus headache or positive migraine history may not exclude the need for a complete ear, nose, and throat (ENT) workup, including head/sinus CT imaging	Moderate		
Eross et al., 2007 The Sinus, Allergy and Migraine Study (S AMS)	A majority of patients with self-diagnosed "sinus headache" have migraine or probable migraine conditions. In those patients with migraine, the most common reasons for misdiagnosis include headache triggers, pain location, and associated features ("guilt by provocation, location, and association") commonly attributed to sinus headache	Moderate		
Cady et al., 2005 Sinus headache: a neurology, otolaryngology, allergy, and primary care consensus on diagnosis and treatment	Prominent rhinogenic symptoms with headache as one of several symptoms should be evaluated carefully for otolaryngolic conditions, especially those with signs of infection	Low		

Recommendation Rating: 3B—Consensus recommendation for the intervention based on low quality evidence
Justification: Risk of bias (review articles and studies with small sample size) sufficient to downgrade QOE

Rating Definitions:
Quality of Evidence: High quality = **1**; Moderate quality = **2**; Low quality = **3**; Very low quality = **4**
Strength of Recommendation: A = Strength of Recommendation from Consistent Evidence; **B** = Strength of Recommendation from Panel Consensus

Conclusion: "Sinus headache" is a popular label as many migraineurs have cranial autonomic symptomatology (e.g. sinus symptoms-rhinorrhea, congestion, pressure) with migraine attacks. Adults who present with headache and self-reported "sinus headache" are likely migraineurs who will respond to migraine therapy. Nonetheless, if fever, sinus pain and purulent nasal discharge are not resolving with antimicrobial therapy or previous evidence of sinus pathology is present, CT imaging without contrast is diagnostically more accurate than conventional radiography (x-ray) and can be done with low radiation-dose protocols (Kirsch, 2019). Contrast is useful when abscess, osteomyelitis, tumor, venous thrombosis or vessel involvement is suspected (CT venography, angiography).

Final Recommendation: 3B—CT imaging of the sinuses is recommended **only** when the following criteria are present: Adults with headache and signs and/or symptoms of sinusitis (fever, purulent nasal discharge or previous evidence of sinus pathology) not resolved by pharmacological or other conservative therapy. NOTE: Most patients with self-reported 'sinus headache' have a primary headache disorder, most commonly migraine.

PICO #4: In adults with sudden onset and severe headache, does CT offer adequate sensitivity to identify subarachnoid hemorrhage (SAH)?

SEMPI Grading QOE—Table 8A.4a—Summary of Findings						
PICO #4: In adults with sudden onset and severe headache, does CT offer adequate sensitivity to identify subarachnoid hemorrhage (SAH)?						
Author/Year/Title	Design	Population	Intervention Vs Comparator	Results	Conclusion Summary	SEMPI QOE Rating
Tulla et al., 2019 Is there a role for lumbar puncture in early detection of subarachnoid hemorrhage after negative head CT?	Retrospective single center cohort study	N=647 with suspected SAH who underwent CT head w/wo LP. N=539 with suspected SAH with negative CT head and then underwent LP	CT vs LP	Non contrast CT (overall) Sensitivity: 95% (95% CI 89-98%) Specificity:99% (95% CI 97-99.7%) NPV:99% (95% CI 97-99.6%) Performed within 24 hours: Sensitivity: 100% (95% CI 95-100%) Specificity:99% (95% CI 96-99.7%) NPV:99% (95% CI 98-100%)	CT of the head has high sensitivity and specificity in the diagnosis of subarachnoid hemorrhage (SAH) when performed within 24 h of symptom onset. After 24 hours, the sensitivity decreases, and lumbar puncture may identify additional cases.	Low
Dubosh et al., 2016 Sensitivity of Early Brain Computed Tomography to Exclude Aneurysmal Subarachnoid Hemorrhage	Systematic review with meta-analysis	N= 8907 adults (5 studies)	CT versus lumbar puncture (LP)	Pooled Analysis CT sensitivity: 0.987 (0.971–0.994) CT specificity: 0.999 (0.993–1.0) 13 of 8907 who underwent **CT** within 6 hours had a missed SAH (incidence 1.46 per 1000) LR of a + CT was 921.9 (139– 6103) LR of a - CT was 0.010 (0.003–0.034)	CT of the head is the preferred imaging modality in individuals with sudden and severe headaches as it has nearly 100% sensitivity and specificity for identifying subarachnoid hemorrhage (SAH) in neurologically intact patients within 6 hours of headache onset.	Moderate
Carpenter et al., 2016 Spontaneous Subarachnoid Hemorrhage: A Systematic Review and Meta-Analysis Describing the Diagnostic Accuracy of History, Physical Exam,	Systematic review with meta-analysis	N= 22 studies	Head CT with LP for negative CT versus time from HA onset	Pooled sensitivity of CT to detect Subarachnoid Hemorrhage (SAH) Within 6 hrs. = 100% Beyond 6 hrs. = 89% CT within 6 hours: (+LR 230 [6-8700]) (-LR 0.01 [0-0.04]) CT beyond 6 hours: (-LR 0.07 [.01-.61])	Unenhanced CT of the head is first-line imaging in patients with headache and suspected subarachnoid hemorrhage (SAH), particularly within 6 hours of symptom onset.	Moderate

Imaging, and Lumbar Puncture with an Exploration of Test Thresholds						
Verma et al., 2013 Detecting subarachnoid hemorrhage: comparison FLAIR/SWI versus CT	Retrospective study	N=25 patients with acute SAH Causes head trauma (n=9), ruptured aneurysm (n=6), ruptured arteriovenous malformation (n=2), and spontaneous bleeding (n=8)	CT vs MR (CT and MRI within 6 days after symptom onset))	SAH detected in 146 subarachnoid regions. CT identified 110 (75.3%), FLAIR 127 (87%) SWI 129 (88.4%) Combined FLAIR and SWI identifi ed all 146 detectable regions (100%) FLAIR showed sensitivity for frontal-parietal, temporal-occipital and Sylvian cistern SAH, while susceptibility weighted imaging (SWI) was particularly sensitive for interhemispheric and intraventricular hemorrhage	MR (combining susceptibility weighted imaging (SWI) and fluid attenuated inversion recovery (FLAIR)) has a higher detection rate for SAH than CT	Low
da Rocha et al., 2006 Comparison of Magnetic Resonance Imaging with Computed Tomography to detect low-grade subarachnoid hemorrhage	Prospective (consecutive enrollment)	N=42 patients with clinically suspected low-grade SAH (2 groups; traumatic (25) and spontaneous (17) SAH)	CT vs MR (2 radiologists, blinded to clinical data, 26 regions in intracranial subarachnoid space studied)	**Sensitivity for acute SAH (< 4 days):** CT: 71.8% T2* sequences: 37.5% FLAIR sequences: 100% **Sensitivity for subacute SAH (4-15 days):** CT: 50% T2* sequences: 30% FLAIR sequences: 100%	FLAIR sequence is superior for diagnosis and localization of acute (< 4 days) and subacute (4-15 days) low-grade SAH	Moderate
Yuan et al., 2005 Detection of subarach noid hemorrhage at acute and subacute/chronic stages: comparison of four magnetic resonance imaging pulse sequences and computed tomography	Prospective study	N=22 patients with SAH due to ruptured aneurysm (n = 11), trauma (3), or unknown origin (all patients underwent MR and CT)	CT vs MR (MRI (1.5-T) pulse sequences comprised spin-echo T1-weighted, fast spin-echo T2-weighted, FLAIR, and gradient-echo (GE) T2-weighted images)	**Acute-stage group (MR within 5 days):** High signal intensities: T1-weighted images: 36.4% (not significant) T2 weighted images: 18.2% (not significant) FLAIR images: 100% (p= 0.008) CT - 90.9% (p= 0.012) GE T2*-weighted images: 90.9% (p=0.012)	Fluid attenuated inversion recovery (FLAIR), GE T2 MRI pulse sequences, and CT scans have comparable accuracy for acute onset (<= 5 days) SAH. GE T2-weighted images are significant indicators of subacute-to-chronic SAH	Moderate

				Subacute/chronic group (MR within 6-30 days) T1-weighted images: 36.4% (not significant) T2 weighted images: 9.1% (not significant) FLAIR images: 33.3% (not significant) CT: 45.5% (not significant) GE T2*-weighted images: 100% (p=0.001)		
Initial QOE Score Across Studies for PICO #4: **Moderate (2)**						

SEMPI Grading QOE—Table 8A.4b—Risk of Bias		
PICO #4: In adults with sudden onset and severe headache, does a CT offer adequate sensitivity to identify subarachnoid hemorrhage (SAH)?		
Evaluate Outcome for Risk of Bias Across Studies		
Initial QOE Score Across Studies for PICO: **MODERATE**		
Criteria	**Assessment**	**Reason for Assessment**
Negative Bias		
Risk of Bias	Not Serious	Some retrospective data, tertiary care settings, single center
Inconsistency	Not Serious	
Indirectness	Not Serious	Variable time frame (6-24 hours) Role of MR better studied in subacute settings.
Imprecision	Not Serious	
Positive Bias		
Strength of Association	Moderate	High negative predictive value, sensitivity and specificity
Other Considerations	No	
Overall Effect of Bias on Initial QOE Grade: No change		
Final QOE Grade for Outcome Across Studies: **MODERATE**		
High – Very confident the true effect lies close to that of the estimate of the effect **Moderate** – Moderately confident in the effect estimate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different) **Low** – Confidence in the effect estimate is limited (the true effect may be substantially different from the estimate of effect) **Very Low** – Very little confidence in the effect estimate (the true effect is likely to be substantially different from the estimate of effect)		

SEMPI Grading QOE—Table 8A.4c—Evidence to Recommendations

PICO #4: In adults with sudden onset and severe headache, does a CT offer adequate sensitivity to identify subarachnoid hemorrhage (SAH)?

SEMPI Quality of Evidence (QOE) & Recommendation Strength

Author/Year/Title	Highlights	SEMPI QOE Rating	Final QOE Category	Recommendation Strength
Tulla et al., 2019 Is there a role for lumbar puncture in early detection of subarachnoid hemorrhage after negative head CT?	CT of the head has high sensitivity and specificity in the diagnosis of subarachnoid hemorrhage (SAH) when performed within 24 h of symptom onset. After 24 hours, the sensitivity decreases, and lumbar puncture may identify additional cases.	Low	Moderate (2)	Strong (A)
Dubosh et al., 2016 Sensitivity of Early Brain Computed Tomography to Exclude Aneurysmal Subarachnoid Hemorrhage	CT of the head is the preferred imaging modality in individuals with sudden and severe headaches as it has nearly 100% sensitivity and specificity for identifying subarachnoid hemorrhage (SAH) in neurologically intact patients within 6 hours of headache onset.	Moderate		
Carpenter et al., 2016 Spontaneous Subarachnoid Hemorrhage: A Systematic Review and Meta-analysis Describing the Diagnostic Accuracy of History, Physical Examination, Imaging, and Lumbar Puncture With an Exploration of Test Thresholds	Unenhanced CT of the head is first-line imaging in patients with headache and suspected subarachnoid hemorrhage (SAH), particularly within 6 hours of symptom onset.	Moderate		
Verma et al., 2013 Detecting subarachnoid hemorrhage: comparison FLAIR/SWI versus CT	MR (combining susceptibility weighted imaging (SWI) and fluid attenuated inversion recovery (FLAIR)) has a higher detection rate for SAH than CT	Low		
da Rocha et al., 2006 Comparison of Magnetic Resonance Imaging with Computed Tomography to detect low-grade subarachnoid hemorrhage	FLAIR sequence is superior for diagnosis and localization of acute and subacute low-grade SAH	Moderate		
Yuan et al., 2005 Detection of subarachnoid hemorrhage at acute and subacute/chronic stages: comparison of four magnetic resonance imaging pulse sequences and computed tomography	Fluid attenuated inversion recovery (FLAIR), GE T2 MRI pulse sequences, and CT scans have comparable accuracy for acute onset SAH. GE T2-weighted images are significant indicators of subacute-to-chronic SAH	Moderate		

Recommendation Rating: 2A—Strong recommendation for the intervention based on moderate quality evidence **Justification:** Risk of bias insufficient to downgrade QOE as CT remains the preferred modality in emergent setting
Rating Definitions: **Quality of Evidence:** High quality = **1**; Moderate quality = **2**; Low quality = **3**; Very low quality = **4** **Strength of Recommendation: A** = Strength of Recommendation from Consistent Evidence; **B** = Strength of Recommendation from Panel Consensus
Conclusion: Severe headache of sudden onset described as 'worst headache' of the patient's life is a characteristic manifestation of subarachnoid hemorrhage (SAH). Non-contrast CT is very sensitive for identifying acute hemorrhage and is considered the reference standard. The pooled sensitivity is 94% (95% CI: 91%–96%) and when the sensitivity is stratified by time, it is 100% for <6 hours (95% CI: 98%–100%) and 89% for >6 hours (95% CI: 83%–93%) (Carpenter et al, 2016). Previous literature and recommendations have supported or suggested that as the sensitivity of CT decreases over time, a negative CT at longer latencies should be followed with lumbar puncture (LP) to exclude SAH (ACEP 2008) in patients who present to the ED with non-traumatic headache and have concerns for SAH. However, more recent literature has questioned the benefits of LP after a negative, non-contrast CT, given its low diagnostic yield (Gill et al., 2016; Migdal et al., 2015). Magnetic resonance (MR) imaging of the brain offers comparable diagnostic accuracy for SAH but requires more time to perform, is less widely available, and more costly (Hodel et al., 2015).
Final Recommendation: 2A—In adults with sudden onset and severe headache, CT of head (non-contrast) is recommended within the first 6 hours to evaluate for subarachnoid hemorrhage (SAH). In the subacute setting, the sensitivity of CT head decreases, and follow-up with LP (and possibly MRI) is warranted.

PICO #5: In adults with headache and minimal to mild traumatic brain injury (Glasgow coma scale 13, 14 or 15) should CT of the head be used to identify significant pathology for optimal patient management?

SEMPI Grading QOE—Table 8A.5a—Summary of Findings						
PICO #5: In adults with headache and minimal to mild traumatic brain injury (Glasgow coma scale 13, 14 or 15) should CT of the head be used to identify significant pathology for optimal patient management?						
Author/Year/Title	Design	Population	Intervention Vs Comparator	Results	Conclusion Summary	SEMPI QOE Rating
Foks et al., 2019 Risk of Intracranial Complications in Minor Head Injury: The Role of Loss of Consciousness and Post-Traumatic Amnesia in a Multi-Center Observational Study	Prospective, multicenter, observational cohort study 6 Dutch sites Loss of consciousness (LOC) Post-trauma amnesia (PTA) Glasgow coma scale (GCS)	N=3914 Does LOC or PTA impact minor head injury (MHI) with GCS score=15 re neurosurgery and/or complications	LOC, PTA present vs LOC, PTA absent in MHI with GCS=15	1360 (34%)—LOC or PTA present 2249 (58%)—no LOC nor PTA 305 (8%)—unknown LOC or PTA Traumatic brain injury on imaging: With LOC/PTA—153/1360 (11%) No LOC/PTA—67/2249 (3%) Potential neurosurgical lesion: No LOC/PTA—5/2249 Neurosurgical intervention: No LOC/PTA—1/2249	Patients with minor head injury, Glasgow Coma Scale score=15, and neither loss of consciousness nor post-trauma amnesia are still at risk for neurosurgical lesions requiring neurosurgical intervention	Moderate
Singata & Candy, 2018 Is computed tomography of the head justified in patients with minor head trauma presenting with Glasgow Coma Scale 15/15?	Retrospective Performed after new protocol proposed for minor head injury (MHI) patients with Glasgow Coma Scale (GCS) of 15	N=460 MHI: loss of consciousness (LOC) < 30 mins, and/or reversible amnesia, GCS=15 **2012 Kimberly Hospital Rule**: CT of head can be delayed for 8h for MHI+GCS=15	N/A "Clinically significant CT": Sub- or epidural or subarachnoid hematoma, brain contusion, cerebral edema, herniation, pneumocranium, skull fracture	140/460 (30%)-abnormal head CT 33/460 (7%)-clinically significant—22 brain contusion, 11 skull fractures (depressed or basilar); 0 indicated need for urgent neurosurgical intervention Of 33 with clinically significant CT: 19 had "alerting" symptoms—vomiting (5), HA (7), dizziness (7)	Retrospective data suggests that CT imaging of the head may be delayed (up to 8 hours) in patients older than 13 years of age with minor head injury and a Glasgow Coma Scale score of 15, when access to advanced medical resources is limited. Prospective trial data is needed to confirm this observation.	Low

Waganekar et al., 2018 Computed Tomography Profile and its Utilization in Head Injury Patients in Emergency Department: A Prospective Observational Study	Prospective observational	N=1782 patients 12-month period GCS: Group 1: GCS 13–15 (MHI); Group 2: GCS 9–12 (moderate head injury); and Group 3: GCS ≤8 (severe head injury)	CT (positivity for findings)	CT positivity was 50.9%. In minor head injury (MHI), CT positivity rate was 38%. The study showed significant association of CT positivity with five variables: Loss of consciousness >5 min, vomiting, seizures, ear bleed, and nosebleed	CT imaging of the head is indicated in all patients with moderate and severe head injury (GCS ≤ 12). A low threshold for CT imaging of the head is advisable in elderly and alcohol-intoxicated patients. CT imaging is also indicated if any one of the following risk factors is present—loss of consciousness > 5 min, a history of vomiting, or seizures, or ear bleed, or nosebleed	Moderate
Easter et al., 2015 Will Neuroimaging Reveal a Severe Intracranial Injury in This Adult with Minor Head Trauma? The Rational Clinical Examination Systematic Review	Systematic review	N=14 studies (23079 patients) patients having GCS scores between 13 and 15 and 50% or more older than 18 years	Exam findings vs intracranial injuries on CT	Severe intracranial injury findings in patients with minor head trauma: Examination findings suggestive of skull fracture (likelihood ratio (LR), 16; 95% CI, 3.1-59; specificity, 99%) GCS score of 13 (LR, 4.9; 95% CI, 2.8-8.5; specificity, 97%) 2 or more vomiting episodes (LR, 3.6; 95% CI, 3.1-4.1; specificity, 92%) Decline in GCS score (LR range, 3.4-16; specificity range, 91%-99%;) Pedestrians struck by motor vehicles (LR range, 3.0-4.3; specificity range, 96%-97%)	Physical exam findings suggestive of skull fracture, Glasgow Coma Scale (GCS) score of 13 or less, 2 or more vomiting episodes, a decrease in GCS score, and pedestrians struck by motor vehicles, can identify those at increased risk of severe intracranial injury who warrant emergent neuroimaging	Moderate
Sharif-Alhoseini et al., 2011 Indications for brain computed tomography scan after minor head injury	Prospective study	N= 642 patients over age 2 with blunt head trauma and GCS 13 or higher	CT with no comparator	Odds ratio for abnormal CT Headache-5.68 Loss of consciousness or amnesia-13.8 Alcohol intoxication-17.13	Headache, vomiting, loss of consciousness, amnesia and alcohol intoxication can increase the likelihood of positive CT findings in those with minor head trauma	Moderate

Saboori et al., 2007 Indications for brain CT scan in patients with minor head injury	Prospective cohort	N= 682 patients with Glasgow coma scale (GCS) of 15	CT with no comparator Clinical symptoms compared to CT results to identify risk factors for abnormal results	Odds ratio for abnormal CT Loss of consciousness- 2.371 Posttraumatic amnesia- 2.654 Confusion-3.940 Vomiting-8.333 Headache-2.125 Skull fracture- 8.873 Age >60-4.971	In patients with minor head injury, the presence of at least one of the following risk factors correlates with abnormal findings on head CT: Age over 60, Skull fracture, Vomiting, Confusion, Post-trauma amnesia, Loss of consciousness, Headache	Moderate
Smits et al., 2007 Predicting Intracranial Traumatic Findings on Computed Tomography in Patients with Minor Head Injury: The CHIP Prediction Rule	Prospective observational. Data obtained to develop clinical prediction rule	N= 3181 patients	CT with no comparator	Odds ratio (95% CI) for abnormal CT **Signs of skull fracture** =10 (5.9-18) GCS of 13 =3.9 (2.4-6.6) GCS of 14 =2.1 (1.4-2.9) **Persistent anterograde amnesia**= 1.5 (1.1-2.2) **Contusion of the skull**=1.8 (1.3-2.4) **Vomiting**=2.4 (1.7-3.5) Pt age 16 per 10 yrs.=1.2 (1.1-1.3) **Posttraumatic amnesia** 2-4 hours=1.6 (0.6-4.5) **Posttraumatic amnesia** >4 hours=7.5 (1.5-37) **Loss of consciousness**= 1.8 (1.3-2.5) **Neurologic deficit**= 1.5 (1.0-2.3) **Fall from any elevation**=1.7 (1.2-2.4) **Use anticoagulant therapy**=2.4 (1.2-4.6) **Pedestrian or cyclist versus vehicle**=3.6 (2.4-5.3) **Ejected from vehicle**=3.1 (1.3-7.2) **Posttraumatic seizure**=2.3 (0.7-8.2)	Use of a verified prediction tool (CHIP rule) can facilitate identification of those patients who warrant CT imaging after minor head injury	Moderate

Gómez et al., 1996 [Mild head injury: differences in prognosis among patients with a Glasgow Scale score of 13-15 and analysis of factors associated with abnormal CT findings]	Retrospectiv e consecutive	N= 2484 Patients with head trauma, over age 15 and Glasgow coma scale (GCS) of 13, 14 or 15	CT with no comparator Clinical symptoms compared to CT results to identify risk factors for abnormal results	Skull fracture, focal neurological deficit and GCS are all associated with abnormal CT results	Following mild head injury, patients with a Glasgow Coma Scale score of 13-14 warrant an unenhanced CT of the head	Low
Initial QOE Score Across Studies for PICO #5: **Moderate (2)**						

SEMPI Grading QOE—Table 8A.5b—Risk of Bias		
PICO #5: In adults with headache and minimal to mild traumatic brain injury (Glasgow coma scale 13, 14 or 15) should CT of the head be used to identify significant pathology for optimal patient management?		
Evaluate Outcome for Risk of Bias Across Studies		
Initial QOE Score Across Studies for PICO: **MODERATE**		
Criteria	**Assessment**	**Reason for Assessment**
Negative Bias		
Risk of Bias	Not Serious	Retrospective, small N, missing data on mechanism of injury
Inconsistency	Not Serious	
Indirectness	Not Serious	
Imprecision	Serious	Studies looked at different predictors
Positive Bias		
Strength of Association	Moderate	Similar results in all studies
Other Considerations	No	
Overall Effect of Bias on Initial QOE Grade: No change		
Final QOE Grade for Outcome Across Studies: **MODERATE**		

High – Very confident the true effect lies close to that of the estimate of the effect
Moderate – Moderately confident in the effect estimate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different)
Low – Confidence in the effect estimate is limited (the true effect may be substantially different from the estimate of effect)
Very Low – Very little confidence in the effect estimate (the true effect is likely to be substantially different from the estimate of effect)

SEMPI Grading QOE—Table 8A.5c—Evidence to Recommendations				
PICO #5: In adults with sudden onset and severe headache should CT be the preferred modality for identifying significant intracranial pathology/abnormality for optimal patient outcome(s)?				
SEMPI Quality of Evidence (QOE) & Recommendation Strength				
Author/Year/Title	Highlights	SEMPI QOE Rating	Final QOE Category	Recommendation Strength
Foks et al., 2019 Risk of Intracranial Complications in Minor Head Injury: The Role of Loss of Consciousness and Post-Traumatic Amnesia in a Multi-Center Observational Study	Patients with minor head injury, Glasgow Coma Scale score=15, and neither loss of consciousness nor post-trauma amnesia are still at risk for neurosurgical lesions requiring neurosurgical intervention	Moderate	Moderate (2)	Strong (A)
Singata & Candy, 2018 Is computed tomography of the head justified in patients with minor head trauma presenting with Glasgow Coma Scale 15/15?	Retrospective data suggests that CT imaging of the head may be delayed (up to 8 hours) in patients older than 13 years of age with minor head injury and a Glasgow Coma Scale score of 15, when access to advanced medical resources is limited. Prospective trial data is needed to confirm this observation.	Low		
Waganekar et al., 2018 Computed Tomography Profile and its Utilization in Head Injury Patients in Emergency Department: A Prospective Observational Study	CT imaging of the head is indicated in all patients with moderate and severe head injury (GCS ≤ 12). A low threshold for CT imaging of the head is advisable in elderly and alcohol-intoxicated patients. CT imaging is also indicated if any one of the following risk factors is present loss of consciousness > 5 min, a history of vomiting, or seizures, or ear bleed, or nosebleed	Moderate		
Easter et al., 2015 Will Neuroimaging Reveal a Severe Intracranial Injury in This Adult with Minor Head Trauma? The Rational Clinical Examination Systematic Review	Physical exam findings suggestive of skull fracture, Glasgow Coma Scale (GCS) score of 13 or less, 2 or more vomiting episodes, a decrease in GCS score, and pedestrians struck by motor vehicles, can identify those at increased risk of severe intracranial injury who warrant emergent neuroimaging	Moderate		
Sharif-Alhoseini et al., 2011 Indications for brain computed tomography scan after minor head injury	Headache, vomiting, loss of consciousness, amnesia and alcohol intoxication can increase the likelihood of positive CT findings in those with minor head trauma	Moderate		

Saboori et al., 2007 Indications for brain CT scan in patients with minor head injury	In patients with minor head injury, the presence of at least one of the following risk factors correlates with abnormal findings on head CT: Age over 60, Skull fracture, Vomiting, Confusion, Post-trauma amnesia, Loss of consciousness, Headache	Moderate		
Smits et al., 2007 Predicting Intracranial Traumatic Findings on Computed Tomography in Patients with Minor Head Injury: The CHIP Prediction Rule	Use of a verified prediction tool (CHIP rule) can facilitate identification of those patients who warrant CT imaging after minor head injury	Moderate		
Gómez et al., 1996 Mild head injury: differences in prognosis among patients with a Glasgow Scale score of 13-15 and analysis of factors associated with abnormal CT findings	Following mild head injury, patients with a Glasgow Coma Scale score of 13-14 warrant an unenhanced CT of the head	Low		

Recommendation Rating: 2A— Strong recommendation for the intervention based on moderate quality evidence

Justification: Consistent evidence for use of CT in mild to moderate head injury with risk factors although there is some disagreement about specific symptoms.

Rating Definitions:

Quality of Evidence: High quality = **1**; Moderate quality = **2**; Low quality = **3**; Very low quality = **4**

Strength of Recommendation: A = Strength of Recommendation from Consistent Evidence; **B** = Strength of Recommendation from Panel Consensus

Conclusion: CT imaging of the head (brain) for minimal or mild traumatic brain injury is an area of potential over-utilization because of the dramatic consequences of misdiagnosing a serious injury. Traditionally, the use of the Glasgow Coma Scale (GCS) has been used to classify the severity of head injuries. However, patients with GCS scores of 14 or 15 may have significant brain injury despite being classified as “minimal” or “mild” by the GCS. In response to this realization, decision rules have been developed to decrease the likelihood of missing a clinically significant brain injury. Studies have found that the Canadian CT Head Rule, the New Orleans Criteria and the National Emergency- XR Utilization Study have all proven to be highly sensitive (but not highly specific) in the diagnosis of significant brain injury (Mower et al., 2017; Ro et al., 2011). Therefore, it is important to look at the entire clinical picture when deciding to image a patient with a GCS of 13, 14, or 15. A validated decision rule/scale is needed when considering neuroimaging in “mild/minimal” head trauma patients as consensus is lacking, especially in patients with a GCS score of 15. Preliminary data suggest that in mild head injury patients with a GCS score of 15 and no focal deficits, neuroimaging can be safely delayed (e.g. up to 8 hours) in areas with limited medical resources; however, prospective trial evidence is warranted to confirm these observations. Conversely, other studies demonstrate that even those without loss of consciousness or post-traumatic amnesia and a GCS of 15, may be at increased risk for brain trauma requiring neurosurgical evaluation/intervention and thus warrant head CT imaging. Although it has been proposed that “pregnancy” should be added to the list of indications warranting neuroimaging to identify secondary headache disorders, this is not without serious issues and the proper alternatives are not supported by strong evidence (Micieli & Kingston, 2019; Ramchandren et al., 2007; Robbins et al., 2015; Sandoe & Lay, 2019). Depending on urgency/availability/clinical findings, unenhanced CT imaging with adequate shielding to minimize fetal radiation exposure, can be performed as an alternative to MR imaging in pregnant patients

presenting with a new headache or one that has changed in severity or symptomatology. Therefore, pregnancy represents a clinical scenario in which consultation between radiologist, ordering provider, and, if possible, obstetrician is required to optimize imaging accuracy while ensuring maximal safety.
Final Recommendation: 2A—In adults with minimal to mild traumatic brain injury (Glasgow coma scale 13, 14 or 15), imaging is usually not recommended. CT imaging of the head is recommended for optimal patient management when any of the following parameters are present: • Loss of consciousness • Vomiting • Signs of skull fracture • Significant mechanism of injury (car vs. pedestrian or bike; ejection from vehicle)

PICO #6: In adults with moderate to severe head injury should initial evaluation include CT of the head for optimal patient management?

SEMPI Grading QOE—Table 8A.6a—Summary of Findings						
PICO #6: In adults with moderate to severe head injury should initial evaluation include CT of the head for optimal patient management?						
Author/Year/Title	Design	Population	Intervention Vs Comparator	Results	Conclusion Summary	SEMPI QOE Rating
Waganekar et al., 2018 Computed Tomography Profile and its Utilization in Head Injury Patients in Emergency Department: A Prospective Observational Study	Prospective observational study	N=1782 patients over a 12-month period. Group 1: GCS 13–15 (MHI); Group 2: GCS 9–12 (moderate head injury); and Group 3: GCS ≤8 (severe head injury)	CT positivity in head injury patients	Overall CT positivity was 50.9%. Strong association was found between CT positivity and severity of head injury based on GCS score with $P < 0.05$.	CT imaging of the head is indicated in all patients with moderate and severe head injury (GCS ≤ 12). A low threshold for CT imaging of the head is advisable in elderly and alcohol-intoxicated patients. CT imaging is also indicated if any one of the following risk factors is present—loss of consciousness > 5 min, a history of vomiting, or seizures, or ear bleed, or nosebleed	Moderate
Miller et al., 2004 Initial Head Computed Tomographic Scan Characteristics Have a Linear Relationship with Initial Intracranial Pressure after Trauma	Retrospective review	N=82 adult patients with severe closed head injury (GCS < 8) who required ventriculostomy (patients requiring surgery were excluded)	Initial ICP (Intracranial Pressure) readings and CT findings were compared to determine whether a significant linear relationship existed between the above CT findings and ICPs	Initial head CT characteristics show a linear relationship to baseline ICPs	Initial CT imaging of patients with severe head injury is necessary per the Brain Trauma Foundation which recommends ICP monitoring in those patients with a GCS score < 8 and abnormal CT as well as in those with a normal CT if age > 40 years and systolic blood pressure < 90 mm Hg, or if posturing is present	Low

Bulger et al., 2002 [Management of severe head injury: institutional variations in care and effect on outcome]()	Retrospective study of consecutive patients	Adult patients with severe closed head injury and a GCS score of 8 or less	Variations in care were assessed, including prehospital intubation, intracranial pressure monitoring, use of osmotic agents, hyperventilation, and **computed tomography utilization**. Centers were classified as aggressive or non-aggressive in their treatment of head-injured patients (see paper for criteria). Primary outcome variables were mortality, functional status at discharge, and length of stay	There were significantly higher rates of head CT utilization, neurosurgical consultation, intubation on admission, use of osmotic agents, hyperventilation, and ventriculostomy in aggressive centers. In the management of severely head injured patients (GCS 8 or less), the liberal use of head CT imaging (by 'aggressive' institutions) was associated in part with a significant reduction in mortality as compared to 'non-aggressive institutions	CT of the head is used liberally by institutions with the best outcomes for severe head-injury patients, supporting their use in the initial evaluation and management of patients with severe head injury	Low
Arienta et al., 1997 [Management of head-injured patients in the emergency department: a practical protocol]()	Retrospective analysis	N=10,000 head-injured patients (253 classified as moderate to severe head injury)	Findings of head CT versus clinical outcome	In 205 patients classified with **moderate head injury** 85 (41%) had intracranial lesions. Of the 85 with intracranial lesions, 23 (27%) required operation and 6 patients died (7%). In 48 patients classified with **severe head injury** (GCS 3-8) every patient (100%) had intracranial lesions. Of these 48, 34 (71%) required operation and 14 died (29%). Of these 799 patients with **minor head injury** and symptoms (LOC, amnesia, emesis, etc.), 592 (74%) received a head CT and 21 (3.5%) were found to have an intracranial lesion. 3 (14%) of these 21 patients required operation and no deaths were observed	Patients with moderate and severe head injuries have a high incidence of intracranial injury and therefore should be evaluated with head CT diagnostically to identify surgical candidates	Low

Gentry et al., 1988 Prospective comparative study of intermediate-field MR and CT in the evaluation of closed head trauma	Prospective observational study	N=40 patients with acute closed head trauma GCS range (3-14)	Patients were evaluated by both head CT and head MRI and the diagnostic efficacies of these two techniques were compared	Sensitivity for the detection of hemorrhagic lesions: CT = 89.8% T1 MR=87.1% T2 MR = 92.5% Intraventricular hemorrhage was consistently seen with both imaging studies, but subarachnoid hemorrhage was detected much more frequently with CT Sensitivity for the detection of non-hemorrhagic lesions: CT = 17.7% T1 MR = 67.6% T2 MR =93.3%	Although CT and MR imaging are highly sensitive in the detection of hemorrhagic lesions, CT detects significantly more subarachnoid hemorrhage and is more rapid in identifying lesions requiring surgical intervention in patients with closed head trauma	Moderate
Initial QOE Score Across Studies for PICO #6: **Moderate (2)**						

SEMPI Grading QOE—Table 8A.6b—Risk of Bias		
PICO #6: In adults with moderate to severe head injury should initial evaluation include CT of the head for optimal patient management?		
Evaluate Outcome for Risk of Bias Across Studies		
Initial QOE Score Across Studies for PICO: **MODERATE**		
Criteria	**Assessment**	**Reason for Assessment**
Negative Bias		
Risk of Bias	Serious	'Pre-selected' patient population Incomplete data in several studies - lack of long-term follow-up
Inconsistency	Serious	Imaging studies were often performed at various lengths of hospital stay yet were compared, making it difficult to decide if findings were due to primary injury, treatment-related secondary injury, or abnormality
Indirectness	Serious	Appropriate study population and tests of interest studied. In some instances, conclusions were gleaned from the study data and were slightly different than the study's conclusion
Imprecision	Not Serious	Studies often lack a gold standard for head injury lesions (e.g. surgical path), however, not deemed serious
Positive Bias		
Strength of Association	Moderate	Acceptable confidence intervals in observational study
Other Considerations	No	
Overall Effect of Bias on Initial QOE Grade: Downgraded to LOW		
Final QOE Grade for Outcome Across Studies: **LOW**		
High – Very confident the true effect lies close to that of the estimate of the effect **Moderate** – Moderately confident in the effect estimate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different) **Low** – Confidence in the effect estimate is limited (the true effect may be substantially different from the estimate of effect) **Very Low** – Very little confidence in the effect estimate (the true effect is likely to be substantially different from the estimate of effect)		

SEMPI Grading QOE—Table 8A.6c—Evidence to Recommendations

PICO #6: In adults with moderate to severe head injury should initial evaluation include CT of the head for optimal patient management?

SEMPI Quality of Evidence (QOE) & Recommendation Strength

Author/Year/Title	Highlights	SEMPI QOE Rating	Final QOE Category	Recommendation Strength
Waganekar et al., 2018 Computed Tomography Profile and its Utilization in Head Injury Patients in Emergency Department: A Prospective Observational Study	CT imaging of the head is indicated in all patients with moderate and severe head injury (GCS ≤ 12). A low threshold for CT imaging of the head is advisable in elderly and alcohol-intoxicated patients. CT imaging is also indicated if any one of the following risk factors is present loss of consciousness > 5 min, a history of vomiting, or seizures, or ear bleed, or nosebleed	Moderate	Low (3)	Strong (A)
Miller et al., 2004 Initial Head Computed Tomographic Scan Characteristics Have a Linear Relationship with Initial Intracranial Pressure after Trauma	Initial CT imaging of patients with severe head injury is necessary per the Brain Trauma Foundation which recommends ICP monitoring in those patients with a GCS score < 8 and abnormal CT as well as in those with a normal CT if age > 40 years and systolic blood pressure < 90 mm Hg, or if posturing is present	Low		
Bulger et al., 2002 Management of severe head injury: Institutional variations in care and effect on outcome	CT of the head is used liberally by institutions with the best outcomes for severe head-injury patients, supporting their use in the initial evaluation and management of patients with severe head injury	Low		
Arienta et al., 1997 Management of head-injured patients in the emergency department: a practical protocol	Patients with moderate and severe head injuries have a high incidence of intracranial injury and therefore should be evaluated with head CT diagnostically to identify surgical candidates	Low		
Gentry et al., 1988 Prospective Comparative Study of intermediate-field MR and CT in the evaluation of closed head trauma	Although CT and MR imaging are highly sensitive in the detection of hemorrhagic lesions, CT detects significantly more subarachnoid hemorrhage and is more rapid in identifying lesions requiring surgical intervention in patients with closed head trauma	Moderate		

Recommendation Rating: 3A—Strong recommendation for the intervention based on low quality evidence

Justification: Risk of bias is sufficient to downgrade the Quality of Evidence

Rating Definitions: **Quality of Evidence:** High quality = **1**; Moderate quality = **2**; Low quality = **3**; Very low quality = **4** **Strength of Recommendation: A** = Strength of Recommendation from Consistent Evidence; **B** = Strength of Recommendation from Panel Consensus
Conclusion: Evaluation of patients with moderate to severe head injury with head computed tomography (CT) has been routine practice since the 1980's, the effectiveness of CT in identifying surgically correctable lesions is rarely in question. Magnetic resonance (MR) imaging has recently been compared to CT in the evaluation for head trauma patients and has been found to be of value in the identification of soft tissue injury, cerebral edema, diffuse axonal injury, and delayed presentations of intracranial blood (Mutch et al., 2016). However, MR imaging is not well suited for the emergent evaluation of patients. The goal of initial care is to identify patients who might require surgical intervention or invasive monitoring and for this, CT is ideally suited MR imaging takes more time and requires that no ferrous metals are present—which may not be possible to ascertain in severely injured patients. As such, the ability of CT to accurately and rapidly assess the cranial vault for space occupying as well as the size of cerebral ventricles make it the imaging study of choice for the emergent evaluation of patients with moderate to severe head injury.
Final Recommendation: 3A—In adults with moderate to severe head injury, CT of the head is recommended to identify potential surgical candidates for optimal patient management.

PICO #7: In adults with persistent headache and suspected post-concussive syndrome does neuroimaging impact patient management?

SEMPI Grading QOE—Table 8A.7a—Summary of Findings						
PICO #7: In adults with persistent headache and suspected post-concussive syndrome does neuroimaging impact patient management?						
Author/Year/Title	Design	Population	Intervention Vs Comparator	Results	Conclusion Summary	SEMPI QOE Rating
Rose et al., 2017 [Utilization of conventional neuroimaging following youth concussion]	Retrospective cohort study	N=1953 subjects with concussion (1652 no imaging and 301 imaging ordered: 176 CT only, 108 MR only and 26 CT followed by MR)	CT vs MR	Predictors of CT utilization included loss of consciousness, amnesia and vomiting (all p <0.001). Prior concussion (p = 0.002) and continued participation in activity after injury (p = 0.03) predicted greater MRI utilization. Neuroimaging with either CT (p = 0.024, hazard ratio = 1.2) or MR (p < 0.001, hazard ratio = 2.75) was associated with prolonged symptoms. Only 3.1% of CTs and 1.5% of MRs demonstrated signs of traumatic brain injury.	In youth concussion settings CT imaging is preferred in acutely while magnetic resonance (MR) imaging is used in the sub-acute and chronic post-concussion periods. Delayed neuroimaging (months to years) for "post-concussion headache" has limited clinical yield	Moderate
Dean et al., 2015 [Multimodal imaging of mild traumatic brain injury and persistent postconcussion syndrome]	Convenience sample from a large cross section study	N=25 participants: 8 mTBI + PCS participants (suffered an mTBI and have persistent PCS); 8 mTBI-PCS participants (mTBI but no PCS); 9 Control participants (no history of brain injury and no PCS)	MR	Individuals with mTBI and ongoing PCS exhibited the greatest differences compared to controls, with reduced BOLD response in working memory-related areas (left IFG/MFG during PVSAT) and declarative memory and visual processing areas (right inferior/medial temporal areas during n-Back). Increased PCS symptom report correlated with reduced BOLD response in declarative memory and visual processing areas (right inferior/medial temporal areas during n-Back), DMN-related areas (PCC and precuneus during PVSAT), as well as increased BOLD response in attention-related areas (ACC during n-Back)	Magnetic resonance imaging may help improve detection of brain abnormalities after mild traumatic brain injury, but larger, prospective studies are needed to confirm this	Low

Datta et al., 2009 Post-concussion syndrome: Correlation of neuropsychological deficits, structural lesions on magnetic resonance imaging and symptoms	Prospective observational cohort	N=20 patients	MR with no comparator. Attempted to correlate patient symptoms for MRI results	MR normal in 9/20 subjects No statistically significant results found	Structural lesions may influence the degree or severity of symptoms in patients with post-concussion headache	Moderate
Levin et al., 1992 Serial MRI and neurobehavioral findings after mild to moderate closed head injury	Prospective cohort	N=50 patients	CT vs MR	40 subjects had abnormalities on initial MR- 13 of these patients had normal CT. 9 subjects had lesions on CT that were not visualized on MR	There is no correlation between brain lesion size and/or type on CT imaging and performance on neurobehavioral tests after mild-moderate head injury	Low
Initial QOE Score Across Studies for PICO #7: **Moderate (2)**						

SEMPI Grading QOE—Table 8A.7b—Risk of Bias		
PICO #7: In adults with persistent headache and suspected post-concussive syndrome does neuroimaging impact patient management?		
Evaluate Outcome for Risk of Bias Across Studies		
Initial QOE Score Across Studies for PICO: **MODERATE**		
Criteria	**Assessment**	**Reason for Assessment**
Negative Bias		
Risk of Bias	Not Serious	Small sample size may have resulted in statically insignificant results, decrease taken as part of indirectness
Inconsistency	Serious	Considerable heterogeneity of patient population between studies
Indirectness	Serious	Studies do not include moderate or severe head trauma and does not address whether imaging findings change management
Imprecision	Not Serious	
Positive Bias		
Strength of Association	Low	
Other Considerations	No	
Overall Effect of Bias on Initial QOE Grade: Downgraded to LOW		
Final QOE Grade for Outcome Across Studies: **LOW**		
High – Very confident the true effect lies close to that of the estimate of the effect **Moderate** – Moderately confident in the effect estimate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different) **Low** – Confidence in the effect estimate is limited (the true effect may be substantially different from the estimate of effect) **Very Low** – Very little confidence in the effect estimate (the true effect is likely to be substantially different from the estimate of effect)		

SEMPI Grading QOE—Table 8A.7c—Evidence to Recommendations

PICO #7: In adults with persistent headache and suspected post-concussive syndrome does neuroimaging impact patient management?

SEMPI Quality of Evidence (QOE) & Recommendation Strength

Author/Year/Title	Highlights	SEMPI QOE Rating	Final QOE Category	Recommendation Strength
Rose et al., 2017 Utilization of conventional neuroimaging followin g youth concussion	In youth concussion settings CT imaging is preferred in acutely while magnetic resonance (MR) imaging is used in the sub-acute and chronic post-concussion periods. Delayed neuroimaging (months to years) for "post-concussion headache" has limited clinical yield	Moderate	Low (3)	Strong (A)
Dean et al., 2015 Multimodal imaging of mild traumatic brain injury and persistent postconcussion syndrome	Magnetic resonance imaging may help improve detection of brain abnormalities after mild traumatic brain injury, but larger, prospective studies are needed to confirm this	Low		
Datta et al., 2009 Post-concussion syndrome: Correlation of neuropsychological deficits, structural lesions on magnetic resonance imaging and symptoms	Structural lesions may influence the degree or severity of symptoms in patients with post-concussion headache	Moderate		
Levin et al., 1992 Serial MRI and neurobehavioural findings after mild to moderate closed head injury	There is no correlation between brain lesion size and/or type on CT imaging and performance on neurobehavioral tests after mild-moderate head injury	Low		

Recommendation Rating: 3A—Strong recommendation for the intervention based on low quality evidence

Justification: Small sample sizes and heterogeneous study populations lower quality of evidence.

Rating Definitions:

Quality of Evidence: High quality = **1**; Moderate quality = **2**; Low quality = **3**; Very low quality = **4**

Strength of Recommendation: A = Strength of Recommendation from Consistent Evidence; **B** = Strength of Recommendation from Panel Consensus

Conclusion: The evidence does not support imaging for post-concussive syndrome due to a lack of correlation between symptoms and imaging findings. In acute concussive head injury**,** the American Association of Neurology and the American Medical Society of Sports Medicine Guidelines, recommend that imaging should only be performed if there are concerns regarding skull fracture, intracranial hemorrhage, or other intracranial pathology based on clinical exam (Giza et al., 2013; Harmon et al., 2013). Conversely post concussive headache (occurring at a latency period of weeks to months) generally does not warrant imaging.

Although it has been proposed that “pregnancy” should be added to the list of indications warranting neuroimaging to identify secondary headache disorders, this is not without serious issues and the proper alternatives are not supported by strong evidence (Micieli & Kingston, 2019; Ramchandren et al., 2007; Robbins et al., 2015; Sandoe & Lay, 2019). Depending on urgency/availability/clinical findings, unenhanced CT imaging with adequate shielding to minimize fetal radiation exposure, can be performed as an alternative to MR imaging in pregnant patients presenting with a new headache or one that has changed in severity or symptomatology. Therefore, pregnancy represents a clinical scenario in which consultation between radiologist, ordering provider, and, if possible, obstetrician is required to optimize imaging accuracy while ensuring maximal safety.
Final Recommendation: 3A—In adults with persistent headache and suspected post-concussive syndrome, routine neuroimaging is not recommended as it rarely impacts patient management.

PICO #8: In adults with headache, what clinical predictors warrant MR imaging of the brain for optimal patient management?

<table>
<tr><th colspan="7">SEMPI Grading QOE—Table 8A.8a—Summary of Findings</th></tr>
<tr><td colspan="7">PICO #8: In adults with headache, what clinical predictors warrant MR imaging of the brain for optimal patient management?</td></tr>
<tr><th>Author/Year/Title</th><th>Design</th><th>Population</th><th>Intervention Vs Comparator</th><th>Results</th><th>Conclusion Summary</th><th>SEMPI QOE Rating</th></tr>
<tr><td>Budweg et al., 2016
Factors associated with significant MRI findings in medical walk-in patients with acute headache</td><td>Retrospective Cohort</td><td>N=513 patients that received an MRI for acute headache</td><td>Significant results on MRI vs No significant results on HA</td><td><u>Odds Ratio for significant findings</u>
Female-3.08 Ophthalmologic symptoms-3.93 Syncope-31.38 Vomiting-7.45</td><td>In patients presenting with headache, a history of syncope within the last 3 days or at least 2 other risk factors (vomiting, ophthalmologic symptoms, female) should be evaluated by magnetic resonance neuroimaging</td><td>Low</td></tr>
<tr><td>Gilbert et al., 2012
Atraumatic headache in US emergency departments: recent trends in CT/MRI utilisation and factors associated with severe intracranial pathology</td><td>Retrospective cohort from USA National hospital ambulatory medical care survey 1998-2008</td><td>N=15,062 records examined</td><td>CT/MR results correlated with clinical predictors</td><td><u>Odds Ratios for statistically significant variables</u>

Sensory disturbance-6.04 Speech disturbance-10.54 Vision disturbance-3.02 Motor disturbance-11.67 Neurological weakness-8.46</td><td>Sensory, speech, vision and motor disturbances along with neurological weakness are statistically significant indicators of intracranial pathology</td><td>Low</td></tr>
<tr><td>Chen et al., 2009
Cough headache: a study of 83 consecutive patients</td><td>Prospective Cohort</td><td>N=83 patients</td><td>MRI or CT</td><td>9/83 had intracranial lesion(s)
MRI: 80 pts
CT: 3 pts
91.6% with contrast (MRI 74, CT 2)</td><td>A significant number of patients with cough headache (i.e., with Valsalva) have intracranial lesions thought to be the underlying cause</td><td>Low</td></tr>
<tr><td>Kernick et al., 2008
Imaging for suspected brain tumour: guidance for primary care</td><td>Systematic Review</td><td>N/A</td><td>N/A</td><td><table><tr><th>Clinical feature</th><th>Likelihood ratio, 95% CI</th><th>Risk of tumor (primary care%)</th></tr><tr><td>HA waking from sleep</td><td>98 (10-960)</td><td>9</td></tr><tr><td>Dizziness</td><td>49 (3-710)</td><td>4</td></tr><tr><td>Increasing headache freq.</td><td>12 (3-48)</td><td>1</td></tr></table></td><td>Patients in whom there is a greater than 1% chance of a brain tumor should be imaged and includes patients with:
-papilledema
-significant alterations in consciousness or mental status</td><td>Moderate</td></tr>
</table>

				Abnormal neuro exam | 5.3 (2.4-12) | 0.5 Focal neuro Sx | 3.1 (0.37-25) | 0.3 Aggravated by Valsalva | 2.3 (1.4-3.8) | 0.2 Associated vomiting | 1.8 (1.2-2.6) | 0.2 Worsening headache | 1.6 (0.23-10) | 0.1	-new seizures -new cluster headaches -HA with history of cancer -HA with other neurologic symptoms. Patients with a 0.1-1% chance of a tumor should have a low threshold for imaging including: -HA not diagnosed after 8 weeks -HA aggravated by exertion or Valsalva -HA with vomiting -chronic HA that has changed significantly -new onset HA and over 50 years of age -HA that wakes patient from sleep	
Detsky et al., 2006 Does this patient with headache have a migraine or need neuroimaging	Systematic review	11 studies with N=3725 patients	N/A	Significant Likelihood Ratios Cluster type headache-11 Abnormal neurologic exam- 5.3 Undefined headache type- 3.8 Headache with aura-3.2 Headache worsened by exertion or Valsalva-like maneuver-2.3 Headache with vomiting-1.8	Patients with abnormal findings on neurologic examinations, cluster type headache, headache with aura, headache that is not clearly defined, headache with vomiting or headache aggravated by exertion of Valsalva-like maneuver should undergo neuroimaging	Moderate
Cohen et al., 2006 Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) or cranial autonomic features (SUNA) –a prospective clinical study of SUNCT and SUNA	Prospective Cohort	N=43 SUNCT patients N=9 SUNA patients	MR	11/43 SUNCT patients had significant abnormalities in intracranial imaging 1/9 SUNA patient had significant abnormalities in intracranial imaging	Trigeminal autonomic cephalgias are significant indicators of abnormal intracranial lesions	Low

Tsushima & Endo, 2005 MR imaging in the evaluation of chronic or recurrent headache	Retrospective review	N=306 adults with chronic or recurrent headache who were evaluated by MR imaging	MRI findings were placed in 3 groups: no abnormality, minor abnormality, clinically important abnormality	**3 groups:** 1) 169 (55.2%): no abnormality on MR 2) 135 44.1%): minor abnormality on MR 3) 2 (0.7%): clinically important MR finding that may explain headaches Clinically important infarctions were noted on MR images in five (26.3%) of 19 patients with complicated migraine.	Magnetic resonance (MR) imaging has low diagnostic yield in the evaluation of patients with chronic or recurrent headache and normal neurologic findings. Neither contrast enhancement nor repeated MR imaging produces higher diagnostic yield in these populations	Low
Quality Standards Subcommittee of the American Academy of Neurology, 1994 Report of the Quality Standards Subcommittee of the American Academy of Neurology--Practice parameter: the utility of neuroimaging in the evaluation of headache in patients with normal neurological examinations	Systematic review of the literature	Adults with headache and normal neurologic exams	Clinical exam versus imaging versus outcome	There is insufficient evidence to define the role of CT and MR in the evaluation of patients with headache that is not consistent with migraine	Neither CT nor MR is warranted in adult patients whose headaches (HA) fit a broad definition of recurrent migraine and who have **not** demonstrated the following: -recent change in HA pattern -history of seizures -presence of focal neurological signs	Moderate
Initial QOE Score Across Studies for PICO #8: **Moderate (2)**						

SEMPI Grading QOE—Table 8A.8b—Risk of Bias		
PICO #8: In adults with headache, what clinical predictors warrant MR imaging of the brain for optimal patient management?		
Evaluate Outcome for Risk of Bias Across Studies		
Initial QOE Score Across Studies for PICO: **MODERATE**		
Criteria	**Assessment**	**Reason for Assessment**
Negative Bias		
Risk of Bias	Not Serious	Meta-analysis and systematic reviews (Some studies had small sample size)
Inconsistency	Serious	Studies evaluated different outcomes
Indirectness	Serious	Conclusions extrapolated from authors findings
Imprecision	Not Serious	
Positive Bias		
Strength of Association	Moderate	Similar predictors inferred
Other Considerations	No	
Overall Effect of Bias on Initial QOE Grade: Downgraded to LOW		
Final QOE Grade for Outcome Across Studies: **LOW**		

High – Very confident the true effect lies close to that of the estimate of the effect
Moderate – Moderately confident in the effect estimate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different)
Low – Confidence in the effect estimate is limited (the true effect may be substantially different from the estimate of effect)
Very Low – Very little confidence in the effect estimate (the true effect is likely to be substantially different from the estimate of effect)

SEMPI Grading QOE—Table 8A.8c—Evidence to Recommendations				
PICO #8: In adults with headache, what clinical predictors warrant MR imaging of the brain for optimal patient management?				
SEMPI Quality of Evidence (QOE) & Recommendation Strength				
Author/Year/Title	Highlights	SEMPI QOE Rating	Final QOE Category	Recommendation Strength
Budweg et al., 2016 Factors associated with significant MRI findings in medical walk-in patients with acute headache	In patients presenting with headache, a history of syncope within the last 3 days or at least 2 other risk factors (vomiting, ophthalmologic symptoms, female) should be evaluated by magnetic resonance neuroimaging	Low	Low (3)	Consensus (B)
Gilbert et al., 2012 Atraumatic headache in US emergency departments: recent trends in CT/MRI utilisation and factors associated with severe intracranial pathology	Sensory, speech, vision and motor disturbances along with neurological weakness are statistically significant indicators of intracranial pathology	Low		
Chen et al., 2009 Cough headache: a study of 83 consecutive patients	A significant number of patients with cough headache (i.e., with Valsalva) have intracranial lesions thought to be the underlying cause	Low		
Kernick et al., 2008 Imaging patients with suspected brain tumour: guidance for primary care	Patients in whom there is a greater than 1% chance of a brain tumor should be imaged and includes patients with: -papilledema -significant alterations in consciousness/mental status -new seizures -new cluster headaches -HA with history of cancer -HA with other neurologic symptoms. Patients with a 0.1-1%% chance of a tumor should have a low threshold for imaging including: -HA not diagnosed after 8 weeks -HA aggravated by exertion or Valsalva -HA with vomiting -chronic HA that has changed significantly -new onset HA and over 50 years of age -HA that wakes patient from sleep	Moderate		

Detsky et al., 2006 Does this patient with headache have a migraine or need neuroimaging	Patients with abnormal findings on neurologic examinations, cluster type headache, headache with aura, headache that is not clearly defined, headache with vomiting or headache aggravated by exertion of Valsalva-like maneuver should undergo neuroimaging	Moderate		
Cohen et al., 2006 Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) or cranial autonomic features (SUNA) –a prospective clinical study of SUNCT and SUNA	Trigeminal autonomic cephalgias are significant indicators of abnormal intracranial lesions	Low		
Tsushima & Endo, 2005 MR imaging in the evaluation of chronic or recurrent headaches	Magnetic resonance (MR) imaging has low diagnostic yield in the evaluation of patients with chronic or recurrent headache and normal neurologic findings. Neither contrast enhancement nor repeated MR imaging produces higher diagnostic yield in these populations	Low		
Quality Standards Subcommittee of the American Academy of Neurology, 1994 Report of the Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: the utility of neuroimaging in the evaluation of headache in patients with normal neurologic examinations	Neither CT nor MR is warranted in adult patients whose headaches (HA) fit a broad definition of recurrent migraine and who have **not** demonstrated the following: -recent change in HA pattern -history of seizures -presence of focal neurological signs	Moderate		

Recommendation Rating: 3B—Consensus recommendation for the intervention based on low quality evidence

Justification: Lack of quality clinical trials and inconsistent imaging recommendations among available studies warrants a downgrade of QOE and a consensus recommendation

Rating Definitions:

Quality of Evidence: High quality = **1**; Moderate quality = **2**; Low quality = **3**; Very low quality = **4**

Strength of Recommendation: A = Strength of Recommendation from Consistent Evidence; **B** = Strength of Recommendation from Panel Consensus

Conclusion: While CT has emerged as the neuroimaging modality of choice in emergent situations (i.e. following trauma or amidst concern for SAH within the first 6 hours), it offers lower value outside of the emergency department (ED) for identifying the wide array of secondary headache etiologies and provides poor visualization of the posterior fossa. Indications for magnetic resonance (MR) imaging are not as well defined. Even though MR imaging is frequently used in patients with headache, there are no well-established guidelines for the appropriate use of MR. MR is considered most accurate for the identification of intracranial lesions and secondary causes of headache when symptom onset is greater than 6 hours or outside of the ED. Some studies have considered the likelihood ratio for specific symptoms and suggest imaging based on the increased probability of finding significant intracranial abnormalities. It is prudent to only image patients who have an increased likelihood of abnormality based on their clinical signs/symptoms.

Although it has been proposed that "pregnancy" should be added to the list of indications warranting neuroimaging to identify secondary headache disorders, this is not without serious issues and the proper alternatives are not supported by strong evidence (Micieli & Kingston, 2019; Ramchandren et al., 2007; Robbins et al., 2015; Sandoe & Lay, 2019). Depending on urgency/availability/clinical findings, unenhanced CT imaging with adequate shielding to minimize fetal radiation exposure, can be performed as an alternative to MR imaging in pregnant patients presenting with a new headache or one that has changed in severity or symptomatology. Therefore, pregnancy represents a clinical scenario in which consultation between radiologist, ordering provider, and, if possible, obstetrician is required to optimize imaging accuracy while ensuring maximal safety.
Final Recommendation: 3B—MR imaging of the head (brain) is recommended for optimal patient management in adults with non-emergent headache in presence of any of the following clinical predictors: • Papilledema • New seizures • Headache aggravated or precipitated by exertion or Valsalva • Headache with unusual/different aura • Chronic headache that has changed in nature/intensity • History of cancer • Abnormal (or focal) neurologic findings • Cluster headache or other trigeminal autonomic cephalgia (TAC) • New headache during pregnancy

PICO #9: In adults with headache and suspected meningitis, is CT of the head warranted prior to lumbar puncture (LP) for optimal patient management?

SEMPI Grading QOE—Table 8A.9a—Summary of Findings						
PICO #9: In adults with headache and suspected meningitis, is CT of the head warranted prior to lumbar puncture (LP) for optimal patient management?						
Author/Year/Title	Design	Population	Intervention Vs Comparator	Results	Conclusion Summary	SEMPI QOE Rating
Glimåker et al., 2018 Lumbar puncture performed promptly or after neuroimaging in acute bacterial meningitis in adults: a prospective national cohort study evaluating different guidelines	Retrospective cohort study Prospectively registered adults (17 years and older) with community - acquired bacterial meningitis Multicenter (29 Swedish clinics)	N=815 Charts review to include mortality and outcome—favorable vs not favorable Assess effect on outcome of adherence to 3 different national guidelines regarding neuroimaging prior to lumbar puncture (LP)	Swedish, ESCMID, and IDSA guidelines compared	Indications for CT pre-LP: Swedish: 7% ESCMID: 32% IDSA: 65% Adjusted Odds ratios (95% CI) for mortality/favorable (++) outcome: Swedish: 0.48 (0.26-0.89) and 1.52 (1.08-2.12) ESCMID: 0.68 (0.38-1.23) and 1.05 (0.75-1.47) IDSA: 1.09 (0.61-1.95) and 0.59 (0.42-0.82) LP without CT / LP with prior CT: mortality 4% / 10%, p < 0.001 ++ outcome—62% /43%, p < 0.001 No difference in mortality or outcomes when LP without CT performed in Pts with decreased mental status, immunosuppression, or seizures.	Adherence to guidelines that promote prompt lumbar puncture (without prior CT imaging of the head) is associated with lower mortality and higher rates of favorable outcomes. Specifically, immunosuppression, mental status, and new-onset seizures do not warrant delaying lumbar puncture with neuroimaging in adults with suspected bacterial meningitis	Moderate
Costerus et al., 2018 Cranial Computed Tomography, Lumbar Puncture, and Clinical Deterioration in Bacterial Meningitis: A Nationwide Cohort Study	Prospective cohort study Multicenter Evaluate head CT findings in those with CNS deterioration after LP vs control group	N= 1533 episodes of bacterial meningitis GCS=Glasgow Coma Scale LP-lumbar puncture	Evaluate head CT findings in those with CNS deterioration after LP versus Control group (no CNS deterioration after LP)	100/1533 died within 7 days of presentation (58=GCS 8 or higher; 42=GCS< 8); and 53/100 excluded from final analysis Of 47, 29 (GCS 8+) deteriorated after LP and 18 (GCS < 8) deteriorated after LP Head CT done in 43/47 prior to LP Control group=43 with CT prior to LP without deterioration	Cerebral herniation caused by lumbar puncture (LP) is uncommon, and performing an LP is safe in the majority of patients with suspected bacterial meningitis. CT imaging should be selective (for patients with contraindications for LP) and **antimicrobial therapy should be initiated PRIOR to CT imaging (not delayed)**.	Moderate

	(no CNS deterioration 4 readers			6/43 (14%) with deterioration post-LP had contraindications on head CT 5/43 (11%) without deterioration post-LP had contraindications on head CT Interrater reliability moderate at 0.47		
Salazar & Hasbun, 2017 Cranial Imaging Before Lumbar Puncture in Adults wit h Community-Acquired Meningitis: Clinical Utility and Adherence to the Infectious Diseases Society of America Guidelines	Retrospective study	N=614 patients with meningitis (207 head CT indicated; 407 head CT not indicated)	CT performed according to IDSA guidelines versus CT performed not according to IDSA guidelines	Indications for undergoing head Computed Tomography prior to lumbar puncture in 614 Patients with Community-Acquired Meningitis as per Infectious Diseases Society of America Criteria -Abnormal consciousness 118(19.1%) -Immunocompromised 83 (13.4%) -Focal neurologic deficit 43 (6.9%) -New-onset seizures 26 (4.2%) -History of CNS disease 18 (2.9%) -Papilledema 1 (0.2%) CT not indicated by IDSA guidelines- 66.3% CT indicated by IDSA guidelines-33.7% CT ordered before LP- 89% Clinician non-adherence to IDSA guidelines- 60% CT ordered when not indicated- 64% CT not ordered when indicated 0.6% Intracranial abnormalities on CT in patients with indication for CT- 18.1% Intracranial abnormalities on CT in patients without indication for CT- 0.05%(P < .05) Major intracranial findings- 2.7% (all with an indication for brain imaging). Only 8/614 had abnormalities that affected clinical management	Most clinicians do not adhere to IDSA guidelines, delaying diagnostic LP and increasing costs. Usefulness of head CT in patients with CAM without an indication for imaging is limited and has no impact in clinical management.	Moderate

van de Beek et al., 2016 ESCMID guideline: diagnosis and treatment of acute bacterial meningitis	Systematic review of the literature	Adults with/being evaluated for bacterial meningitis	Examination +/- head CT prior to LP versus outcome	-The risk of cerebral herniation after lumbar puncture in patients with suspected bacterial meningitis is increased compared to normal individuals -Clinical characteristics can be used to identify patients with an increased risk for space- occupying lesions associated with increased risk of cerebral herniation due to lumbar puncture When hydrocephalus or space-occupying lesions, such as subdural empyema, brain abscess or intracerebral hemorrhages, are detected on cranial imaging, neurosurgical intervention may be warranted to prevent cerebral herniation and sometimes remove the lesion. In most patients with obstructive hydrocephalus, placement of an external ventricular drain is indicated.	It is strongly recommended to perform CT cranial imaging before lumbar puncture in patients with: -Focal neurologic deficits -New-onset seizures. -Severely altered mental status (GCS <10) -Immunocompromised state In patients lacking these characteristics, cranial imaging before lumbar puncture is not recommended	Moderate
Hasbun et al., 2001 Computed tomography of the head before lumbar puncture in adults with suspected meningitis	Prospective cohort study	N=235 adults with suspected meningitis who underwent head CT prior to LP	Examination versus head CT prior to LP	56/235 (24%) had an abnormal CT of which 11/235 (5%) had evidence of a mass effect. Clinical features associated with an abnormal CT were age >/= 60 yrs., immunocompromise, history of CNS disease, seizure, and neuro abnormalities. The Modified National Institutes of Health Stroke Scale – 9 items: all of these clinical items were not present in 96 of 235 (41%). Of these 96, the CT was negative in 93, NPV of 97% Herniations- 2 in patients with severe mass effect on CT who did not have LP No herniations in patients who had LP	In adults with suspected meningitis, clinical features can be used to identify those who should be evaluated by CT prior to LP. These include: -Age >/= 60 years -Immunocompromised -History of CNS disease -New Seizure (within 1 wk.) -Focal neurologic deficit	Moderate

Gopal et al., 1999 Cranial computed tomography before lumbar puncture: a prospective clinical evaluation	Prospective consecutive enrollment cohort study	N=113 adults with urgent need for lumbar puncture (LP) (42.3% r/o SAH 36.9% r/o meningitis 20.7% other)	Examination & clinical impression versus head CT prior to LP	New lesions identified on CT in 17/111 (15.3%) of which 3/111 (2.7%) had absolute contraindications to LP. The remaining 14 underwent uneventful LP. 3 statistically significant predictors of new intracranial lesions identified: -altered mental status LR 2.2 -focal neuro exam LR 4.3 -papilledema LR 11.1 -clinical impression LR 18.8	3 clinical predictors to identify patients with the greatest risk of having intracranial lesions. -Altered mental status -Focal neurologic deficit -Papilledema CT detected 3 patients (2.7%) in whom LP would not be safe and thus LP was avoided	Low
Initial QOE Score Across Studies for PICO #9: **Moderate (2)**						

SEMPI Grading QOE—Table 8A.9b—Risk of Bias		
PICO #9: In adults with headache and suspected meningitis, is CT of the head warranted prior to lumbar puncture (LP) for optimal patient management?		
Evaluate Outcome for Risk of Bias Across Studies		
Initial QOE Score Across Studies for PICO: **MODERATE**		
Criteria	**Assessment**	**Reason for Assessment**
Negative Bias		
Risk of Bias	Serious	Variable populations across studies—some with confirmed dx of acute bacterial meningitis (not "suspected"), non-randomized, significant numbers of eligible patients had missing data; largely retrospective application of guidelines to data prospectively collected
Inconsistency	Serious	
Indirectness	Serious	Non-meningitis (e.g., SAH) populations evaluated
Imprecision	Not Serious	
Positive Bias		
Strength of Association	Low	
Other Considerations	No	
Overall Effect of Bias on Initial QOE Grade: Downgraded to LOW		
Final QOE Grade for Outcome Across Studies: **LOW**		
High – Very confident the true effect lies close to that of the estimate of the effect **Moderate** – Moderately confident in the effect estimate (the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different) **Low** – Confidence in the effect estimate is limited (the true effect may be substantially different from the estimate of effect) **Very Low** – Very little confidence in the effect estimate (the true effect is likely to be substantially different from the estimate of effect)		

SEMPI Grading QOE—Table 8A.9c—Evidence to Recommendations

PICO #9: In adults with headache and suspected meningitis, is CT of the head warranted prior to lumbar puncture (LP) for optimal patient management?

SEMPI Quality of Evidence (QOE) & Recommendation Strength

Author/Year/Title	Highlights	SEMPI QOE Rating	Final QOE Category	Recommendation Strength
Glimåker et al., 2018 Lumbar puncture performed promptly or after neuroimaging in acute bacterial meningitis in adults: a prospective national cohort study evaluating different guidelines	Adherence to guidelines that promote prompt lumbar puncture (without prior CT imaging of the head) is associated with lower mortality and higher rates of favorable outcomes. Specifically, immunosuppression, mental status, and new-onset seizures do not warrant delaying lumbar puncture with neuroimaging in adults with suspected bacterial meningitis	Moderate	Low (3)	Strong (A)
Costerus et al., 2018 Cranial Computed Tomography, Lumbar Puncture, and Clinical Deterioration in Bacterial Meningitis: A Nationwide Cohort Study	Cerebral herniation caused by lumbar puncture (LP) is uncommon, and performing an LP is safe in the majority of patients with suspected bacterial meningitis. CT imaging should be selective (for patients with contraindications for LP) and **antimicrobial therapy should be initiated PRIOR to CT imaging (not delayed)**.	Moderate		
Salazar & Hasbun, 2017 Cranial Imaging Before Lumbar Puncture in Adults with Community-Acquired Meningitis: Clinical Utility and Adherence to the Infectious Diseases Society of America Guidelines	In patients with suspected community acquired meningitis who demonstrate altered level of consciousness, focal neurologic deficit, seizures, papilledema, a hx of CNS disease or immunocompromise, CT should be performed prior to lumbar puncture	Moderate		
van de Beek et al., 2016 ESCMID guideline: diagnosis and treatment of acute bacterial meningitis	It is strongly recommended to perform CT cranial imaging before lumbar puncture in patients with: -Focal neurologic deficits -New-onset seizures. -Severely altered mental status (GCS <10) -Immunocompromised state	Moderate		
Hasbun et al., 2001 Computed tomography of the head before lumbar puncture in adults with suspected meningitis	Adults with suspected meningitis, clinical features to identify those should be evaluated by CT prior to LP are: -Age >/= 60 years -Immunocompromised -History of CNS disease -New Seizure (within 1 wk.) -Focal neurologic deficit	Moderate		

Gopal et al., 1999 Cranial computed tomography before lumbar puncture: a prospective clinical evaluation	3 clinical predictors to identify patients with the greatest risk of having intracranial lesions: -Altered mental status -Focal neurologic deficit -Papilledema	Low		

Recommendation Rating: 3A—Strong recommendation for the intervention based on low quality evidence

Justification: Low quality of evidence due to indirectness but consistent conclusions support the recommendation.

Rating Definitions:

Quality of Evidence: High quality = **1**; Moderate quality = **2**; Low quality = **3**; Very low quality = **4**

Strength of Recommendation: A = Strength of Recommendation from Consistent Evidence; **B** = Strength of Recommendation from Panel Consensus

Conclusion: The practice of "CT then LP" is commonly used in the investigation of meningitis because of the risk of brain herniation associated with lumbar puncture procedure. This practice has led to an increased utilization of CT scans. It is important to note this catastrophic complication occurs in 3-5% of patients with acute bacterial meningitis (Costerus et al., 2018; Joffe, 2007). Professional society guidelines including IDSA 2004, ESCMID 2016, Swedish 2015 have recommended a selective approach to identify at risk patients to balance the uncommon risk of herniation with the risks of CT delaying LP and starting antibiotics (Tunkel et al., 2004; Glimåker et al., 2015; van de Beek et al., 2016). One Swedish retrospective study suggests that delays in meningitis treatment due to obtaining CT in this patient population may increase mortality, although this might reflect confounding by indication (Glimåker et al., 2018).

Final Recommendation: 3A—In adults with headache and suspected meningitis, CT of the head is recommended prior to lumbar puncture (LP) in selected patients with risk factors such as signs of herniation, focal neurological deficit, papilledema, severely altered mental status (Glasgow Coma Scale < 10), age equal to or greater than 60 years.

REFERENCES

Agid, R., Shelef, I., Scott, J.N., & Farb, R.I. (2008). Imaging of the intracranial venous system. *The neurologist*, *14*(1), 12-22.

Arienta, C., Caroli, M., & Balbi, S. (1997). Management of head-injured patients in the emergency department: a practical protocol. *Surgical Neurology, 48*(3), 213-219.

Bley, T. A., Reinhard, M., Hauenstein, C., Markl, M., Warnatz, K., Hetzel, A., . . . Langer, M. (2008). Comparison of duplex sonography and high-resolution magnetic resonance imaging in the diagnosis of giant cell (temporal) arteritis. *Arthritis & Rheumatism*, *58*(8), 2574-2578.

Budweg, J., Sprenger, T., De Vere-Tyndall, A., Hagenkord, A., Stippich, C., & Berger, C.T. (2016). Factors associated with significant MRI findings in medical walk-in patients with acute headache. *Swiss Medical Weekly*, *146*, w14349.

Bulger, E.M., Nathens, A.B., Rivara, F.P., Moore, A., MacKenzie, E.J., Jurkovich, G.J., & Brain Trauma Foundation. (2002). Management of severe head injury: institutional variations in care and effect on outcome. *Critical Care Medicine*, *30*(8), 1870-1876.

Cady, R.K., Dodick, D.W., Levine, H.L., Schreiber, C.P., Eross, E.J., Setzen, M., . . . Durham, P.L. (2005). Sinus headache: a neurology, otolaryngology, allergy, and primary care consensus on diagnosis and treatment. In *Mayo Clinic Proceedings* (Vol. 80, No. 7, pp. 908-916). Elsevier.

Carpenter, C.R., Hussain, A.M., Ward, M.J., Zipfel, G.J., Fowler, S., Pines, J.M., & Sivilotti, M.L. (2016). Spontaneous Subarachnoid Hemorrhage: A Systematic Review and Meta-analysis Describing the Diagnostic Accuracy of History, Physical Examination, Imaging, and Lumbar Puncture with an Exploration of Test Thresholds. *Academic Emergency Medicine*, *23*(9), 963-1003.

Chen, P.K., Fuh, J.L., & Wang, S.J. (2009). Cough headache: a study of 83 consecutive patients. *Cephalalgia*, *29*(10), 1079-1085.

Clarke, C.E., Edwards, J., Nicholl, D.J., & Sivaguru, A. (2010). Imaging results in a consecutive series of 530 new patients in the Birmingham Headache Service. *Journal of neurology*, *257*(8), 1274-1278.

Cohen, A.S., Matharu, M.S., & Goadsby, P.J. (2006). Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) or cranial autonomic features (SUNA)—a prospective clinical study of SUNCT and SUNA. *Brain*, *129*(10), 2746-2760.

Costerus, J.M., Brouwer, M.C., Sprengers, M.E., Roosendaal, S.D., van der Ende, A., & van de Beek, D. (2018). Cranial Computed Tomography, Lumbar Puncture, and Clinical Deterioration in Bacterial Meningitis: A Nationwide Cohort Study. *Clinical Infectious Diseases, 67*(6), 920-926.

da Rocha, A.J., da Silva, C.J., Gama, H.P.P., Baccin, C.E., Braga, F.T., de Araújo Cesare, F., & Veiga, J.C.E. (2006). Comparison of magnetic resonance imaging sequences with computed tomography to detect low-grade subarachnoid hemorrhage: role of fluid-attenuated inversion recovery sequence. *Journal of computer assisted tomography, 30*(2), 295-303.

Datta, S.G., Pillai, S.V., Rao, S.L., Kovoor, J.M., & Chandramouli, B.A. (2009). Post-concussion syndrome: Correlation of neuropsychological deficits, structural lesions on magnetic resonance imaging and symptoms. *Neurology India, 57*(5), 594.

Dean, P.J., Sato, J.R., Vieira, G., McNamara, A., & Sterr, A. Multimodal imaging of mild traumatic brain injury and persistent post-concussion syndrome. (2015). *Brain and Behavior*, *5*(1), 45-61.

Dejaco, C., Ramiro, S., Duftner, C., Besson, F.L., Bley, T.A., Blockmans, D., . . . Schmidt, W.A. (2018). EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. *Annals of the Rheumatic Diseases*, annrheumdis-2017.

Detsky, M.E., McDonald, D.R., Baerlocher, M.O., Tomlinson, G.A., McCrory, D.C., Booth, C.M. (2006). Does this patient with headache have a migraine or need neuroimaging? *Journal of American Medical Association*, *296*(10), 1274-1283.

Diamantopoulos, A.P., Haugeberg, G., Hetland, H., Soldal, D.M., Bie, R., & Myklebust, G. (2014). Diagnostic value of color Doppler ultrasonography of temporal arteries and large vessels in giant cell arteritis: a consecutive case series. *Arthritis care & research*, *66*(1), 113-119.

Do, T.P., Remmers, A., Schytz, H.W., Schankin, C., Nelson, S.E., Obermann, M., . . . Schoonman, G.G. (2019). Red and orange flags for secondary headaches in clinical practice: SNNOOP10 list. *Neurology, 92*(3), 134-144.

Dodick, D. W. (2003). Diagnosing headache: clinical clues and clinical rules. *Advanced Studies Medicine*, *3*(2), 87-92.

Dubosh, N.M., Bellolio, M.F., Rabinstein, A.A., & Edlow, J.A. (2016). Sensitivity of Early Brain Computed tomography to Exclude Aneurysmal Subarachnoid Hemorrhage: A Systematic Review and Meta-Analysis. *Stroke*, STROKEAHA-115.

Duftner, C., Dejaco, C., Sepriano, A., Falzon, L., Schmidt, W.A., & Ramiro, S. (2018). Imaging in diagnosis, outcome prediction and monitoring of large vessel vasculitis: a systematic literature review and meta-analysis informing the EULAR recommendations. *Rheumatic Musculoskeletal Disorders (RMD) open*, *4*(1), e000612.

Easter, J.S., Haukoos, J.S., Meehan, W.P., Novack, V., & Edlow, J.A. (2015). Will neuroimaging reveal a severe intracranial injury in this adult with minor head trauma?: the rational clinical examination systematic review. *Journal of American Medical Association, 314*(24), 2672-2681.

Edlow, J.A., Panagos, P.D., Godwin, S.A., Thomas, T.L., Decker, W.W., & American College of Emergency Physicians. (2008). Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute headache. *Annals of Emergency Medicine*, *52*(4), 407-436.

El-Shehally, A.A., & Sobh, K. (2014). Is it rhinogenic headache or migraine? The role of sino-nasal endoscope and sinus CT. *Al-Azhar Assiut Medical Journal (AAMJ)*, *12*(4).

Eross, E., Dodick, D., & Eross, M. (2007). The Sinus, Allergy and Migraine Study (SAMS) CME. *Headache: The Journal of Head and Face Pain, 47*(2), 213-224.

Evans, R.W. (1996). Diagnostic testing for the evaluation of headaches. *Neurologic clinics*, *14*(1), 1-26.

Foks, K.A., Dijkland, S.A., Lingsma, H.F., Polinder, S., van den Brand, C.L., Jellema, K., . . . Dippel, D.W. (2019). Risk of Intracranial Complications in Minor Head Injury: The Role of Loss of Consciousness and Post-Traumatic Amnesia in a Multi-Center Observational Study. *Journal of neurotrauma*, *36*(16), 2377-2384.

Gentry, L.R., Godersky, J.C., Thompson, B., & Dunn, V.D. (1988). Prospective comparative study of intermediate-field MR and CT in the evaluation of closed head trauma. *American Journal of Roentgenology*, *150*(3), 673-682.

Gilbert, J.W., Johnson, K.M., Larkin, G.L., & Moore, C.L. (2012). Atraumatic headache in US emergency departments: recent trends in CT/MRI utilisation and factors associated with severe intracranial pathology. *Emergency Medicine Journal*, *29*(7), 576-581.

Gill, H.S., Marcolini, E.G., Barber, D., & Wira, C.R. (2018). Focus: Sensory Biology and Pain: The Utility of Lumbar Puncture After a Negative Head CT in the Emergency Department Evaluation of Subarachnoid Hemorrhage. *The Yale journal of biology and medicine, 91*(1), 3.

Giza, C.C., Kutcher, J.S., Ashwal, S., Barth, J., Getchius, T.S., Gioia, G.A., . . . McKeag, D.B. (2013). Summary of evidence-based guideline update: evaluation and management of concussion in sports: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology, 80*(24), 2250-2257.

Glimåker, M., Johansson, B., Grindborg, Ö., Bottai, M., Lindquist, L., Sjölin, J. (2015). Adult bacterial meningitis: earlier treatment and improved outcome following guideline revision promoting prompt lumbar puncture. *Clinical Infectious Diseases: an official publication of the Infectious Diseases Society of America*, *60*(8),1162-9.

Glimåker, M., Sjölin, J., Åkesson, S., & Naucler, P. (2018). Lumbar puncture performed promptly or after neuroimaging in acute bacterial meningitis in adults: a prospective national cohort study evaluating different guidelines. *Clinical Infectious Diseases*, *66*(3), 321-328.

Goldstein, J.N., Camargo, C.A., Pelletier, A.J., & Edlow, J.A. (2006). Headache in United States emergency departments: demographics, work-up and frequency of pathological diagnoses. *Cephalalgia*, *26*(6), 684-690.

Gómez, P.A., Lobato, R.D., Ortega, J.M., & De La Cruz, J. (1996). Mild head injury: differences in prognosis among patients with a Glasgow Coma Scale score of 13 to 15 and analysis of factors associated with abnormal CT findings. *British Journal of Neurosurgery*, *10*(5), 453-460.

Gopal, A.K., Whitehouse, J.D., Simel, D.L., & Corey, G.R. (1999). Cranial computed tomography before lumbar puncture: a prospective clinical evaluation. *Archives of internal medicine*, *159*(22), 2681-2685.

Harmon, K.G., Drezner, J., Gammons, M., Guskiewicz, K., Halstead, M., Herring, S., . . . Roberts, W. (2013). American Medical Society for Sports Medicine position statement: concussion in sport. *Clinical Journal of Sport Medicine, 23*(1), 1-18.

Hasbun, R., Abrahams, J., Jekel, J., & Quagliarello, V.J. (2001). Computed tomography of the head before lumbar puncture in adults with suspected meningitis. *New England Journal of Medicine*, *345*(24), 1727-1733.

Hodel, J., Aboukais, R., Dutouquet, B., Kalsoum, E., Benadjaoud, M.A., Chechin, D., . . . Leclerc, X. (2015). Double Inversion Recovery MR Sequence for the Detection of Subacute Subarachnoid Hemorrhage. *American Journal of Neuroradiology, 36*(2), 251–258.

Hunder, G.G., Bloch, D.A., Michel, B.A., Stevens, M.B., Arend, W.P., Calabrese, L.H., . . . Lie, J.T. (1990). The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. *Arthritis & Rheumatology*, *33*(8), 1122-1128.

Ifediora, C.O. (2018). Insights into radiographic investigations for headaches in general practice. *Family practice*, *35*(4), 412-419.

Jayawardena, A.D., & Chandra, R. (2018). Headaches and facial pain in rhinology. *American journal of rhinology & allergy, 32*(1), 12-15.

Joffe, A.R. (2007). Lumbar puncture and brain herniation in acute bacterial meningitis: a review. *Journal of intensive care medicine*, *22*(4), 194-207.

Karassa, F.B., Matsagas, M.I., Schmidt, W.A., & Ioannidis, J.P. (2005). Meta-analysis: test performance of ultrasonography for giant-cell arteritis. *Annals of Internal Medicine*, *142*(5), 359-369.

Kernick, D.P., Ahmed, F., Bahra, A., Dowson, A., Elrington, G., Fontebasso, M., . . . Goadsby, P.J. (2008). Imaging patients with suspected brain tumour: guidance for primary care. *The British journal of general practice: the journal of the Royal College of General Practitioners*, *58*(557), 880-885.

Kirsch, C.F. (2019). Headache Caused by Sinus Disease. *Neuroimaging Clinics, 29*(2), 227-241.

Klink, T., Geiger, J., Both, M., Ness, T., Heinzelmann, S., Reinhard, M., . . . Bley, T.A. (2014). Giant cell arteritis: diagnostic accuracy of MR imaging of superficial cranial arteries in initial diagnosis-results from a multicenter trial. *Radiology*, *273*(3), 844-852.

Sobri, M., Lamont, A.C., Alias, N.A., & Win, M.N. (2003). Red flags in patients presenting with headache: clinical indications for neuroimaging. *The British journal of radiology*, *76*(908), 532-535.

Levin, H.S., Williams, D.H., Eisenberg, H.M., High, W.M., Guinto, F.C. (1992). Serial MRI and neurobehavioural findings after mild to moderate closed head injury. *Journal of Neurology, Neurosurgery & Psychiatry*, *55*(4), 255-262.

Lohiya, S.S., Patel, S.V., Pawde, A.M., Bokare, B.D., & Sakhare, P.T. (2016). Comparative study of diagnostic nasal endoscopy and CT paranasal sinuses in diagnosing conic rhinosinusitis. *Indian Journal of Otolaryngology and Head & Neck Surgery, 68*(2), 224-229.

Luqmani, R., Lee, E., Singh, S., Gillett, M., Schmidt, W.A., Bradburn, M., . . . Hutchings, A. (2016). The Role of Ultrasound Compared to Biopsy of Temporal Arteries in the Diagnosis and Treatment of Giant Cell Arteries (TABUL): a diagnostic accuracy and cost-effectiveness study. *Health Technol Assess*, *20*(90), 1-238.

Mehle, M.E., & Kremer, P.S. (2008). Sinus CT scan findings in “sinus headache” migraineurs. *Headache: The Journal of Head and Face Pain*, *48*(1), 67-71.

Micieli, A., & Kingston, W. (2019). An Approach to Identifying Headache Patients That Require Neuroimaging. *Frontiers in Public Health*, *7*, 52.

Migdal, V.L., Wu, W.K., Long, D., McNaughton, C.D., Ward, M.J., & Self, W.H. (2015). Risk-benefit analysis of lumbar puncture to evaluate for nontraumatic subarachnoid hemorrhage in adult ED patients. *The American journal of emergency medicine, 33*(11), 1597-1601

Miller, M.T., Pasquale, M., Kurek, S., White, J., Martin, P., Bannon, K., . . . Li, M. (2004). Initial head computed tomographic scan characteristics have a linear relationship. *Journal of Trauma and Acute Care Surgery*, *56*(5), 967-973.

Miller, D.G., Vakkalanka, P., Moubarek, M.L., Lee, S., & Mohr, N.M. (2018). Reduced computed tomography use in the emergency department evaluation of headache was not followed by increased death or missed diagnosis. *Western Journal of Emergency Medicine*, *19*(2), 319.

Mitchell, C.S., Osborn, R.E., Grosskreutz, S.R. (1993). Computed tomography in the headache patient: is routine evaluation really necessary? *Headache, 33*(2), 82-86.

Mitchell, P., Wilkinson, I.D., Hoggard, N., Paley, M.N., Jellinek, D.A., Powell, T., . . . Griffiths, P.D. (2001). Detection of subarachnoid haemorrhage with magnetic resonance imaging. *Journal of Neurology, Neurosurgery & Psychiatry*, *70*(2), 205-211.

Mower, W.R., Gupta, M., Rodriguez, R., & Hendey, G.W. (2017). Validation of the sensitivity of the National Emergency X-Radiography Utilization Study (NEXUS) Head computed tomographic (CT) decision instrument for selective imaging of blunt head injury patients: An observational study. *PLoS medicine*, *14*(7), e1002313.

Mutch, C.A., Talbott, J.F., & Gean, A. (2016). Imaging evaluation of acute traumatic brain injury. *Neurosurgery Clinics*, *27*(4), 409-439.

Patel, Z.M., Kennedy, D.W., Setzen, M., Poetker, D.M., & DelGaudio, J.M. (2013). "Sinus headache": rhinogenic headache or migraine? An evidence-based guide to diagnosis and treatment. In *International forum of allergy & rhinology* (Vol. 3, No. 3, pp. 221-230).

Pedram, D., Jennifer, H.G., & John, M.D. (2016). Sinus Headache in Chronic Rhinosinusitis (CRS): An Analysis of Otolaryngology Initiated Treatment Efficacy of Migraine in the CRS Patient. *Journal of Sinusitis. Migraine*, *1*, 1.

Perry, J.J., Stiell, I.G., Sivilotti, M.L., Bullard, M. J., Émond, M., Symington, C., . . . Wells, G.A. (2011). Sensitivity of computed tomography performed within six hours of onset of headache for diagnosis of subarachnoid haemorrhage: prospective cohort study. *British Medical Journal*, *343*, d4277.

Quality Standards Subcommittee of the American Academy of Neurology. (1994). Practice parameter: the utility of neuroimaging in the evaluation of headache in patients with normal neurologic examinations (summary statement). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology, 44*(7), 1353-4.

Ramchandren, S., Cross, B.J., Liebeskind, D.S. (2007). Emergent headaches during pregnancy: correlation between neurologic examination and neuroimaging. *American journal of neuroradiology*, *28*(6), 1085-1087.

Ro, Y.S., Shin, S.D., Holmes, J.F., Song, K.J., Park, J.O., Cho, J.S., . . . Traumatic Brain Injury Research Network of Korea (TBI Network). (2011). Comparison of clinical performance of cranial computed tomography rules in patients with minor head injury: a multicenter prospective study. *Academic Emergency Medicine*, *18*(6), 597-604.

Robbins, M.S., Farmakidis, C., Dayal, A.K., & Lipton, R.B. (2015). Acute headache diagnosis in pregnant women: a hospital-based study. Neurology, 85(12), 1024-1030.

Rose, S.C., Schaffer, C.E., Young, J.A., McNally, K.A., Fischer, A.N., & Heyer, G.L. (2017). Utilization of conventional neuroimaging following youth concussion. *Brain Injury*, *31*(2), 260-266.

Saboori, M., Ahmadi, J., Farajzadegan, Z. (2007). Indications for brain CT scan in patients with minor head injury. *Clinical neurology and neurosurgery*, *109*(5), 399-405.

Sait, M.R., Lepore, M., Kwasnicki, R., Allington, J., Balasubramanian, R., Somasundaram, S.K., . . . Barkeji, M. (2017). The 2016 revised ACR criteria for diagnosis of giant cell arteritis–Our case series: Can this avoid unnecessary temporal artery biopsies? *International Journal of Surgery Open, 9*, 19-23.

Salazar, L., & Hasbun, R. (2017). Cranial Imaging Before Lumbar Puncture in Adults With Community Acquired Meningitis: Clinical Utility and Adherence to the Infectious Diseases Society of America Guidelines. *Clinical Infectious diseases: an official publication of the Infectious Diseases Society of America, 64*(12), 1657-1662.

Sammel, A.M., Hsiao, E., Schembri, G., Nguyen, K., Brewer, J., Schrieber, L., . . . Laurent, R. (2019). Diagnostic Accuracy of PET/CT Scan of the Head, Neck and Chest for Giant Cell Arteritis: The Double-Blinded Giant Cell Arteritis and PET Scan (GAPS) Study. *Arthritis & Rheumatology, 71*(8), 1319-1328.

Sandoe, C.H., & Lay, C. (2019). Secondary headaches during pregnancy: When to worry. *Current neurology and neuroscience reports, 19*(6), 27.

Sempere, A.P., Porta-Etessam, J., Medrano, V., Garcia-Morales, I., Concepcion, L., Ramos, A., . . . Botella, C. (2005). Neuroimaging in the evaluation of patients with non-acute headache. *Cephalalgia*, *25*(1), 30-35.

Sharif-Alhoseini, M., Khodadadi, H., Chardoli, M., Rahimi-Movaghar, V. (2011). Indications for brain computed tomography scan after minor head injury. *Journal of emergencies, trauma, and shock*, *4*(4), 472.

Singata, C., & Candy, S. (2018). Is computed tomography of the head justified in patients with minor head trauma presenting with Glasgow Coma Scale 15/15? *SA Journal of Radiology*, *22*(1).

Smits, M., Dippel, D.W., Steyerberg, E.W., de Haan, G.G., Dekker, H.M., Vos, P.E., . . . Hunink, M.G. (2007). Predicting intracranial traumatic findings on computed tomography in patients with minor head injury: the CHIP prediction rule. *Annals of internal medicine*, *146*(6), 397-405.

Starling, A.J. (2018). Diagnosis and management of headache in older adults. In *Mayo Clinic Proceedings* (Vol. 93, No. 2, pp. 252-262). Elsevier.

Tsushima, Y., & Endo, K. (2005). MR Imaging in the Evaluation of Chronic or Recurrent Headache 1. *Radiology*, *235*(2), 575-579.

Tulla, M., Tillgren, T., & Mattila, K. (2019). Is there a role for lumbar puncture in early detection of subarachnoid hemorrhage after negative head CT? *Internal and emergency medicine, 14*(3), 451-457.

Tunkel, A.R., Hartman, B.J., Kaplan, S.L., Kaufman, B.A., Roos, K.L., Scheld, W.M., & Whitley, R.J. (2004). Practice Guidelines for the Management of Bacterial Meningitis. *Clinical Infectious Diseases*, *39*,1267–84.

van de Beek, D., Cabellos, C., Dzupova, O., Esposito, S., Klein, & Kloek, A.T. (2016). ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. *Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases*, *22*(Suppl 3), S37-S62.

Verma, R.K., Kottke, R., Andereggen, L., Weisstanner, C., Zubler, C., Gralla, J., . . . El-Koussy, M. (2013). Detecting subarachnoid hemorrhage: comparison of combined FLAIR/SWI versus CT. *European journal of radiology, 82*(9), 1539-1545.

Waganekar, A., Sadasivan, J., Prabhu, A.S., & Harichandrakumar, K.T. (2018). Computed Tomography Profile and its Utilization in Head Injury Patients in Emergency Department: A Prospective Observational Study. *Journal of emergencies, trauma, and shock*, *11*(1), 25.

Wang, R., Liu, R., Dong, Z., Su, H., Ao, R., Liu, Y., . . . Yu, S. (2019). Unnecessary Neuroimaging for Patients with Primary Headaches. *Headache: The Journal of Head and Face Pain*, *59*(1), 63-68.

Westerlaan, H.E., van Dijk, J.M.C., Jansen-van der Weide, M.C., de Groot, J.C., Groen, R.J., Mooij, J.J., & Oudkerk, M. (2011). Intracranial aneurysms in patients with subarachnoid hemorrhage: CT angiography as a primary examination tool for diagnosis—systematic review and meta-analysis. *Radiology*, *258*(1), 134-145.

Young, N.P., Elrashidi, M.Y., McKie, P.M., & Ebbert, J.O. (2018). Neuroimaging utilization and findings in headache outpatients: Significance of red and yellow flags. *Cephalalgia*, *38*(12), 1841-1848.