

Provider Led Entity

CDI Quality Institute PLE Headache AUC

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Appropriateness of advanced imaging procedures* in patients with headache and the following clinical presentations:

*including MRI with and/or without IV contrast, CT with and/or without IV contrast, MRA, MRV, CTA, CTV, SPECT, and PET

Abbreviation list:

AAN	American Academy of Neurology	PET	Positron emission tomography
ACEP	American College of Emergency Physicians	PLE	Provider Led Entity
ACR	American College of Radiology	RCVS	Reversible cerebral vasoconstriction syndrome
AUC	Appropriate Use Criteria	SAH	Subarachnoid hemorrhage
CSF	Cerebrospinal fluid	SFEMC	French Society for the Study of Migraine and Headache Disorders
CT	Computed tomography	SFN	French Society of Neurology
CTA	Computed tomography angiography	SIGN	Scottish Intercollegiate Guidelines Network
CTP	Computed tomography perfusion	SPECT	Single-photon emission computed tomography
CTV	Computed tomography venography	SUNA	Short-lasting unilateral neuralgiform headache attacks with cranial autonomic features
EFNS	European Federation of Neurological Societies	SUNCT	Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing
EHF	European Headache Federation	SWI	Susceptibility-weighted imaging
FLAIR	Fluid-attenuated inversion recovery	TBI	Traumatic brain injury
ICHD-3	International Classification of Headache Disorders 3 rd edition	TCH	Thunderclap headache
ICSI	Institute for Clinical Systems Improvement	TOP	Toward Optimized Practice
MRA	Magnetic resonance angiography		
MRI	Magnetic resonance imaging		
MRV	Magnetic resonance venography		
NICE	National Institute for Health and Care Excellence		

Chronic headache (including migraine, tension, chronic daily, new daily persistent or medication overuse/rebound headaches) *without* a change in pattern, seizure, or neurological signs/symptoms:

- **Green** –
- **Yellow** –
- **Orange** –
- **Red** – MRI; CT; MRA; CTA; MRV; CTV; PET; SPECT

Level of Evidence: CT and MRI: moderate level of evidence; for MRA, CTA, MRV and CTV: low level of evidence; SPECT and PET: PLE expert panel consensus opinion.

Notes concerning applicability and/or patient preferences: None.

Guideline and PLE expert panel consensus opinion summary:

In adult patients with migraine, with no recent change in pattern, no history of seizures, and no other focal neurological signs or symptoms, the routine use of neuroimaging is not warranted (Douglas, et al. [ACR] 2014; Sandrini et al. [EFNS] 2011).

Neuroimaging is not indicated in patients with a clear history of migraine, without red flag features for potential secondary headache, and a normal neurological examination (*SIGN* 2008, grade D recommendation).

As the diagnostic yield of neuroimaging in patients with typical recurrent migraine attacks is very low, neuroimaging is not indicated in patients with recurrent headaches with the clinical features of migraine, a normal neurological examination, and no red flags for potential causes of secondary headache (*TOP Clinical Practice Guideline* 2016).

Do not refer people diagnosed with tension-type headache, migraine, or medication overuse headache for neuroimaging solely for reassurance (*NICE* 2015).

The *American College of Radiology (ACR)* assigned a rating of 4 for MRI head with or without IV contrast, 3 for CT with or without IV contrast, and 2 for MRA or CTA for the imaging of chronic headache with no new features and a normal neurologic examination (Douglas et al. [ACR] 2014).

Clinical notes:

- Primary headaches are headache disorders that are not due to another underlying medical condition and include migraine, tension, cluster, chronic daily, new daily persistent and medication overuse headaches (*SIGN* 2008).
- Clinicians should use a detailed headache history that includes duration of attacks and the exclusion of secondary causes as the principal means to diagnose primary headache. Additional testing in patients without atypical symptoms or an abnormal neurologic examination is unlikely to be helpful (Beithon et al. [ICS] 2013).
- Most primary headache can be managed in primary care and investigations are rarely needed (*SIGN* 2008).

- Sinus and cervical spine imaging is not recommended for the routine evaluation of patients with migraine headaches (*TOP Clinical Practice Guideline 2016*, expert opinion).
- The yield of CT and MRI in patients referred with isolated nontraumatic headache is approximately 0.4% (Douglas et al. [ACR] 2014; *SIGN 2008*).
- In frequent conditions, performing low-yield studies is more likely to result in false-positive results, with the consequent risk of additional and unnecessary procedures (Douglas et al. [ACR] 2014).
- Clinicians requesting neuroimaging should be aware that both MRI and CT can identify incidental neurological abnormalities which may result in patient anxiety as well as practical and ethical dilemmas with regard to management (*SIGN 2008*, grade D recommendation).
- Red flag features for the identification of secondary headaches include (*NICE 2015; TOP Clinical Practice Guideline 2016; SIGN 2008*):
 - New onset or change in headache in patients who are older than 50 years of age;
 - change in headache frequency, characteristics and/or associated symptoms;
 - new onset cognitive dysfunction or change in personality;
 - new onset neurological symptoms and/or abnormal neurological examination;
 - papilledema and/or impaired level of consciousness;
 - thunderclap headache;
 - headache changing with posture or that awakens;
 - headache precipitated by physical exertion, sexual activity or Valsalva maneuver;
 - patients with risk factors for cerebral venous sinus thrombosis;
 - symptoms suggestive of giant cell arteritis;
 - symptoms suggestive of acute narrow angle glaucoma;
 - patients with jaw claudication or visual disturbance;
 - neck stiffness and/or fever; or
 - new onset in patients with history of HIV or cancer
- Patients with headache and red flag features for secondary headache should be referred to an appropriate specialist for further assessment (*NICE 2015; TOP Clinical Practice Guideline 2016; SIGN 2008*).
- Medication overuse headaches are associated with analgesic (prescription and over-the-counter) and migraine-specific medication use (Beithon et al. [ICSI] 2013; *TOP Clinical Practice Guideline 2016*).
- When medication overuse is suspected, the patient should also be evaluated for the presence of psychiatric comorbidities ... and drug dependence ... (*TOP Clinical Practice Guideline 2016*).
- Patients with medication overuse headache who have psychiatric comorbidity or dependence behavior should have these conditions treated independently (*SIGN 2008*, grade C recommendation).
- In patients with new daily persistent headache, specialist referral should be considered for investigation and treatment (*TOP Clinical Practice Guideline 2016; SIGN 2008*).

Evidence update (2014-present):

Honningsvag et al., in a 2016 epidemiological study, evaluated the relationship between intracranial abnormalities and headache among 864 adults (age 50-65) in the general population. Based on the responses to the HUNT 3 Questionnaire, respondents were categorized as having migraine, tension-type headache, or unclassified headache. Intracranial abnormalities were found to be more common in headache sufferers than in headache-free individuals (29% vs. 22%, respectively; $p = 0.041$). Adjusted multivariate analyses revealed that those with tension-type headache had higher odds of having minor

abnormalities (odds ratio, 2.13; 95% CI = 1.18-3.85). This association disappeared when those with only white matter hyperintensities were removed from the analysis. The authors conclude that neuroimaging of headache sufferers in the general population yields few findings of clinical importance (moderate level of evidence).

Al-Nabhani et al., in a 2014 retrospective study reported on the usefulness of CT in 142 patients with non-localized headache (without neurological deficits, history of cancer or history of trauma). Only 4% of patients showed clinically significant findings. 70% had normal CT scans and 26% incidental positive findings (low level of evidence).

Tung et al., in a 2014 retrospective study, evaluated the efficiency of Rothrock criteria in predicting clinically significant findings on CT. The prevalence of significant findings was 10.1%. The Rothrock criteria (age > 60, new onset focal neurologic deficit, headache with vomiting or altered mental status) had a sensitivity of 97.1% (identifying 34 of 35 significant findings) among the 346 patients. The one false negative case was in a patient with known metastatic melanoma without focal neurological signs or symptoms. Although 100% sensitivity was not achieved, these results may contribute to the evidence that in the absence of focal neurologic deficit, headache with vomiting or altered mental status in patients aged < 60 years cranial tomography can be refrained from. Further research might validate patient history as a parameter (low level of evidence).

Headache with atypical features, an abrupt increase in severity or frequency, or an abrupt pattern change:

- **Green** – MRI brain with and without IV contrast; MRI brain without IV contrast
- **Yellow** – MRI brain with IV contrast to characterize abnormalities seen on a previous MRI brain without IV contrast
- **Yellow** – CT head with and without IV contrast if the patient is unable to undergo MRI or if MRI is unavailable
- **Yellow** – CT head without IV contrast if there is a suspicion of hemorrhage, if the patient is unable to undergo MRI, or if MRI is not available
- **Yellow** – CT head with IV contrast if the patient is unable to undergo MRI, if MRI is not available, or to characterize abnormalities detected on previous CT head without IV contrast
- **Yellow** – MRA head, CTA head, MRV head, or CTV head if clinical or imaging suspicion of a vascular lesion
- **Red** – SPECT; PET

Level of Evidence: MRI and CT: low level of evidence; SPECT and PET: PLE expert panel consensus opinion.

Notes concerning applicability and/or patient preferences: None.

Guideline and PLE expert panel consensus opinion summary:

Patients with headaches that do not fit the typical pattern of migraine or tension-type headache, and patients with a major change in headache pattern should be considered for specialist consultation and/or neuroimaging, depending on the clinical judgment of the practitioner (*TOP Clinical Practice Guideline 2016; NICE 2008; SIGN 2008*).

In case of unusual headache that came on or worsened within the last 7 days, brain imaging should be performed rapidly to search for an expansive intracranial process or a vascular cause. Ideally, brain MRI with T1, T2, FLAIR, and T1 injected sequences will be performed to search for contrast uptake and signs of venous thrombosis (Moisset et al. [*SFEMC & SFN*] 2016, professional agreement).

Selective testing including neuroimaging..., lumbar puncture, cerebrospinal fluid and blood studies may be indicated to evaluate for secondary headache if causes of concern have been identified in the patient history or physical examination. MRI with and without contrast is more sensitive than a CT of the head (Beithon et al. [*ICS/*] 2013). The American Academy of Neurology recommends against the use of electroencephalography (EEG) for the evaluation of headaches (Langer-Gould et al. 2013).

In patients with atypical headache patterns, a history of seizures, or neurological signs or symptoms, MRI may be indicated (Sandrini et al. [*EFNS*] 2011).

When neuroimaging is warranted, the most sensitive method should be used, and we recommend MRI and not CT in these cases (Sandrini et al. [*EFNS*] 2011).

Unless there is an emergency, and if MRI is easily accessible, CT is not needed. If MRI accessibility is limited, a brain CT without contrast injection should be performed (Moisset et al. [*SFEMC & SFN*] 2016, professional agreement).

In ruling out secondary causes of headache, MRI is more sensitive than CT in identifying white matter lesions and developmental venous anomalies (*SIGN* 2008).

The *American College of Radiology* recommends MRI head without and with IV contrast (8), MRI head without IV contrast (7), CT head without IV contrast (7), and CTA head without and with IV contrast (5) for the imaging of chronic headache with new feature or neurologic deficit (Douglas et al. [*ACR*] 2014).

The ACR states that in patients with suspected brain tumor, MRI with and without IV contrast is the study of choice. If there are contraindications to MRI, CT with IV contrast is recommended (Douglas et al. [*ACR*] 2014).

In patients with headaches associated with atypical features, an abrupt increase in severity or frequency, or an abrupt pattern change, CT with IV contrast should be considered if tumor is suspected and the patient is unable to undergo MRI (PLE expert panel/PLE multidisciplinary committee consensus opinion).

In patients with headaches associated with atypical features, an abrupt increase in severity or frequency, or an abrupt pattern change, CT without IV contrast should be considered if hemorrhage is suspected, or if the patient is unable to undergo MRI and has a moderate or severe allergy to CT contrast (PLE expert panel consensus opinion).

Clinical notes:

- Atypical features of migraine headaches may include hemimotor symptoms, hemisensory symptoms outlasting the headache episode (ictus), diplopia, and onset of new aura after the age of 40 (PLE expert panel consensus opinion).
- Further investigation is recommended for migraine patients with poor balance, visual symptoms affecting only one eye or decreased level of consciousness (*NICE* 2015).
- A gradual increase in the frequency of migraine headaches over time is typical and does not need additional imaging (Mitsikostas, et al. [*EHF*] 2016; PLE expert panel consensus opinion).
- Headaches that worsen with time may be due to a progressive intracranial lesion such as a tumor, subdural hematoma or hydrocephalus (Beithon et al. [*JCSI*] 2013).

Evidence update (2014-present): There were no new articles that significantly affected the recommendations or conclusions found in the guidelines referenced above.

Headache with neurologic signs, neurologic symptoms, or seizures:

- **Green** – MRI brain with and without IV contrast; MRI brain without IV contrast
- **Yellow** – MRI brain with IV contrast to characterize abnormalities seen on a previous MRI brain without IV contrast
- **Yellow** – CT head with and without IV contrast if the patient is unable to undergo MRI or if MRI is unavailable
- **Yellow** – CT head without IV contrast if there is a suspicion of hemorrhage, if the patient is unable to undergo MRI, or MRI is not available
- **Yellow** – CT head with IV contrast if the patient is unable to undergo MRI, if MRI is not available, or to characterize abnormalities detected on previous CT head without IV contrast
- **Yellow** – MRA head, CTA head, MRV head, or CTV head if clinical or imaging suspicion of a vascular lesion
- **Red** – SPECT; PET

Level of Evidence: CT and MRI for focal neurologic signs and symptoms: moderate level of evidence; MRA, CTA, MRV, CTV, SPECT and PET: PLE expert panel consensus opinion.

Notes concerning applicability and/or patient preferences: None.

Guideline and PLE expert panel consensus opinion summary:

Patients with headaches and new onset neurological symptoms and/or abnormal neurological examination should be considered for specialist consultation and/or neuroimaging, depending on the clinical judgment of the practitioner (*TOP Clinical Practice Guideline 2016; NICE 2008; SIGN 2008*, grade D recommendation).

In the non-urgent setting [in patients with unexplained focal neurological signs and recurrent headache], brain magnetic resonance imaging (MRI) is the neuroimaging of choice, but a non-contrast brain CT is usually adequate to exclude a space-occupying lesion as a cause of headache (*TOP Clinical Practice Guideline 2016*).

CT scans are widely accepted for acute diagnostic purposes and for planning acute treatment. They are recommended for abnormal mental status, focal neurologic deficits, or acute seizure (*CO Division of Workers' Compensation Medical Treatment Guidelines 2012*).

In patients with atypical headache patterns, a history of seizures, or neurological signs or symptoms, MRI may be indicated (Sandrini et al. [*EFNS*] 2011).

When neuroimaging is warranted, the most sensitive method should be used, and we recommend MRI and not CT in these cases (Sandrini et al. [*EFNS*] 2011).

A patient who presents with sudden-onset headache or headache associated with a neurological deficit should have an emergency CT scan (Moisset et al. [*SFEMC & SFN*] 2016, grade B recommendation).

Patients presenting to the emergency department with headache and new abnormal findings on neurologic examination (e.g., focal deficit, altered mental status, altered cognitive function) should undergo emergent noncontrast head CT (Edlow et al. [*ACEP*] 2008, level B recommendation).

The *American College of Radiology* recommends MRI head without and with IV contrast (8), MRI head without IV contrast (7), CT head without IV contrast (7), and CT head without and with IV contrast (5) for the imaging of chronic headache with new feature or neurologic deficit (Douglas et al. [ACR] 2014).

The ACR states that in patients with suspected brain tumor, MRI with and without IV contrast is the procedure of choice. If there are contraindications to MRI, CT with IV contrast is recommended (Douglas et al. [ACR] 2014).

In patients with headache associated with neurologic signs, neurologic symptoms or seizures, CT with IV contrast should be considered if tumor is suspected and the patient is unable to undergo MRI or MRI is not available (PLE expert panel/PLE multidisciplinary committee consensus opinion).

In patients with headache associated with neurologic signs, neurologic symptoms, or seizures, CT without IV contrast should be considered if hemorrhage is suspected, or if the patient is unable to undergo MRI and has a moderate or severe allergy to CT contrast (PLE expert panel consensus opinion).

Clinical notes:

- Atypical features of migraine headaches may include hemimotor symptoms, hemisensory symptoms outlasting the headache episode (ictus), diplopia, and onset of new aura after the age of 40 (PLE expert panel consensus opinion).
- Neuroimaging in patients with headache and an abnormal neurological examination is significantly more likely to reveal an underlying cause (*SIGN* 2008).
- For patients with unusual aura symptoms, consider referral to a neurologist for diagnosis and possible investigation (*TOP Clinical Practice Guideline* 2016).

Evidence update (2014-present): There were no new articles that significantly affected the recommendations or conclusions found in the guidelines referenced above.

Sudden onset of severe headache (thunderclap headache):

- **Green** – CT head without IV contrast; CT head with and without IV contrast
- **Green** - CTA head and neck or MRA head and neck with and/or without IV contrast
- **Yellow** – MRI brain without IV contrast or MRI brain with and without IV contrast *
- **Yellow** – MRV head or CTV head in patients with suspected venous sinus thrombosis
- **Orange** – CT head with IV contrast, except to characterize abnormalities detected on previous CT head without IV contrast
- **Orange** – MRI brain with IV contrast, except to characterize abnormalities seen on a previous MRI brain without IV contrast
- **Red** – SPECT; PET

MRI for thunderclap headache should only be performed when radiology expertise is available and MR imaging equipment support the use of fluid-attenuated inversion recovery (FLAIR), gradient-recalled T2 and/or susceptibility-weighted (SWI) sequences.

Level of Evidence: MRI and CT: moderate level of evidence; MRA, CTA, MRV, CTV: low level of evidence; SPECT and PET: PLE expert panel consensus opinion.

Notes concerning applicability and/or patient preferences: None.

Guideline and PLE expert panel consensus opinion summary:

Patients presenting with severe headache of sudden onset should be sent to an emergency department with urgent computerized tomography (CT) capability for immediate investigation to exclude subarachnoid hemorrhage (*TOP Clinical Practice Guideline* 2016; *SIGN* 2008, grade D recommendation; Edlow et al. [*ACEP*] 2008/level B recommendation).

A patient who presents with sudden-onset headache or headache associated with a neurological deficit should have an emergency CT scan (Moisset et al. [*SFEMC & SFN*] 2016, grade B recommendation).

The multidisciplinary committee thought that MRI with FLAIR, gradient-recalled T2* and susceptibility-weighted (SWI) sequences were equally sensitive to subarachnoid hemorrhage and could be used in the initial evaluation of patients with thunderclap headache, although in most circumstances CT would be more readily available and efficient (PLE multidisciplinary committee consensus opinion; Mitchell et al. 2001; Yuan et al. 2005; Abdel Ghaffar et al. 2014; Lummel et al. 2011).

Patients diagnosed with acute subarachnoid hemorrhage require MRA, computed tomography angiography (CTA), and/or catheter angiography to evaluate for an aneurysm or arteriovenous malformations (AVM). CTA has gained popularity and is frequently used for its noninvasiveness and sensitivity and specificity comparable to that of cerebral angiography (Douglas et al. [*ACR*] 2014).

[In patients with a thunderclap headache and] no vascular malformation, the etiological search should focus on a reversible cerebral vasoconstriction syndrome (RCVS). Diagnosis requires demonstration of typical arterial anomalies on the CT or MRI angiogram. The first imaging exploration may be normal if

performed early during the first 4-5 days after symptom onset. Anomalies reach a maximum 2-3 weeks after the first symptoms (Moisset et al. [*SFEMC & SFN*] 2016, professional agreement).

CT without IV contrast is recommended in patients with thunderclap headache to exclude subarachnoid hemorrhage. With the recognition of reversible cerebral vasoconstriction syndrome (RCVS), CTA or MRA is also indicated for the initial workup of thunderclap headache (PLE expert panel consensus opinion).

If the CTA or MRA findings are consistent with RCVS, then repeat CTA or MRA should be obtained in 3 months to see if the findings have resolved in order to confirm the diagnosis. If the CTA or MRA findings are negative or equivocal for RCVS, then CT and CTA or MRA should be repeated at the time of the first recurrent headache (PLE expert panel consensus opinion).

The *American College of Radiology (ACR; (Douglas, et al., 2014))* recommends CT head without IV contrast (9), CTA head with IV contrast (8), MRA head without and with IV contrast (7), MRA head without IV contrast (7), MRI head without IV contrast (7), MRI head without and with IV contrast (6), and CT head without and with IV contrast (5) for the imaging of sudden onset of severe headache (Douglas et al. [*ACR*] 2014).

In patients previously treated with an aneurysm clip, coil or stents, an MRA with IV contrast is indicated [instead of CTA or MRA without contrast because of metal artifact] (Douglas et al. [*ACR*] 2014).

If subarachnoid hemorrhage is not present, specialist involvement and further neuroimaging may also be necessary as the differential diagnosis includes arterial dissection, dural sinus thrombosis, pituitary apoplexy and reversible cerebral vasoconstriction syndrome (*TOP Clinical Practice Guideline 2016*).

Thunderclap headache can also be the inaugural sign of cervical artery dissection, cerebral venous thrombosis, or pituitary apoplexy, with a normal physical examination, CT, and CSF. Other explorations must be proposed when the CT angiogram of the supra-aortic trunks and the CSF analysis are normal; exploration of the cervical vessels and a brain MRI are needed (Moisset et al. [*SFEMC & SFN*] 2016).

Clinical notes:

- Thunderclap headache is defined as severe head pain of abrupt onset, reaching maximum intensity in < 1 minute (*ICHD-3 2013; TOP Clinical Practice Guideline 2016*) or < 5 minutes (*SIGN 2008; NICE 2015*).
- New headache upon waking does not meet the classification of a thunderclap headache (PLE expert panel consensus opinion).
- Differential diagnoses include subarachnoid hemorrhage (SAH) or other intracranial bleeding, brain infarction, reversible cerebral vasoconstriction syndrome (RCVS), cerebral venous thrombus, cervical arterial dissection, meningitis and/or encephalitis, hypertensive encephalopathy and eclampsia, pituitary necrosis, and temporal arteritis. Other causes can also produce the same clinical presentation: CSF hypotension, angina pectoris or intra-ventricular tumor (Moisset et al. [*SFEMC & SFN*] 2016).
- Headaches that present suddenly, “like a thunderclap”, may indicate one of several serious intracranial processes including subarachnoid hemorrhage (SAH), venous sinus thrombosis, bacterial meningitis, carotid dissection or hypertensive encephalopathy (Beithon et al. [*ICS/*] 2013).
- RCVS has been diagnosed in 45% of patients presenting with thunderclap headaches. RCVS is attributed to transient reversible abnormal regulation of cerebral arterial tone, which triggers

multifocal diffuse vasoconstriction and vasodilatation. It can be triggered by vasoactive substances such as cannabis, cocaine, ecstasy, amphetamines, LSD, antidepressants (SSRI and SNRI drugs), nasal decongestants, triptans and ergotamine (Moisset et al. [SFEMC & SFN] 2016; ICHD-3 2013).

- Patients with a first presentation of a thunderclap headache should be referred immediately to hospital for same day specialist assessment; thunderclap headache is a medical emergency as it may be caused by subarachnoid hemorrhage (*SIGN* 2008, grade D recommendation).
- Sensitivity of CT for subarachnoid hemorrhage is 98% at 12 hours, dropping to 93% by 24 hours (*SIGN* 2008).
- Sensitivity of CT is decreased for detecting subarachnoid hemorrhage in patients with “minor leaks” and those with normal neurologic examination results. The sensitivity also decreases with time from onset of headache (Edlow et al. [*ACEP*] 2008).
- LP may no longer be indicated to exclude a subarachnoid hemorrhage following a negative CT as the accuracy of CT for subarachnoid hemorrhage has increased significantly in the interval (Dubosh et al. 2016). With modern CT equipment, a negative CT within 6 hours of onset effectively excludes subarachnoid hemorrhage (PLE expert panel consensus opinion).
- If the patient is to undergo lumbar puncture to exclude SAH, neuroimaging should be performed prior to lumbar puncture (*SIGN* 2008).

Technical notes:

- If an MRI is obtained to evaluate a thunderclap headache, it should include fluid-attenuated inversion recovery (FLAIR), gradient recalled T2* and/or SWI sequences (PLE expert panel consensus opinion).

Evidence update (2014-present) and select articles from guideline bibliographies:

Dubosh et al., in a 2016 systematic review of 5 articles concerning the accuracy of CT for subarachnoid hemorrhage (SAH), reported an overall sensitivity of 0.987 (95% confidence intervals, 0.971-0.994) and specificity of 0.999 (95% confidence intervals, 0.993-1.0). The pooled likelihood ratio of a negative CT was 0.010 (95% confidence intervals, 0.003-0.034). The authors concluded that for patients presenting with thunderclap headache and normal neurological examination, normal brain CT within 6 hours of headache is extremely sensitive in ruling out aneurysmal SAH (high level of evidence).

Greenberg et al. (2010) conducted a meta-analysis on the accuracy of CTA and CT perfusion (CTP) for cerebral vasospasm in patients with acute SAH using digital subtraction angiography (DSA) as the gold standard. 10 research studies met the inclusion criteria. 6 CTA studies and 3 CTP studies had sufficient data for statistical analysis. CTA pooled estimates were 79.1% sensitivity, 93.1% specificity, 18.1 LR+, and 0.2 LR-. CTP pooled estimates were 74.1% sensitivity, 93% specificity, 9.3 LR+ and 0.2 LR-. The area under the ROC curve was 98 for CTA and 97 for CTP. The authors concluded that CTA and CTP have a high diagnostic accuracy for the diagnosis of cerebral vasospasm in patients with acute SAH (high level of evidence).

Mathon et al. in 2014 presented the imaging findings in 30 prospective consecutive patients <50 years with convexity subarachnoid and intracerebral hemorrhages. 19 patients were diagnosed with reversible cerebral vasoconstriction syndrome (RCVS), 7 with cerebral venous sinus thrombosis (CVST) and 4 with bleeding mycotic aneurysms (moderate level of evidence).

Cheng et al. in 2014 presented imaging findings in 31 prospective consecutive patients with SAH. 24

(72.7%) of these patients fulfilled the criteria for thunderclap headache (TCH). RCVS was confirmed in 14 (45.2%) of patients with SAH and in 11 (45.8%) of patients with TCH. The authors concluded that RCVS is a common cause of SAH and TCH (moderate level of evidence).

Grooters et al., in a 2014 study of 34 patients with TCH without aneurysmal subarachnoid hemorrhage in CT, found RCVS in 3 patients (8.8%). The authors concluded that RCVS is an under recognized condition, and additional imaging should be performed in every patient with TCH (moderate level of evidence).

Alons et al. conducted a 2015 retrospective study on the utility of CT angiography in 70 consecutive patients reporting to the ED with acute severe headache. Patients with neurologic deficits, subdural or subarachnoid hemorrhage on CT and increased CSF bilirubin concentration were excluded. 13 (19%) of patients had vascular abnormalities on CT: 4 with a prior aneurysm or CVT, 8 with an unruptured intracranial aneurysm (UIA), 2 with CVT (3%), 2 with RCVS (3%) and 1 with cerebral ischemia (1%). The authors concluded that patients with a history of UIA or CVT should undergo CTA despite normal CT and LP (low level of evidence).

Cooper et al. conducted a 2016 retrospective study of 517 consecutive neurologically patients presenting to the ED with sudden onset acute severe headache. 510/517 underwent CT for the diagnosis of SAH. 27/510 patients had an abnormal CT: 13 positive for SAH and 14 positive for other diagnoses. 309/491 patients underwent LP: 11 positive for SAH (only one of which had a positive angiogram), 16 for viral meningitis and one for nonocclusive sagittal sinus thrombosis. 6/13 patients with SAH had abnormal angiogram findings. The authors concluded that the decision to follow a negative CT with an LP in all cases needs careful consideration, as CSF results may only rarely confer therapeutic benefit to patients suspected of SAH (low level of evidence).

Han et al., in 2013 in retrospective study, reported on the utility of CTA in 512 patients with sudden-onset of acute severe headache, no severe neurological deficits and no abnormalities on noncontrast CT. Thirty-four (6.6%) of the 512 patients had intracranial vascular lesions on CTA, including 33 aneurysms (2 patients had 2 aneurysms each), 2 with Moyamoya disease and 1 with arterial dissection (low level of evidence).

Graff-Radford et al., in a 2016 retrospective study, presented the imaging findings in 88 patients with non-traumatic cSAH. The most common causes were RCVS (26, 29.5%), cerebral amyloid angiopathy (CAA) (23, 26.1%), indeterminate (14, 15.9%), and endocarditis (9, 10.2%) (low level of evidence).

Geraldes et al., in a 2014 retrospective study, presented the imaging findings in 15 consecutive patients with cSAH. The authors found 2 cases of RCVS. Other diagnoses included ICA atheromatous stenosis in 5, CAA in 2, cerebral venous thrombosis in 1, dural fistulae in 2 and undetermined in 3 (low level of evidence).

Perry et al., in a 2017 prospective cohort study, assessed the accuracy, clinical acceptability and potential effect on rates of neuroimaging of the Ottawa SAH Rule (patients with one of the following – neck pain or stiffness, age > 40 yrs., witnessed loss of consciousness, onset during exertion, thunderclap headache and limited neck flexion upon exam) in consecutive patients with acute headache visiting the ED. Treating physicians enrolled 1153 of 1743 (66.2%) eligible patients (alert and neurologically intact), and scored the rule before investigations were started. A total of 67 patients had SAH. The Ottawa SAH Rule had 100% sensitivity (95% CI: 94.6%-100%) with specificity of 13.6% (95% CI: 13.1%-15.8%),

whereas neuroimaging rates were 87%. The authors conclude that the Ottawa SAH Rule was sensitive for identifying SAH, and can be used to rule out this diagnosis, thereby decreasing number of cases missed and constraining rates of neuroimaging (moderate level of evidence).

Chu et al., in a 2017 cross-sectional study, described characteristics of 847 headache presentations (median age 39; range 18-92 years) to the ED. Headache peaked ≤ 1 hour in 44% and it was “worst ever” in 37%. Persisting neurologic deficit was found in 6.5%. CT head scan was performed in 38% and lumbar puncture in 4.7%. Overall, there were 18 SAH, six intraparenchymal hemorrhages, one subdural hematoma, one newly diagnosed brain metastasis, and two bacterial meningitis. Migraine was diagnosed in 23% and “primary headache not further specified” in 45%. The authors conclude that a majority of patients had a benign diagnosis, with intracranial hemorrhage and bacterial meningitis accounting for only 3%. As over one-third of presentations underwent CT scans, the authors note there is scope to rationalize diagnostic testing to rule out life-threatening conditions (low level of evidence).

New headache with systemic symptoms, suspected encephalitis, or suspected meningitis:

- **Green** – CT head without IV contrast
- **Green** – MRI brain with and without IV contrast or MRI brain without IV contrast
- **Yellow** – MRI brain with IV contrast to characterize abnormalities seen on a previous MRI brain without IV contrast
- **Yellow** – CT head with and without IV contrast or CT head with IV contrast if the patient is unable to undergo MRI or if MRI is not available
- **Yellow** – MRA head, CTA head, MRV head, or CTV head to evaluate for suspected vascular involvement or vascular complications
- **Red** – SPECT; PET

Level of Evidence: CT and MRI: low level of evidence; MRA/MRV, CTA/CTV, SPECT and PET: PLE expert panel consensus opinion.

Notes concerning applicability and/or patient preferences: None.

Guideline and PLE expert panel consensus opinion summary:

Patients with suspected bacterial meningitis should be sent immediately to an emergency department with urgent CT and lumbar puncture capability for investigation and treatment (*TOP Clinical Practice Guideline* 2016).

CT scan is performed before lumbar puncture to determine if there is elevated intracranial pressure (Douglas et al. [ACR] 2014).

If encephalitis is suspected, MRI of brain with and without contrast is the study of choice. MRI is more sensitive and specific than CT for detecting encephalitis and complications of meningitis. CT of the brain with and without IV contrast should be performed only if MRI is contraindicated or unavailable (Douglas et al. [ACR] 2014).

The *American College of Radiology* recommends MRI head without and with IV contrast (8), MRI head without IV contrast (7), CT head with IV contrast (6), CT head without and with IV contrast (6), and CT head without IV contrast (5) for the imaging of new headache, suspected meningitis/encephalitis (Douglas et al. [ACR] 2014).

Clinical notes:

- Headache is typically associated with neck stiffness, nausea, fever and changes in mental state and/or other neurological symptoms and/or signs (*ICHD-3* 2013).
- Patients who present with headache and features suggestive of CNS infection should be referred immediately for same day specialist appointment (*SIGN* 2008, grade D recommendation).

Evidence update (2014-present): There were no new articles that significantly affected the recommendations or conclusions found in the guidelines referenced above.

New headache or change in headaches in a cancer patient or immunocompromised patient:

- **Green** – MRI brain with and without IV contrast; MRI brain without IV contrast
- **Yellow** – MRI brain with IV contrast to characterize abnormalities seen on a previous MRI brain without IV contrast
- **Yellow** – CT head with and without IV contrast or CT head with IV contrast if the patient is unable to undergo MRI or if MRI is unavailable
- **Yellow** – CT head without IV contrast if there is a suspicion of hemorrhage, if the patient is unable to undergo MRI, or if MRI is not available
- **Yellow** – MRA head, CTA head, MRV head, or CTV head to evaluate for suspected vascular involvement or complications
- **Orange** – FDG-PET or Thallium 201 SPECT, except to differentiate tumor from infection
- **Red** –

Level of Evidence: MRI and CT: low level of evidence; MRA/CTA, MRV/CTV, PET and SPECT: PLE expert panel consensus opinion.

Notes concerning applicability and/or patient preferences: None.

Guideline and PLE expert panel consensus opinion summary:

Patients with new-onset headache or a major change in headache pattern and a systemic illness (cancer, HIV, etc.) that may indicate a serious cause for the headache may require urgent specialist consultation and/or investigation/[neuroimaging] (*TOP Clinical Practice Guideline 2016; NICE 2015*).

Patients with known cancer should also be scanned when a headache develops or if there is a change in headache characteristics (Douglas et al. [ACR] 2014).

In patients with symptomatic illness such as tumors, acquired immunodeficiency syndrome (AIDS) and neurofibromatosis, MRI may be indicated (Sandrini et al. [EFNS] 2011).

HIV-positive patients with a new type of headache should be considered for an emergent neuroimaging study (Edlow et al. [ACEP] 2008).

In patients with underlying neoplasm or suspected brain tumor, MRI with and without contrast is the study of choice. If there are contraindications to MRI, contrast-enhanced CT is a good alternative (Douglas et al. [ACR] 2014).

The *American College of Radiology* recommends MRI head without and with IV contrast (9), MRI head without IV contrast (7), CT head without and with IV contrast (6), CT head with IV contrast (6), MRA head without IV contrast (5), MRA head without and with IV contrast (5), CT head without IV contrast (5), and CTA head with IV contrast (5) for the imaging of new headache in cancer patient or immunocompromised individual (Douglas et al. [ACR] 2014).

Although single-photon emission CT (SPECT) and PET are not currently routinely used in the evaluation of patients with headache, FDG-PET or thallium-201 SPECT may be useful in differentiating tumor from infection in high-risk patients (Douglas et al. [ACR] 2014).

CT with IV contrast should be considered if there is a suspicion of intracranial neoplasm, encephalitis or complications of meningitis and the patient is unable to undergo MRI (PLE expert panel/PLE multidisciplinary committee consensus opinion).

CT without IV contrast should be considered if hemorrhage is suspected, or if the patient is unable to undergo MRI and has a moderate or severe allergy to CT contrast (PLE expert panel consensus opinion).

Clinical notes:

- Immunosuppressed individuals are at increased risk of infection, lymphoma, leukemia and complications of immunosuppressive therapy (Douglas et al. [ACR] 2014).

Evidence update (2014-present): There were no new articles that significantly affected the recommendations or conclusions found in the guidelines referenced above.

Cluster headaches/ trigeminal autonomic cephalgias (SUNCT/SUNA, chronic paroxysmal hemicranias, and hemicrania continua):

- **Green** – MRI brain with and without IV contrast
- **Yellow** - MRI brain without IV contrast in patients who are unable to receive or refuse IV contrast
- **Yellow** – MRI brain with IV contrast to characterize abnormalities seen on MRI brain without IV contrast
- **Yellow** – CT head with IV contrast or CT head with and without IV contrast in patients unable to undergo MRI or if MRI is unavailable
- **Yellow** – CT head without IV contrast in patients who are unable to undergo MRI and who are unable to receive or refuse IV contrast
- **Yellow** – MRA head following an MRI brain or CTA head following a CT head with IV contrast
- **Red** –MRV; CTV; SPECT; PET

Level of Evidence: MRI and CT: very Low level of evidence; MRA, CTA, MRV, CTV, SPECT, PET: PLE expert panel consensus opinion.

Notes concerning applicability and/or patient preferences: None.

Guideline and PLE expert panel consensus opinion summary:

Brain MRI should be considered in patients with cluster headache/trigeminal autonomic cephalgia, paroxysmal hemicrania or SUNCT, in order to exclude the wide variety of secondary causes (*SIGN* 2008, Grade D recommendation; Sandrini et al. [*EFNS*] 2011; Douglas et al. [*ACR*] 2014).

When neuroimaging is warranted, the most sensitive method should be used, and we recommend MRI and not CT in these cases (Sandrini et al. [*EFNS*] 2011).

For patients presenting a first cluster headache, brain magnetic resonance imaging (MRI) and MRA or CTA of the head and neck should be performed (Moisset et al. [*SFEMC & SFN*] 2016, professional agreement).

The *American College of Radiology* recommends MRI head without and with IV contrast (8), MRI head without IV contrast (7), CT head without and with IV contrast (6), CT head without IV contrast (5), CT head with IV contrast (5), MRA head without IV contrast (5), and CTA head with IV contrast (5) for the imaging of headache of trigeminal autonomic origin (Douglas et al. [*ACR*] 2014).

CT without IV contrast should be considered if the patient is unable to undergo MRI and has a moderate or severe allergy to CT contrast (PLE expert panel consensus opinion).

Clinical notes:

- Cluster headache is characterized by repeated short-lasting (lasting 15-180 minutes and occurring from once every other day to eight times a day (*ICHD-3* 2013)) but excruciating intense attacks of strictly unilateral peri-orbital pain associated with local autonomic symptoms or signs. The most striking feature of cluster headache is the unmistakable circadian and circannual periodicity (Beithon et al. [*ICSI*] 2013; Douglas et al. [*ACR*] 2014; *SIGN* 2008, grade D recommendation).

- Trigeminal autonomic cephalgia is a group of primary headache disorders characterized by pain in unilateral trigeminal distribution in association with ipsilateral cranial autonomic signs and symptoms. Cluster headache is the only relative common member of this family (Douglas et al. [ACR] 2014).
- In patients with new onset cluster headache or another trigeminal autonomic cephalgia, hemicranias continua, or new daily persistent headache, specialist referral should be considered for investigation and treatment (*TOP Clinical Practice Guideline* 2016; *SIGN* 2008, grade D recommendation; *NICE* 2015).
- Cluster headaches are associated with pituitary macroadenomas in 5-10% of patients. Therefore, an MRI of the brain is recommended at least once in the patient's lifetime. Head MRA and CTA are not usually indicated initially (Douglas et al. [ACR] 2014).
- Discuss the need for neuroimaging for people with a first bout of cluster headache with a general practitioner with a special interest in headache or a neurologist (*NICE* 2015).

Evidence update (2014-present): There were no new articles that significantly affected the recommendations or conclusions found in the guidelines referenced above.

New headache with patient over 50:

- **Green** – MRI brain with and without IV contrast; MRI brain without IV contrast
- **Yellow** – MRI brain with IV contrast to characterize abnormalities seen on MRI brain without IV contrast
- **Yellow** - CT head with IV contrast or CT head with and without IV contrast if the patient is unable to undergo MRI or if MRI is unavailable
- **Yellow** – CT head without IV contrast if there is a suspicion of hemorrhage, if the patient is unable to undergo MRI, or if MRI is not readily available
- **Yellow** – MRA head, CTA head, MRV head, or CTV head if clinical or imaging suspicion of a vascular lesion
- **Red** – SPECT; PET

Level of Evidence: Low level of evidence.

Notes concerning applicability and/or patient preferences: None.

Guideline and PLE expert panel consensus opinion summary:

Patients who are older than 50 years and presenting with new type of headache but with a normal neurologic examination should be considered for an urgent neuroimaging study (Edlow et al. [ACEP] 2008, level C recommendation; *TOP Clinical Practice Guideline* 2016).

Causes for concern must be evaluated irrespective of the patient's past history of headache. Warning signs of possible disorder other than primary headache [include] headache of new onset after age 50. Many patients who do have the onset of a new headache disorder after age 50 years will merit brain imaging (Beithon et al. [JCSJ] 2013).

Warning signs or red flags for potential secondary headache requiring further investigation [neuroimaging] include new onset or change in headache in patients who are aged over 50 (*SIGN* 2008).

Elderly patients with a new headache and a recent subacute (days to weeks) decline in cognition may have a subacute or chronic hematoma. A history of head injury is not always present. They require urgent specialist referral and/or neuroimaging (*TOP Clinical Practice Guideline* 2016).

In patients over 50 with new onset headache, CT without IV contrast should be considered if hemorrhage is suspected, or if the patient is unable to undergo MRI and has a moderate or severe allergy to CT contrast (PLE expert panel consensus opinion).

Clinical notes:

- Patients who present with headache and red flag features for potential secondary headache should be referred to a specialist appropriate to their symptoms for further assessment (*SIGN* 2008, grade D recommendation).

Evidence update (2014-present): There were no new articles that significantly affected the recommendations or conclusions found in the guidelines referenced above.

Headache with symptoms and signs of increased intracranial pressure, including papilledema:

- **Green** – MRI brain with and without IV contrast; MRI brain without IV contrast
- **Yellow** – MRI brain with IV contrast to characterize abnormalities seen on a previous MRI brain without IV contrast
- **Yellow** – CT head with and without IV contrast or CT head with IV contrast if the patient is unable to undergo MRI or if MRI is unavailable
- **Yellow** – CT head without IV contrast if there is a clinical suspicion of hemorrhage, if the patient is unable to undergo MRI, or if MRI is not readily available
- **Yellow** – MRV head or CTV head for suspected dural venous sinus thrombosis or idiopathic intracranial hypertension (IIH)/pseudotumor cerebrii
- **Yellow** – MRA head or CTA head to evaluate for a suspected vascular abnormality
- **Red** – SPECT; PET

Level of Evidence: MRI and CT: moderate level of evidence; MRA, CTA, MRV, CTV, SPECT and PET: PLE expert panel consensus opinion.

Notes concerning applicability and/or patient preferences: None.

Guideline and PLE expert panel consensus opinion summary:

Patients with papilledema, a normal level of consciousness, and no focal neurological signs may have benign intracranial hypertension. They should have urgent specialist referral and will need urgent neuroimaging (*TOP Clinical Practice Guideline 2016*).

Patients with papilledema and altered level of consciousness and/or focal neurological signs may have a space occupying lesion and may be at risk for incipient transtentorial herniation. They should be sent immediately to an emergency department with neuroimaging capability and specialist resources for investigation and treatment (*TOP Clinical Practice Guideline 2016*).

Adult patients with [acute or new onset] headache and exhibiting signs of increased intracranial pressure (e.g., papilledema, altered mental status, focal neurological deficits, signs of meningeal irritation) should undergo a neuroimaging study before having a lumbar puncture (Edlow et al. [*ACEP*] 2008, level C recommendation).

For headache that worsens on lying down, a brain CT or MRI scan can be used to exclude a space-occupying lesion (*TOP Clinical Practice Guideline 2016*).

MRI of the head with and without contrast is the imaging study of choice in the evaluation of patients with papilledema. CT of the head with contrast may be appropriate if MRI is contraindicated or not available (Douglas et al. [*ACR*] 2014).

The *American College of Radiology* recommends MRI head without and with IV contrast (8), MRI head without IV contrast (7), CT head without IV contrast (7), MRA head without and with IV contrast (6), CT head without and with IV contrast (6), MRA head without IV contrast (5), CT head with IV contrast (5),

and CTA head with IV contrast (5) for the imaging of new headache, focal neurologic deficit or papilledema (Douglas et al. [ACR] 2014).

In headache patients with symptoms and signs of increased intracranial pressure, CT with IV contrast should be considered if tumor is suspected and the patient is unable to undergo MRI (PLE expert panel/PLE multidisciplinary committee consensus opinion).

In headache patients with symptoms and signs of increased intracranial pressure, CT without IV contrast should be considered if hemorrhage is suspected, or if the patient is unable to undergo MRI and has a moderate or severe allergy to CT contrast (PLE expert panel consensus opinion).

Clinical notes:

- Headache with nausea and vomiting [can be] signs of increased intracranial pressure and are usually worse in the morning. The presence of bilateral papilledema indicates increased intracranial pressure that is transmitted to the optic nerve sheath (Douglas et al. [ACR] 2014).
- The differential diagnosis of headache with papilledema is broad and includes any entity that results in increased intracranial pressure including tumor, abscess, hematoma, hydrocephalus, idiopathic intracranial hypertension and dural venous sinus thrombosis (Douglas et al. [ACR] 2014).
- Headache secondary to intracranial neoplasm has at least one of the three features: progressive, worse in the morning or after daytime napping, or aggravated by Valsalva-like maneuvers (*ICHD-3* 2013).
- Although the majority of patients with IIH have papilledema, IIH without papilledema has been observed. Other symptoms of IIH include pulse-synchronous tinnitus, transient visual obscurations, neck or back pain and diplopia (*ICHD-3* 2013).
- Patients who present with headache and features suggestive of raised intracranial pressure should be referred urgently to a specialist for assessment (*SIGN* 2008, grade D recommendation).

Evidence update (2014-present): There were no new articles that significantly affected the recommendations or conclusions found in the guidelines referenced above.

Suspected low CSF pressure headache / orthostatic headache:

- **Green** – MRI brain with and without IV contrast
- **Yellow** – MRI brain without IV contrast if the patient is unable to receive or refuses IV contrast
- **Yellow** – MRI brain with IV contrast to characterize abnormalities seen on a previous MRI brain without IV contrast
- **Yellow** – CT head with IV contrast or CT head with and without IV contrast if the patient is unable to undergo MRI or MRI is unavailable
- **Yellow** – CT head without IV contrast if the patient is unable to undergo MRI and is unable to receive or refuses contrast
- **Yellow** – MR myelography or CT myelography of the spine if patient is not responding to treatment
- **Red** – MRA; CTA; MRV; CTV; SPECT; PET

Level of Evidence: MRI and CT: very Low level of evidence; MRA, CTA, MRV, CTV, SPECT, PET: PLE expert panel consensus opinion.

Notes concerning applicability and/or patient preferences: None.

Guideline and PLE expert panel consensus opinion summary:

In patients where orthostatic headache is part of the presentation, brain MRI with injection should be preferred (Moisset et al. [*SFEMC & SFN*] 2016, professional agreement).

For headache that worsens on standing, brain MRI scanning with gadolinium enhancement may be needed to look for indirect evidence of a CSF leak (dural enhancement) (*TOP Clinical Practice Guideline* 2016).

In patients with suspected low pressure/orthostatic headache, consider additional investigation and/or referral to a specialist (*NICE* 2015; *SIGN* 2008).

If MRI of the head is normal and the patient fails initial treatment regimens, MRI or CT of the spine should be obtained and should include MR myelographic sequences (Douglas et al. [*ACR*] 2014).

The *American College of Radiology* recommends MRI head without and with IV contrast (8), MRI head without IV contrast (7), myelography and post myelography CT spine (7), MRI spine include MR myelography (7), CT head without IV contrast (5), CT head with IV contrast (5), and CT head without and with IV contrast (5) for the imaging of positional headache (Douglas et al. [*ACR*] 2014).

In patients with low pressure headache, CT of head with IV contrast is recommended if the patient is unable to undergo MRI or MRI is unavailable. If the patient has a moderate or severe allergy to CT contrast, this can be performed without contrast (PLE multidisciplinary committee consensus opinion).

Clinical notes:

- In patients with spontaneous or iatrogenic intracranial hypotension ... the headache develops or worsens soon after assuming an upright posture and lessens or resolves shortly after lying down. Intracranial hypotension should be considered in all patients with headache developing or worsening after assuming an upright posture (*SIGN* 2008, grade D recommendation).

- Spontaneous intracranial hypotension typically results in orthostatic headache and low opening pressure on lumbar puncture (Douglas et al. [ACR] 2014).
- The main diagnostic criteria of spontaneous intracranial hypotension are the demonstration of extrathecal CSF with CT or MRI of the entire spine, which should include an MR myelography sequence. If no extrathecal CSF is present, then ... the presence of at least one of the following should indicate a diagnosis of spontaneous intracranial hypotension: low opening pressure on lumbar puncture, meningeal diverticulum, or improvement of symptoms with epidural blood patch. (Douglas et al. [ACR] 2014).

Evidence update (2014-present): There were no new articles that significantly affected the recommendations or conclusions found in the guidelines referenced above.

Headache precipitated by cough:

- **Green** – MRI brain with and without IV contrast; MRI brain without IV contrast
- **Yellow** – MRI brain with IV contrast to characterize abnormalities seen on a previous MRI brain without IV contrast
- **Yellow** – CT head with and without IV contrast or CT head with IV contrast in patients who are unable to undergo MRI or if MRI is not available
- **Yellow** - CT head without IV contrast if there is a suspicion for hemorrhage, if the patient is unable to undergo MRI, or if MRI is not available
- **Orange** – MRA head or CTA head, except if there is clinical suspicion of a vascular lesion/abnormality
- **Red** – SPECT; PET; MRV; CTV

Level of Evidence: CT, MRI: very low level of evidence; MRA, CTA, MRV, CTV, SPECT, PET: PLE expert panel consensus opinion.

Notes concerning applicability and/or patient preferences: None

Guideline and PLE expert panel consensus opinion summary:

Patients with headache clearly precipitated by exertion, cough, or Valsalva should be considered for specialist referral and/or a brain MRI scan to exclude a Chiari 1 malformation or a posterior fossa lesion (but it must also be considered that patients with typical migraine may have exertion as one of their headache triggers) (*TOP Clinical Practice Guideline 2016*).

Brain MRI should be carried out in patients presenting with headache which is precipitated, rather than aggravated, by cough (*SIGN 2008*, grade D recommendation).

Brain MRI including the craniocervical junction is recommended to exclude structural abnormalities in patients with primary cough headache. MRA is not generally recommended, however, dynamic MRI CSF studies may be useful (Mitsikostas, et al. [*EHF*] 2016*).

Consider further investigations and /or referral in patients who present with headache triggered by cough, valsalva, sneeze or exercise (*NICE 2015*; Beithon et al. [*ICS*] 2013).

The *American College of Radiology* recommends MRI head without and with IV contrast (8), MRI head without IV contrast (7), CT head without IV contrast (7), MRA head without IV contrast (6), MRA head without and with IV contrast (6), CT head without and with IV contrast (6), CT head with IV contrast (5), and CTA head with IV contrast (5) for the imaging of headache associated with cough, exertion, or sexual activity (Douglas et al. [*ACR*] 2014).

With headache precipitated by cough, CT with IV contrast should be considered if tumor is suspected and the patient is unable to undergo MRI (PLE multidisciplinary committee consensus opinion).

CT without IV contrast should be considered if hemorrhage is suspected, or if the patient is unable to undergo MRI and has a moderate or severe allergy to CT contrast (PLE expert panel consensus opinion).

*This guideline did not pass the Agree II review. It is used here, however because of its direct relevance to these uncommon headache disorders.

Clinical notes:

- The diagnostic criteria for a cough headache are at least two headaches brought on by or occurring only with coughing, straining and/or other Valsalva maneuvers, sudden onset, and lasting between 1 second and 2 hours (*ICHD-3* 2013).
- Symptomatic cough headache may represent a primary headache or may be a sign of an underlying structural abnormality, most commonly a Chiari I malformation or other posterior fossa lesions (Evers et al. [*EFNS*] 2011; *SIGN* 2008).
- Patients who present with headache and red flag features for potential secondary headache should be referred to a specialist appropriate to their symptoms for further assessment (*SIGN* 2008, grade D recommendation).
- Imaging studies reveal pathology in 9.7-43% of cases of headaches associated with cough, exertion or sexual activity (Douglas et al. [*ACR*] 2014).

Evidence update (2014-present) and select articles from guideline bibliographies:

Pascual et al., in a 2008 article, reported the incidence of secondary headache in patients seen in their clinic from 1997 through 2006. 40/68 patients with cough headaches had secondary headaches: 32/40 with Chiari 1 malformation. The remaining 8 had other posterior fossa lesions including 3 subarachnoid cysts, 2 dermoid cysts, 2 meningiomas and one os odontoideum. 2/11 patients with exertional headaches had SAH. 2/18 patients with sexual headaches had secondary headaches: one with hydrocephalus and one with a cervical AVM (moderate level of evidence).

Chen et al., in a 2009 article, reported on the clinical characteristics and outcome in 83 consecutive patients with cough headaches. 9/83 patients had abnormalities on brain imaging. Abnormalities localized to the posterior fossa in 6/9 patients, with Chiari malformation in 2 patients and a cerebellar mass in 4 patients (moderate level of evidence).

Headache precipitated by exertion or sexual activity:

- **Green** – CT head without contrast or CT head with and without IV contrast
- **Green** – CTA head and/or neck; MRA head and/or neck with and/or without IV contrast
- **Yellow** – MRI brain without IV contrast or MRI brain with and without IV contrast*
- **Orange** – CT head with IV contrast, except to characterize abnormalities detected on previous CT head without IV contrast
- **Orange** – MRI brain with IV contrast, except to characterize abnormalities seen on a previous MRI brain without IV contrast
- **Red** – MRV; CTV; SPECT; PET

MRI for thunderclap headache should only be performed when radiology expertise is available and MR imaging equipment support the use of fluid-attenuated inversion recovery (FLAIR), gradient-recalled T2 and/or susceptibility-weighted (SWI) sequences.

Level of Evidence: CT, MRI, MRA, CTA: very low level of evidence; MRV, CTV, SPECT, PET: insufficient level of evidence.

Notes concerning applicability and/or patient preferences: None.

Guideline and PLE expert panel consensus opinion summary:

Headaches associated with sexual activity may be primary or secondary and head CT should be considered to rule out SAH or the patient should be evaluated with MRI (including GRE or SWI sequences) for a more thorough assessment of symptoms (Douglas et al. [ACR] 2014).

On first occurrence of exercise headaches, it is mandatory to exclude subarachnoid hemorrhage, arterial dissection and reversible cerebral vasoconstriction syndrome (RCVS) (ICHD-3 2013).

CT without contrast is recommended to rule out subarachnoid hemorrhage on the initial presentation of a patient with orgasmic sexual headache. The multidisciplinary committee felt that MRI with FLAIR, gradient-recalled T2* and susceptibility-weighted (SWI) sequences were equally sensitive to subarachnoid hemorrhage and could also be used in the initial evaluation of patients with orgasmic type of sexual headache, although in most circumstances CT would be more readily available and efficient (PLE multidisciplinary committee consensus opinion).

Brain MRI, brain MRA and MRA of the carotid/vertebral arteries are recommended to rule out subarachnoid hemorrhage and arterial dissection on the first occurrence of exercise headache (Mitsikostas et al. [EHF] 2016*).

Further investigation should be considered in patients with headaches which are precipitated, rather than aggravated, by exercise. In patients with headache precipitated rather than aggravated by exercise, subarachnoid haemorrhage or arterial dissection need to be excluded on first occurrence. Expert opinion suggests that neuroimaging should be carried out to exclude a structural cause or vascular abnormality in patients with exertional headache (SIGN 2008).

MRI and MRA are recommended to rule out vascular abnormalities or other structural causes particularly [in patients with exercise-induced headaches] if the headaches are of new onset, occur after

age 40, last beyond a few hours, or are accompanied by vomiting or focal neurologic symptoms (Douglas et al. [ACR] 2014).

On the first onset of headache associated with sexual activity, it is mandatory to exclude subarachnoid hemorrhage, arterial dissection and reversible vasoconstriction syndrome (RCVS). Multiple explosive headaches during sexual activities should be considered RCVS until proven otherwise by angiographic studies or transcranial Doppler ultrasonography (*ICHD-3* 2013).

In patients with headaches associated with sexual activity, brain MRI, brain MRA/MRV and ultrasound or MRA of the carotid and vertebral arteries are recommended to rule out arterial dissection or RCVS (Mitsikostas et al. [EHF] 2016*; Yeh et al. 2010).

In patients with exercise headaches or headaches associated with sexual activity, repeat imaging may be indicated: If the initial study is negative, then another study is indicated for first recurrence. If the initial study is positive for RCVS, then a repeat study is recommend for follow-up (PLE expert panel consensus opinion).

The *American College of Radiology* recommends MRI head without and with IV contrast (8), MRI head without IV contrast (7), CT head without IV contrast (7), MRA head without IV contrast (6), MRA head without and with IV contrast (6), CT head without and with IV contrast (6), CT head with IV contrast (5), and CTA head with IV contrast (5) for the imaging of headache associated with cough, exertion, or sexual activity (Douglas et al. [ACR] 2014).

*This guideline did not pass the Agree II review. It is used here, however because of its direct relevance to these uncommon headache disorders.

Clinical notes:

- Primary exercise headache is usually precipitated by sustained physically strenuous exercise, and occurs more commonly in hot weather or at high altitude (*ICHD-3* 2013).
- Exertional or exercise-induced headaches may be primary or secondary. Important differential diagnoses include SAH, cervical artery dissection, and craniocervical abnormalities (Evers et al. [EFNS] 2011; Pascual et al. 2008).
- Headaches associated with sexual activity may increase in intensity with increasing sexual excitement or may explode in intensity just before or with orgasm (*ICHD-3* 2013).
- Headaches precipitated by sexual activity can be primary, however it is essential to exclude SAH and arterial dissection at initial presentation (*SIGN* 2008; Douglas et al. [ACR] 2014; Evers et al. [EFNS] 2011).
- Patients who present with headache and red flag features for potential secondary headache should be referred to a specialist appropriate to their symptoms for further assessment (*SIGN* 2008, grade D recommendation).
- Imaging studies reveal pathology in 9.7-43% of cases of headaches associated with cough, exertion or sexual activity (Douglas et al. [ACR] 2014).
- RCVS has been diagnosed in 45% of patients presenting with thunderclap headaches. RCVS is attributed to transient reversible abnormal regulation of cerebral arterial tone, which triggers multifocal diffuse vasoconstriction and vasodilatation. It can be triggered by vasoactive substances such as cannabis, cocaine, ecstasy, amphetamines, LSD, antidepressants (SSRI and SNRI drugs), nasal decongestants, triptans and ergotamine. RCVS can be triggered by sexual activity or valsalva maneuvers (Moisset et al. [SFEMC & SFN] 2016; *ICHD-3* 2013).

Technical notes:

- If an MRI is obtained to evaluate a headache precipitated by exertion or sexual activity, it should include fluid-attenuated inversion recovery (FLAIR), gradient recalled T2* and/or SWI sequences (PLE expert panel consensus opinion).

Evidence update (2014-present) and select articles from guideline bibliographies:

Pascual et al., in a 2008 article, reported the incidence of secondary headache in patients seen in their clinic from 1997 through 2006. 40/68 patients with cough headaches had secondary headaches: 32/40 with Chiari 1 malformation. The remaining 8 had other posterior fossa lesions including 3 subarachnoid cysts, 2 dermoid cysts, 2 meningiomas and one os odontoideum. 2/11 patients with exertional headaches had SAH. 2/18 patients with sexual headaches had secondary headaches: One with hydrocephalus and one with a cervical AVM (moderate level of evidence)

Yeh et al. (2010) reviewed the findings in 30 patients with headache associated with sexual activity from 2004 to 2009. 20/30 (67%) had secondary causes, 18 with RCVS, one with SAH and one with basilar artery dissection (moderate level of evidence).

Chen et al., in a 2017 systematic review concerning headaches associated with sexual activity (HSA), reported intracranial abnormalities in 3/31 patients: One with an aneurysmal subarachnoid hemorrhage, one with right middle cerebral artery spasm and one with a posterior fossa subarachnoid cyst (low level of evidence).

Vlak et al., in a 2011 study, evaluated the trigger factors in 250 patients with aneurysmal subarachnoid hemorrhage. The authors found 8 triggers. Sexual intercourse had a RR of 11.2 and vigorous physical exercise 2.4. The highest population-attributable risks were found for coffee consumption (10.6%) and vigorous exercise (7.9%) (low level of evidence).

Persistent headache attributed to traumatic injury to the head:

- **Green** – CT head without IV contrast
- **Yellow** – MRI brain with and without IV contrast or MRI brain without IV contrast for patients with new or increasing headache, new or increasing neurologic symptoms/signs, or increasing cognitive deficit
- **Yellow** – CT head with IV contrast for patients with new or increasing headache, new or increasing neurologic symptoms/signs, or increasing cognitive deficit and a previous negative CT head without IV contrast who are unable to undergo MRI
- **Yellow** – MRI brain with IV contrast to characterize abnormalities seen on previous MRI brain without IV contrast
- **Red** – PET; SPECT; MRA; CTA; MRV; CTV

Level of Evidence: PLE expert panel consensus opinion.

Notes concerning applicability and/or patient preferences: None.

Guideline and PLE expert panel consensus opinion summary:

There is insufficient evidence to recommend for or against neuroimaging in patients with persistent headache attributed to head trauma who do not have new focal signs or other red flags to indicate the need for neuroimaging. If, on a case by case basis, it is felt that there may be a need for neuroimaging, consider specialist referral (*TOP Clinical Practice Guideline 2016*).

CT should be considered at least once in patients with mild TBI and a persistent headache or a subsequent decline in cognition to exclude chronic subdural hematoma (PLE expert panel consensus opinion; *TOP Clinical Practice Guideline 2016*).

MRI with and without IV contrast should be considered in patients with chronic post-traumatic headaches which are increasing in severity and in patients with new or increasing neurologic deficits or symptoms (PLE expert panel consensus opinion; see page 7 of this AUC document regarding criteria for patients with new or increasing neurologic deficits).

MRI is the image of choice to detect the late, sub-acute, and chronic structural changes in the brain which underlie abnormal functioning and is a well-accepted technique for follow-up imaging. MRI scans are generally recommended as opposed to CT once the initial acute stage has passed (*CO Division of Workers' Compensation Medical Treatment Guidelines 2012*).

CT scans provide somewhat limited information compared to MRI about intrinsic cerebral damage involving deep brain structures, although many types of intrinsic damages can be seen on CT scans (*CO Division of Workers' Compensation Medical Treatment Guidelines 2012*).

In patients with chronic post-traumatic headache, there is no evidence that an abnormality on CT or MRI changes the prognosis or contributes to treatment. These studies should not be considered routine for patients with ongoing post-traumatic headache. They may be considered on a case-by-case basis (*Ontario Neurotrauma Foundation 2013*).

The *American College of Radiology* recommends MRI head without contrast (9) or CT head without contrast (7) for the imaging of subacute or chronic traumatic brain injury with new cognitive and/or neurologic deficit(s). CT head without contrast is labeled as the first-line procedure in rapidly evolving new neurologic deficits or if MRI is contraindicated (Shetty et al. [ACR] 2016).

MRI is the principle modality for detecting subacute to chronic TBI, with its increased sensitivity to detect and characterize brain injuries, especially atrophy and microhemorrhages, and is recommended in patients with new, persistent, or increasing neurologic deficits (Shetty et al. [ACR] 2016).

Although MRI is superior to CT in detection of chronic sequelae of TBI such as microhemorrhages, head CT may suffice if the aim of imaging is to show areas of atrophy, and CT often helps in documenting the absence of other structural abnormalities (such as an enlarging subacute to chronic subdural hematoma) that might require active intervention (Shetty et al. [ACR] 2016).

The use of intravenous contrast offers no significant advantage in nonvascular neuroimaging for head trauma and is generally not indicated [to exclude subdural hematoma] (Shetty et al. [ACR] 2016).

SPECT is not generally accepted as a diagnostic test for TBI of any severity and is considered investigational for diagnostic purposes. It may provide useful information in some cases in which the prognosis is uncertain and structural neuroimaging is normal (*CO Division of Workers' Compensation Medical Treatment Guidelines 2012*).

PET is not generally accepted as a diagnostic study and should not be used solely to diagnose the presence of TBI (*CO Division of Workers' Compensation Medical Treatment Guidelines 2012*).

Clinical notes:

- Headache is one of the most common symptoms seen in general medical practices; following TBI, 50% or more of injured individuals experience headache. The majority of these are self-limited, but headache persisting for more than three months may occur. Headaches may persist longer when associated with other symptoms such as dizziness, memory problems or weakness. Therefore, every effort should be made to identify the cause and treat headaches and other symptoms as early as possible (*CO Division of Workers' Compensation Medical Treatment Guidelines 2012*).
- The purposes of imaging patients with chronic TBI are to improve identification of underlying injuries, to assist in patient prognosis, and to guide in the need for referral to a specialist (Shetty et al. [ACR] 2016).
- SPECT and PET have revealed focal areas of hypoperfusion without a correlate on MRI or CT. There is ongoing investigation as to whether these abnormalities are of use in the management of patients with subacute or chronic post-traumatic brain injury (Shetty et al. [ACR] 2016).

Evidence update (2014-present): There were no new articles that significantly affected the recommendations or conclusions found in the guidelines referenced above.

Guideline exclusions:

- MR perfusion, CT perfusion;
- Dynamic MRI CSF studies;
- Cervicogenic headache;
- Temporal arteritis;
- Headache associated with sinusitis or mastoiditis;
- Headache of oromaxillofacial (temporomandibular joint disorders (TMJ), odontogenic) origin;
- Headache of suspected orbital or periorbital origin, including suspected acute closed-angle glaucoma;
- Headache associated with pregnancy;
- Acute headache attributed to traumatic injury to the head;
- Investigational MRI techniques, including voxel-based morphometry, magnetic resonance spectroscopy, functional MRI, diffusion tensor imaging, 7 Tesla MRI, and CT perfusion;
- Pediatric patients;
- Patients with prior neurosurgery;
- Patients in whom headache is not the chief complaint or other clinical features are present, which suggest a more specific diagnosis.

AUC Revision History:

<u>Revision Date:</u>	<u>New AUC Clinical Scenario(s):</u>	<u>Posting Date:</u>	<u>Approved By:</u>
09/04/2018	n/a	09/06/2018	CDI Quality Institute's Multidisciplinary Committee

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