Bibliographic Cite	PMID Link	Literature Type	Level of Evidence	Purpose	Population	Intervention and Outcome Measures	Results / Recommendations	Study Limitations
Alons IM, Goudsmit BF, Jellema K, et al. Prediction of vascular abnormalities on CT angiography in patients with acute headache. Brain Behav. 2018; 8(6):e00997.	29741225	Retrospective study	Low	To determine clinical and non-contrast CT (NCCT) criteria to select patients who might benefit from CT-angiography (CTA) for evaluating underlying vascular causes.	All patients (n = 384) who underwent a cerebral and cervical CTA between January 2011 and December 2014 in the emergency department of the Leiden University Hospital (LUMC), a tertiary vascular neurology referral center and university teaching hospital, and the Haaglanden Medical Centre in The Hague, a tertiary vascular referral center and a secondary teaching hospital. Included were all patients who presented with acute headache. Acute headache was headache peaking within 5 min and lasting more than 1 hr. Excluded patients were comatose (EMV < 9), had an ongoing seizure or were otherwise unable to express whether they had headache.	Authors identified factors that increased the probability of finding a vascular abnormality on CTA, performed multivariable regression analyses and determined discrimination with the c-statistic.	NCCT was abnormal in 194 patients. Among these, abnormalities were found in 116 cases of which 99 aneurysms. In the remaining 190 with normal NCCT we found abnormalities in 12 cases; four unruptured aneurysms, three cerebral venous thrombosis', two reversible cerebral vasoconstriction syndromes, two cervical arterial dissections and one cerebellar infarction. In multivariable analysis abnormal NCCT, lowered consciousness and presentation within 6 hr of headache onset were independently associated with abnormal CTA. The c-statistic of abnormal NCCT alone was 0.80 (95% CI: 0.75–0.80), that also including the other two variables was 0.84 (95% CI: 0.80–0.88). If NCCT was normal no other factors could help identify patients at risk for abnormalities. The authors conclude that in patients with acute headache abnormal NCCT is the strongest predictor of a vascular abnormality on CTA. If NCCT is normal no other predictors increase the probability of finding an abnormality on CTA and diagnostic yield is low.	There is a likely selection bias in the performed CTAs limiting the number of CTAs in patients with normal NCCT or normal neurological examination. Due to the retrospective design of our study we do not know why the treating physician chose to perform these CTAs and more importantly, we cannot determine how many patients did not receive a CTA at all. Second, in some subgroups, such as patients with a normal NCCT, the number of abnormalities was small. Due to the limited number of abnormalities there was insufficient power to determine clinically relevant factors. Finally, we had to rely on retrospective chart review and some data, for instance on the presence of nuchal rigidity or evaluation of papillary edema, was missing in a large part of patients, because the performance of such neurological tests may very much depend on the severity of the clinical presentation.
Alons IM, van den Wijngaard IR, Verheul RJ, et al. The value of CT angiography in patients with acute severe headache. Acta Neurol Scand. 2015;131(3):164-8.	25312840	Retrospective study	Low	To evaluate the yield of CTA in patients with acute severe headache with normal neurological examination and no abnormalities at standard CT and CSF analysis	70 consecutive patients presented to the emergency room between January 2008 and May 2011 with acute severe headache and without abnormalities at neurological examination, CT and CSF research, who received a CTA in the diagnostic process in a teaching hospital.	CTA tests were performed. Findings included a vascular abnormality in 13 (19%) of patients. Four had either a prior aneurysm or CVT. Eight patients had an unruptured intracranial aneurysm (UIA) on CTA (11%), two had CVT (3%), two had RCVS (3%) and one had cerebral ischemia (1%).	The authors found a high percentage of vascular abnormalities. A third of these patients had a prior episode of either an aneurysm or CVT. In patients with a history of UIA or CVT performing CTA despite normal CT and LP therefore seems warranted.	The study has several limitations. First, due to the retrospective design of the study, there may be an indication bias. The patients with prior aneurysms and CVT are logical candidates for follow-up by CTA, possibly increasing the chance of finding vascular abnormalities. Second, this study is single center, so the findings may not be generalizable. Tertiary headache centers may find higher yield by referral bias, whereas primary centers may find lower percentages. The assessment of all clinical symptoms, such as detailed headache characteristics, was beyond the scope of this study. Small number of events, single reader, unclear how indeterminate results were handled.
Carey MR, Callaghan BC, Kerber KA, et al. Impact of early headache neuroimaging on time to malignant brain tumor diagnosis: A retrospective cohort study. PLoS One. 2019; 14(2):30211599.	30707721	Retrospective study	Low	To determine the role of early neuroimaging in the identification of malignant brain tumors in individuals presenting to healthcare providers with headaches.	180,623 individuals with incident headaches were included in this retrospective cohort study using administrative claims data (2001–2014) from a US insurer. Individuals were included if they had an outpatient visit for headaches and excluded for prior headache visits, other neurologic conditions, neuroimaging within the previous year, and cancer.	The exposure was early neuroimaging, defined as neuroimaging within 30 days of the first headache visit. A propensity score-matched group that did not undergo early neuroimaging was then created. The primary outcome was frequency of malignant brain tumor diagnoses and median time to diagnosis within the first year after the incident headache visit. The secondary outcome was frequency of incidental findings.	22.2% of 180,623 individuals had early neuroimaging. In the following year, malignant brain tumors were found in 0.28% (0.23–0.34%) of the early neuroimaging group and 0.04% (0.02–0.06%) of the referent group (P<0.001). Median time to diagnosis in the early neuroimaging group was 8 (3–19) days versus 72 (39–189) days for the referent group (P<0.001). Likely incidental findings were discovered in 3.17% (3.00–3.34%) of the early neuroimaging group and 0.66% (0.58–0.74%) of the referent group (P<0.001). The authors conclude that malignant brain tumors in individuals presenting with an incident headache diagnosis are rare and early neuroimaging leads to a small reduction in the time to diagnosis.	The study had several limitations. First, as a retrospective cohort analysis, the early neuroimaging and referent groups, even after matching, almost certainly vary on important outcome predictors such as headache time course and severity. Second, it is difficult to definitively determine whether the neuroimaging studies were truly "for headache" or merely performed in individuals "with headache". Third, our analysis focuses on malignancies—benign tumors may also have clinical relevance, though they are generally less worrisome than gliomas or metastases. Fourth, using administrative data, authors could not identify clinically relevant "red flags", such as an abnormal neurologic examination or other associated symptoms, that would warrant appropriate neuroimaging.
Chen CY, Chen SP, Fuh JL, et al. Vascular wall imaging in reversible cerebral vasoconstriction syndrome - a 3-T contrast-enhanced MRI study. J Headache Pain. 2018; 19(1):74.	30167985	Prospective study	Low	To determine whether absence of arterial wall pathology on imaging is a universal finding in patients with RCVS.	48 patients with RCVS from Taipei Veterans General Hospital from 2010 to 2012, with follow-up until 2017	Authors analyzed the characteristics of vascular wall enhancement in these patients without comparisons to a control group. All participants received vascular wall imaging by contrasted T1 fluidattenuated inversion recovery with a 3-T magnetic resonance machine. The vascular wall enhancement was rated as marked, mild or absent.	Of 48 patients with RCVS, 22 (45.8%) had vascular wall enhancement (5 marked and 17 mild). Demographics, clinical profiles, and cerebral artery flow velocities were similar across patients with versus without vascular wall enhancement, except that patients with vascular wall enhancement had fewer headache attacks than those without (p = 0.04). Follow-up imaging completed in 14 patients (median interval, 7 months) showed reduced enhancement in 9 patients, but persistent enhancement in 5. The authors conclude that almost half of the RCVS patients exhibited imaging enhancement of diseased vessels, and it was persistent for approximately a third of those patients with follow-up imaging. Both acute and persistent vascular wall enhancement may be unhelpful for differentiating RCVS from central nervous system vasculitis or subclinical atherosclerosis.	The present study had several limitations. First, we did not include a control group because doing so would involve unnecessary exposure of subjects to the potential risks of gadolinium deposition in the brain. Second, because we did not recruit patients with secondary causes of RCVS, one should be cautious to extrapolate the findings to the general pathogenesis of RCVS. Third, although follow-up MRA evaluations for confirming vasoconstriction reversibility were obtained for all of our patients, the retention rate for vascular imaging was 70.8%, mainly due to the undesirable requirement of contrast injection. Fourth, the magnitudes of vascular wall enhancement observed in the present study do not correspond precisely with severity levels defined in the previous reports. Fifth, these patients received the same treatment (nimodipine) but the resolution of enhancement was heterogeneous, so we cannot be sure if that enhancement of vascular wall imaging is altered by medical treatment. Sixth, the reluctance of patients to undergo spinal tap in Taiwanese society precluded CSF studies in many patients.

Chen PK, Fuh JL, Wang SJ. Cough headache: A study of 83 consecutive patients. Cephalalgia. 2009; 29(10):1079-1085.	19438909	Prospective study	Moderate	To evaluate patients with cough headache to delineate the differences in headache profiles between primary and secondary cough headache, and to evaluate the efficacy of indomethacin and the predictors for treatment response and prognosis.	Patients with cough headache who visited the headache clinic of Taipei Veterans General Hospital from April 1999 to November 2007. Patients were recruited if they complained of headache induced by cough.	All patients with cough headache filled out a structured questionnaire designed for cough headache. Information included demographics, self-reported medical illnesses, and headache profiles (age at onset; relationship between cough and headache; disease duration; headache location; quality; intensity; other triggers; accompanying symptoms). All patients underwent neurological exam by a physician. All patients received neuroimaging studies, either CT or MRI to investigate for intracranial lesion. Based on imaging findings, patients were classified as either primary or secondary cough headache.	During the study period, 83 of 7100 patients (1.2%) presented at the headache clinic with chief complaint of cough-induced headache (59 males, 24 females; mean age 61.5, range 22-88). Eighty patients underwent MRI of the brain and three underwent CT. Seventy-six of them (91.6%) received contrast enhancement for either CT (n = 2) or MRI (n = 74) studies. Seventy-four patients (89.2%) had primary cough headache, with nine patients having secondary cough headache. Age, gender, age of onset and duration of illness did not differ between the two groups. In the primary group, none of the patients had positive neurological findings, whereas in the secondary group, three patients had ataxic gait with or without dysmetria in the finger-nose test. Six patients with secondary cough (66.7%) had a posterior fossa lesion (four with obstructive hydrocephalus and two with Chiari malformation type I). Of the other three patients, one had subdural hematoma, one multiple brain metastasis and one acute sphenoid sinusitis. The authors conclude that headache profile could not help differentiate primary and secondary cough headache, which supports the clinical rule, i.e. secondary causes should be highly suspect in each patient with cough headache.	The authors note that all headache profiles were self-reported and based on recollection. Bias of subjective recall is assumed. Second, interpretation and generalization of the results shold be cautious, because the study was conducted in a headache clinical rather than in the general population, even though the referral rate was low in the headache clinic.
Cheng, YC, Kuo, KH, Lai, TH. A common cause of sudden and thunderclap headaches: reversible cerebral vasoconstriction syndrome. J Headache Pain. 2014;15:13	24580731	Prospective study	Moderate	Thunderclap headache (TCH) is a sudden headache (SH) with accepted criteria of severe intensity and onset to peak within one minute. It is a well-known presentation for subarachnoid hemorrhage (SAH) but most patients with TCH or SH run a benign course without identifiable causes. Reversible cerebral vasoconstriction syndrome (RCVS), a recently recognized syndrome characterized by recurrent TCH attacks, has been proposed to account for most of these patients.	The authors recruited consecutive patients presenting with SH at the authors' headache clinic. From July 2010 to June 2013, 31 patients with SH were recruited.	Computed tomography and/or magnetic resonance imaging with angiography were performed to exclude structural causes and to identify vasoconstriction. Catheter angiography and lumbar puncture were performed with patients consent. Reversibility of vasoconstriction was confirmed by follow-up study.	Twenty-four (72.7%) of these SH patients exhibited headache fulfilling the TCH criteria. The diagnosis of RCVS was confirmed in 14 (45.2%) of patients with SH and 11 (45.8%) of patients with TCH. Other diagnoses were as follows: primary headaches (SH: 41.9%, TCH: 45.8%) and other secondary causes (SH: 12.9%, TCH: 8.3%). Compared with non-RCVS patients, patients with RCVS were older (50.8+/-9.3 years vs. 40.8+/-10.0 years, P=0.006) and less likely to experience short headache duration of<1 hour (23.1% vs. 78.6%, P=0.007). Patients with RCVS were more likely to cite bathing (42.9% vs. 0%, P=0.004) and less likely to cite exertion (0% vs. 29.4%, P=0.048) as headache triggers. Reversible cerebral vasoconstriction syndrome is a common cause of SH and TCH. Considering the potential mortality and morbidity of RCVS, systemic examination of cerebral vessels should be performed in these patients.	Inconsistent definitions of sudden headache affecting patient ratiosInconsistent application of the catheter angiography
Chu KH, Howell TE, Keijzers G, et al. Acute Headache Presentations to the Emergency Department: A Statewide Cross-sectional Study. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2017;24(1):53-62.	27473746	Cross-sectional study	Low	The objective of this study was to describe demographic and clinical characteristics including features that were consistent with subarachnoid hemorrhage (SAH), use of diagnostic tests, emergency department (ED) discharge diagnoses, and disposition of adult patients presenting with an acute headache to EDs statewide across Queensland, Australia. In addition, potential variations in the presentation and diagnostic workup between principal-referral and city-regional hospitals were examined.	A prospective cross-sectional study of 847 headache patients was conducted over 4 weeks in September 2014. All patients >/= 18 years presenting to one of 29 public and five private hospital EDs across the state with an acute headache were included. The headache had to be the principal presenting complaint and nontraumatic. The 34 study sites attend to about 90% of all ED presentations statewide. The treating doctor collected clinical information at the time of the ED visit including the characteristics of the headache and investigations performed.	A study coordinator retrieved results of investigations, ED discharge diagnoses, and disposition from state databases. Variations in presentation, investigations, and diagnosis between city-regional and principal-referral hospitals were examined.	There were 847 headache presentations. Median (range) age was 39 (18-92) years, 62% were female, and 31% arrived by ambulance. Headache peaked instantly in 18% and </= 1 hour in 44%. It was "worst ever" in 37%, 10/10 in severity in 23%, and associated with physical activity in 7.4%. Glasgow Coma Scale score was < 15 in 4.1%. Neck stiffness was noted on examination in 4.8%. Neurologic deficit persisting in the ED was found in 6.5%. A computed tomography (CT) head scan was performed in 38% (318/841, 95% CI = 35% to 41%) and a lumbar puncture in 4.7% (39/832, 95% CI = 3.4% to 6.3%). 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%. CT head scans were more likely to be performed in principal-referral hospitals (41%) compared to city-regional hospitals (33%). The headache in patients presenting to the latter was less likely to be instantly peaking or associated with activity, but was no less severe in intensity and was more frequently accompanied by nausea and vomiting. Their diagnosis was more likely to be a benign primary headache. Variations in CT scanning could thus be due to differences in the case mix. The median (interquartile range) ED length of stay was 3.1 (2.2 to 4.5) hours. Patients were discharged from the ED or admitted to the ED short-stay unit prior to discharge in 57 and 23% of cases, respectively. CONCLUSIONS: The majority of patients had a benign diagnosis, with intracranial hemorrhage and bacterial meningitis accounting for only 3% of the diagnoses. There are variations in the proportion of patients receiving CT head scans between city-regional and principal-referral hospitals. As 38% of headache presentations overall underwent CT scanning, there is scope to rationalize diagnostic testing to rule out life-threatening conditions.	Patient recruitment was based on the doctors' assessment that the headache was a primary symptom. Eligibility was not verified nor were missing cases specifically sought. Also, no follow up on patients who did not receive neuroimaging to ensure that their diagnosis was correct and that no secondary headaches subsequentluy developed.
Cooper JG, Smith B, Hassan TB. A retrospective review of sudden onset severe headache and subarachnoid haemorrhage on the clinical decision unit: looking for a needle in a haystack? Eur J Emerg Med. 2016;23(5):356-62.	25851332	Retrospective Study	Low	The aims of this study were to describe the prevalence of SAH and to evaluate the performance of CT and LP in a CDU population with sudden onset acute severe headache.	A retrospective review of 517 neurologically pristine patients admitted to a CDU pathway for exclusion of SAH was conducted.	A noncontrast computed tomography (CT) brain scan is the initial investigation of choice, and most would recommend that, if negative, this be followed by a lumbar puncture (LP) and cerebrospinal fluid (CSF) analysis. Many hospitals in the UK have developed Clinical Decision Unit (CDU) pathways to provide a standardized approach to the investigation and management of neurologically normal patients with headache suggestive of SAH.	The overall prevalence of SAH in this population was 14/517 (2.7%). A noncontrast CT of the brain had a negative predictive value of 99.8%, reducing the post-test probability of having an angiogram-positive SAH detected by LP and CSF analysis to 0.21% (95% confidence interval 0.04-0.36%). CONCLUSION: The management of neurologically pristine patients with sudden onset severe headache on a CDU pathway is feasible. In light of the low prevalence of SAH in this population, 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.	The authors note that this study was retrospective and conducted at only two sites, thus the study was subject to limitations with regards to data collection and analysis. They also note that generalizability of their results may be limited, as they looked at a specific cohort of low-risk patients. Finally, they note that CT scans were formally reported by a mixture of general radiologists and specialist neuroradiologists, where interpretation by only the latter would have been preferable.

Graff-Radford, J, Fugate, JE, Klaas, J, et al. Distinguishing clinical and radiological features of non-traumatic convexal subarachnoid hemorrhage. Eur J Neurol. 2016;23(5):839-46.	26910197	Retrospective study	Low	The full spectrum of causes of convexal subarachnoid hemorrhage (cSAH) requires further investigation. Therefore, the authors' objective was to describe the spectrum of clinical and imaging features of patients with non-traumatic cSAH.	A retrospective observational study of consecutive patients with non-traumatic cSAH was performed at a tertiary referral center. In all, 88 patients [median age 64 years (range 25-85)] with non-traumatic cSAH were identified.	The underlying cause of cSAH was characterized and clinical and imaging features that predict a specific etiology were identified. The frequency of future cSAH or intracerebral hemorrhage (ICH) was determined. In all, 88 patients [median age 64 years (range 25-85)] with non-traumatic cSAH were identified.	The most common causes were reversible cerebral vasoconstriction syndrome (RCVS) (26, 29.5%), cerebral amyloid angiopathy (CAA) (23, 26.1%), indeterminate (14, 15.9%) and endocarditis (9, 10.2%). CAA patients commonly presented at an older age than RCVS patients (75 years versus 51 years, P < 0.0001). Thirteen patients (14.7%) had recurrent cSAH, and 12 patients (13.6%) had a subsequent ICH. However, the risk was high amongst those with CAA compared to those caused by RCVS, with recurrent cSAH in 39.1% and subsequent lobar ICH in 43.5% of CAA cases.The study demonstrates the clinical diversity of cSAH. Older age, sensorimotor dysfunction and stereotyped spells suggest CAA as the underlying cause. Younger age and thunderclap headache predict RCVS. Yet, various other causes also need to be considered in the differential diagnosis.	Retrospective Design Small study size in several patient groups
Han A, Yoon DY, Kim ES, et al. Value of CT angiography for the detection of intracranial vascular lesions in patients with acute severe headache. Eur Radiol. 2013;23(6):1443-9.	23263605	Retrospective Study	Low	To retrospectively investigate the prevalence and characteristics of intracranial vascular lesions in patients with acute severe headache with the use of CT angiography (CTA).	The study group consisted of 512 patients; 251 male; mean age 46.2 +/- 12.4 years.	METHODS: The authors systematically searched for neurologically intact patients with acute severe headache and normal unenhanced head CT. The study group consisted of 512 patients; 251 male; mean age 46.2 +/- 12.4 years. All patients underwent CTA between 1 day and 2 months after the headache attack. CTA images were interpreted by two experienced neuroradiologists for the presence of vascular lesions. RESULTS: Thirty-four (6.6%) of the 512 patients had intracranial vascular lesions on CTA, including 33 aneurysms (2 patients had 2 aneurysms each), 2 moyamoya disease and 1 arterial dissection. No gender- or age-related differences were found. Aneurysms arose most commonly on the internal carotid artery (n = 12), followed by the anterior communicating artery (n = 7), and the middle cerebral artery (n = 7). Maximal diameters ranged from 2.0 to 13.1 mm (mean, 3.9 +/- 2.6 mm).	RESULTS: Thirty-four (6.6%) of the 512 patients had intracranial vascular lesions on CTA, including 33 aneurysms (2 patients had 2 aneurysms each), 2 moyamoya disease and 1 arterial dissection. No gender- or age-related differences were found. Aneurysms arose most commonly on the internal carotid artery (n = 12), followed by the anterior communicating artery (n = 7), and the middle cerebral artery (n = 7). Maximal diameters ranged from 2.0 to 13.1 mm (mean, 3.9 +/- 2.6 mm).	The study has several limitations. First, the study did not perform a head-to-head comparison of CTA with the "gold standard", DSA. The overall frequency of false positives (or false negatives) in the study remains unknown, because not all patients underwent DSA to confirm the presence or absence of vascular lesions. Second, we did not investigate the association between the presence of vascular lesions and potential risk factors such as family history, hypertension, alcohol use and smoking. Also, readers were not blinded and highly experienced (tend to increased diagnostic yield relative to target)
Pascual J, Gonzalez-Mandly A, Martin R, Oterino A. Headaches precipitated by cough, prolonged exercise or sexual activity: A prospective etiological and clinical study. J Headache Pain. 2008; 9:259-266.	18751938	Prospective study	Moderate	To delimitate characteristics, etiology, response to treatment and neuroradiological diagnostic protocol of those patients who consult to a general neurological department because of provoked headache.	A total of 6,412 patients consulted due to headache during the 10 years of the study. A total of 68 patients were diagnosed as having cough headache; either primary (n = 28; mean age 60) or secondary (n = 40; mean age 44). Eighteen patients consulted due to headache provoked by sexual activity (mean age 40) - two with secondary sexual activity (mean age 23.5). Sixteen patients presented with primary exertional headache (mean age 40).	Patients who consulted due to provoked headaches were interviewed in depth and followed-up with for at least 1 year. Neuroradiological protocol included craniocervical MRI for all patients with cough headache and dynamic cerebrospinal functional MRI in secondary cough headache cases. In patients with headache provoked by prolonged physical exercise and/or sexual activity, cranial neuroimaging (CT and/or MRI) was performed and, in case of suspicion of subarachnoid bleeding, angioMRI and/or lumbar tap were performed.	A total of 28 patients out of 68 were diagnosed with primary cough headache, while the remaining 40 had secondary cough headache, always due to structural lesions in the posterior fossa, which in most cases was a Chiari type I malformation. Compared to the primary variety, secondary cough headache began earlier, was located posteriorly, lasted longer (5y vs. 11mo), was associated with posterior fossa symptoms/signs and did not respond to indomethacin. All those patients showed difficulties in the cerebrospinal fluid circulation in the foamen magnum region in the dynamic MRI study and preoperative plateau waves, which disappeared after posterior fossa reconstruction. The mean age at onset for primary headaches provoked by physical exercise and sexual activity began at the same age (40y), shared clinical characteristics (bilateral, pulsating) and responded to beta-blockers. Contrary to cough headache, secondary cases are rare and the most frequent etiology was subarachnoid bleeding. In conclusion, these conditions account for a low proportion of headache consultations. These data show the total separation between cough headache versus headache due to physical exercise and sexual activity, confirm that these two latter headaches are clinical variants of the same entity and illustrate the clinical differences between the primary and secondary provoked headaches.	
Perry JJ, Sivilotti ML, Emond M, et al. Prospective implementation of the Ottawa subarachnoid hemorrhage rule and 6-hour computed tomography rule. Stroke. 2020; 51(2):424-430.	31805846	Multicenter prospective study	Moderate	To estimate the clinical impact of the Ottawa SAH rule and the 6-hour-CT rule on testing rates (i.e., CT lumbar puncture, CT angiography); and to validate the 6-hour-CT rule for SAH when applied prospectively in a new cohort of patients.	3672 patients (1743 before and 1929 after implementation) from 6 tertiary-care Academic EDs. Included were consecutive alert patients > 16 years presenting with chief complaint of a nontraumatic, acute headache, or syncope associated with a headache. Patient must have presented to the ED within 14 days of onset. Exclusions were (1) $\geq$ 3 previous similar headaches over > 6 months, (2) confirmed SAH, (3) previously investigated with CT and LP for same headache, (4) papilledema, (5) new focal neurological deficit, (6) previous dx of intracranial aneurysm or SAH, (7) known brain neoplasm, (8) cerebroventricular shunt, (9) headache within 72 hours following LP, and (10) headache described as gradual or peak intensity beyond 1 hour.	During the intervention period, authors asked physicians to utilize the Ottawa SAH rule and the 6 hour-CT rule. For the intervention period, physicians were given a 1 hour lecture, pocket cards, posters were installed, and physicians indicated Ottawa SAH rule criteria when ordering CTs. SAH was defined by blood on CT, xanthochromia in cerebrospinal fluid, or >1×106/L red blood cells in cerebrospinal fluid with aneurysm. Included in the primary analysis of diagnostic accuracy was every consecutive eligible patient with headache during both the control and intervention periods, at all participating sites.	Proportions undergoing CT was unchanged before vs. after implementation (88.0% versus 87.5%; P=0.643). Lumbar puncture use decreased (38.9% versus 25.9% ; P<0.0001). Additional testing following CT (ie, lumbar puncture or CT angiography) decreased (51.3% versus 42.2%; P<0.0001). Admissions declined (9.8% versus 7.4%; P=0.011). Mean emergency department stay was unchanged (6.3±4.0 versus 6.4±4.2 hours; P=0.685). The Ottawa SAH rule was 100% (95% CI, 98.1%–100%) sensitive, and the 6-hour-CT rule was 95.5% (95% CI, 89.8–98.5) sensitive for SAH. The 6-hour-CT rule missed 5 SAHs: 1 radiology misread, 2 incidental aneurysms, 1 nonaneurysmal cause, and 1 profoundly anemic patient. The authors conclude that the Ottawa SAH rule and the 6-hour-CT rule are highly sensitive and can be used routinely when SAH is considered in patients with headache. Implementing both rules was associated with a meaningful decrease in testing and admissions to hospital.	During the control phase, physicians were explicitly told not to follow the Ottawa SAH rule and the 6-hour-CT rule, but rather use their usual care. Nevertheless, since physicians completed study forms, this may have taught physicians to consider SAH more carefully and made them more aware of the Ottawa SAH rule and the 6-hour-CT rule. Authors were unable to control for the temporal trends in the study EDs, including the global phenomenon of ever increasing ED congestion due to access block to in-hospital beds. This, or other temporal factors not controlled for in this study, may explain why the length of stay did not decrease substantially despite less testing in the intervention phase. Finally, the Ottawa SAH rule and 6-hour-CT rule only apply to patients with headache at risk for SAH. They are not designed to assess for other serious etiologies of headache (eg, bacterial meningitis, cerebral venous thrombosis, stroke, etc).

Sahraian S, Beheshtian E, Haj-Mirzaian A, et al. "Worst headache of life" in a migraineur: Marginal value of emergency department CT scanning. J Am Coll Radiol. 2019; 16(%):683-690.	30661996	Retrospective Study	Low	To assess the value of NCCT scanning in patients with known migraine histories and "worst headache of life" (WHOL) or "thunderclap headache" (TCH).	Study consisted of 224 (132 in study group and 92 in comparison group) patients with the chief symptom of WHOL or TCH and a history of migraine. The age of the 132 patients in the main group averaged 43.83 years, and 107 (81.1%) were women. In the comparison group, the mean age of the 92 patients was 44.53 years, and 73 (79.3%) were women.	The ED NCCT scans of all patients reporting WHOL or TCH who had established diagnoses of migraine were retrospectively reviewed over a 5-year period. Patients without known intracranial pathology, cancer, or immunocompromising disease or recent head trauma were included as the main study group. For comparison, patients with any of those factors were included as the comparison group. Scans were graded as (1) normal, (2) minor unimportant findings, (3) findings requiring intervention or follow-up, or (4) critical.	In the main study group, no patients had grade 4 imaging findings (0%), one had a false-positive grade 3 finding (0.8%), and there were no cases of subarachnoid hemorrhage (0%). In the comparison group, six patients had grade 4 imaging findings (6.5%) and three had grade 3 findings (3.3%). The authors conclude that NCCT in known migraineurs with WHOL or TCH who do not have intracranial pathology, cancer, immunocompromising disease, or recent head trauma yielded no critical findings. Therefore, the value of scanning these patients is questionable.	Retrospective sample.
Tulla M, Tillgren T, Mattila K. Is there a role for lumbar puncture in early detection of subarachnoid hemorrhage after negative head CT? Intern Emerg Med. 2019; 14(3):451-457.	30474789	Retrospective Study	Low	To investigate the role of lumbar puncture (LP) after a negative head CT when ruling out subarachnoid hemorrhage (SAH) within 24 hours of symptom onset.	During the 5-year study period, 647 patients who presented to the hospital were identified as being suspected of SAH and underwent head CT or CT and LP. Median age was 47.2 years (range 17–96), and 361 patients (55.8%) were female.	Patients were categorized into four groups depending on the time of symptom onset to initial head CT: 0–6 h, 6–12 h, 12–24 h, and over 24 h. Experienced radiologists interpreted all CT scans. Authors investigated the sensitivity, specificity, and negative predictive value (NPV) of noncontrast CT in detecting SAH. Initial head CT was reported positive for SAH in 108 patients (16.7%). The remaining 539 patients had negative head CT and underwent LP. The initial head CT was performed within 6 h in 132 patients (24.5%), 6–12 h in 99 patients (18.4%), 12–24 h in 49 (9.1%), and over 24 h from symptom onset in 259 patients (48%).	Five patients had positive LP for SAH after a negative head CT (Table 2), and two of these patients had an aneurysm discovered. All five patients had their initial head CT performed more than 24 h after symptom onset. Out of 280 patients who underwent CT within 24 h from symptom onset, none had aSAH. Noncontrast CT had overall sensitivity of 95% (95% CI 89–98%), specificity of 99% (95% CI 97–99.7%), and negative predictive value (NPV) of 99% (95% CI 97–99.6%). When CT was performed within 24 h of symptom onset, it had a sensitivity of 100% (95% CI 95–100%), specificity of 98% (95% CI 96–99.7%), and NPV of 100% (95% CI 98–100%). The authors conclude that modern CT scanners seem to have high sensitivity and specificity in the diagnosis of SAH when performed within 24 h of symptom onset. Beyond this point, CT seems to lack sensitivity and further investigation with LP is required.	The retrospective study design is always inherent to problems relating to proper record keeping. The authors included patients from two different databases. Some patient records did not contain information as to why LP was performed. Selection bias due to occasional poor record keeping was minimized by including these patients with few exceptions. The study also did not include patients who had CT performed for suspicion of SAH but for one reason or another had no LP performed after a negative CT scan.
Tung C, Lindgren A, Siemund R, et al. Emergency room decision-making for urgent cranial computed tomography: selection criteria for subsets of non-trauma patients. Acta Radiologica. 2014;55(7):847-54.	24060816	Retrospective Study	Low	To retrospectively evaluate these selection criteria in a general non-trauma population from a Swedish tertiary hospital, as well as in a nested subgroup that lacks guidelines at present, namely where the chief complaint was not headache, symptoms clearly indicating stroke, seizures, or vertigo.	The authors retrospectively evaluated a general non-trauma population from a Swedish tertiary hospital, as well as in a nested subgroup that lacks guidelines at present, namely where the chief complaint was not headache, symptoms clearly indicating stroke, seizures, or vertigo. Medical records of 346 patients from a general non-trauma population from a Swedish tertiary hospital(114 in the nested group) who had undergone urgent cranial CT were reviewed. Selection criteria as proposed by Rothrock (patient age >=60 years, presence of new onset focal neurologic deficit, headache with vomiting, or altered mental status) were used. Acute cerebral infarction, intracranial hemorrhage, malignancy, infection, cerebral edema, or hydrocephalus were considered significant findings.	The prevalence of significant findings was 10.1%. The Rothrock criteria had a sensitivity of 97.1% (identifying 34 of 35 significant findings) among all 346 patients and 100% (10/10) among the 114 patients in the subgroup and resulted in a potential scan reduction rate of 22.8% and 11.4%, respectively. In the patient with significant pathology, that was not selected for CT, focal neurological symptoms were not described as newly onset.	Although 100% sensitivity was not achieved, The 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, in the general population as well as in the subgroup defined above. Further research might validate patient history as a parameter.	Some limitations of this study include that 29 patients were excluded on the grounds of incomplete medical records. Quality of the medical documentation of neurologic examinations varied and the conclusion that neurologic signs had been ruled out may have based on incomplete description of patient's status. There may be a selection bias due to the fact that only patients that did undergo cranial CT were included, which may influence the results. There was no control group in this study, hence it is unknown how the criteria would have performed on patients suspected of having intracranial pathology but did not undergo an urgent cranial CT. Also retrospective design, no re-read of CT to confirm findings, no evaluation of the patients meeting the Rothrock criteria who did not receive imaging.
Vlak MH, Rinkel GJ, Greebe P, van der Bom JG, Algra A. Trigger factors and their attributable risk for rupture of intracranial aneurysms: A case-crossover study. Stroke. 2011; 42(7):1878-1882.	21546472	Case-Crossover Study	Low	To identify and quantify trigger factors for rupture of intracranial aneurysm (IA) and to determine their attributable risks.	Patients with aneurysmal subarachnoid hemorrhage (SAH) admitted in the Utrecht Stroke Center who were > 18 years of age. Aneurysmal SAH was defined as an abrupt onset of severe headache or loss of consciousness with or without focal neurological signs with subarachnoid blood proven by CT or lumbar puncture and radiologically proven IA. Only patients who completed the questionnaire themselves or with the help of a proxy were included.	Patients completed a structured questionnaire regarding exposure to 30 potential trigger factors in the period soon before subarachnoid hemorrhage (hazard period) and for usual frequency and intensity of exposure. Authors assessed relative risks (RR) of rupture after exposure to triggers with the case-crossover design comparing exposure in the hazard period with the usual frequency of exposure. The authors also calculated population-attributable risks.	A total of 250 patients were included in the study. Eight triggers were found to increase the risk for subarachnoid hemorrhage: coffee consumption (RR, 1.7; 95%CI, 1.2-2.4), cola consumption (RR, 3.4; 95%CI, 1.5-7.9), anger (RR, 6.3; 95%CI, 4.6-25), startline (RR, 23.3; 95%CI, 4.2-128), straining for defecation (RR, 7.3; 95%CI, 2.9-19), sexual intercourse (RR, 11.2; 95%CI, 5.3-24), nose blowing (RR, 2.4; 95%CI, 1.3-4.5), and vigorous physical exercise (RR, 2.4; 95%CI, 1.2-4.2). The highest population-attributable risks were found for coffee consumption (10.6%) and vigorous physical exercise (7.9%). The authors note that all triggers include a sudden and short increase in blood pressure, which seems a possible common cause for aneurysmal rupture.	The authors note that immediately after the SAH, patients are seriously ill and a considerable proportion never recover. This has resulted in an interval between the SAH and completion of the questionnaire of > 2 weeks for two-thirds of the patients. The retrospective assessment, the time lapse between SAH, and completion of the questionnaire and specifically asking for exposure in a prespecified period may have led to recall bias. Second, the inclusion of patients in relatively good clinical condition could have led to survival bias if certain triggers affect prognosis after SAH. A third limitation is the assumption of a 24-hour hazard period for alcohol.
Wang R, Liu R, Dong Z, et al. Unnecessary neuroimaging for patients with primary headaches. Headache. 2019; 59(1):63-68.	30136725	Prospective study	Low	To further verify that primary headache patients do not need neuroimaging, and thus reduce their burden.	The study evaluated 1070 consecutive patients (345 male, 40.05 ± 12.30 years) and 1070 healthy controls (345 male, 40.18 ± 12.46). The age of 2 groups did not significantly differ (P > .05). The types of headache exhibited by the participants included migraine (665, 62.15%), TTH (338, 31.59%), trigeminal autonomic cephalalgias (TACs; 51, 4.77%), and other primary headache disorders (16, 1.50%). The 129 patients with "red flags" shown in the CDSS were excluded from this study.	The primary headache patients were diagnosed by computerized clinical decision support systems, and re-diagnosed by a specialist. All participants were assessed with either computed tomography or magnetic resonance imaging (MRI) scans. The neuroimaging findings were classified as significant abnormalities, non-significant abnormalities, or normal.	All the significant abnormalities were found using MRI scans. Significant abnormalities were identified in 4 primary headache patients (0.58%) and 5 healthy controls (0.73%); the rate of significant abnormalities was not significant different between both groups (P > .05). The authors conclude that the present study found that neuroimaging was unnecessary for the primary headache patients.	First, the healthy controls in the study observed by themselves that they had no headache history. Second, there was a small number of TACs and other primary headaches such as retinal migraine, primary cough headache, and paroxysmal hemicranias. Third, because of reducing to perform neuroimaging examination for headache patients, the misdiagnosis rate and relevant indirect cost such as a cost for delayed diagnosis including additional disability and death would be improved. There was not further consideration in this study. Fourth, whether or not these primary headache patients would get additional benefits from the contrast MRI and MRA was not considered in this study.

Wu, WT, Pan HY, Wu KH, et al. The Ottawa subarachnoid hemorrhage clinical decision rule for classifying emergency department headache patients. Am J Emerg Med. 2020; 38(2):198-202.	30765279	Retrospective Study	Low	To assess the performance of the Ottawa subarachnoid hemorrhage (PSAH) rule in emergency department (ED) headache patients and evaluate its impact on the diagnosis of intracranial hemorrhage (ICH) and other intracranial pathology (ICP).	A total of 913 patients with acute headache with onset within 14 days of the ED visit, were included. The authors excluded patients with head trauma that occurred in the previous 7 days, new onset of abnormal neurologic findings, or consciousness disturbance. The mean age was 46.4 ± 17.9 years; 58.1% were older than 40 years, and 36.5% were male.	A review of health records of consecutive patients presenting with a headache was conducted. The chart data were reviewed and abstracted independently by two emergency physicians. In order to avoid bias by the abstractors, the two emergency physicians were blinded to the study objectives. According to the OSAH rule, patients with any included predictors required further investigation. Authors defined headache secondary to SAH or ICP based on a new neuroimaging finding, such as brain magnetic resonance imaging (MRI), CT, cerebrospinal fluid study, or diagnosed by a neurologist at hospital discharge. The primary outcome was the diagnosis of SAH, and the secondary outcomeswere CT use in the ED, time to CT ordered, and final diagnosis of headache secondary to other ICH and ICP.	Of 913 patients included, 15 of them were diagnosed with SAH. The OSAH rule had 100% (95% CI, 78.2%–100%) sensitivity and 37.0% (95% CI, 33.8–40.2%) specificity for identifying SAH. Twenty-two cases were identified as SAH or ICH with 100% sensitivity (95% CI, 84.6%–100%) and 37.3% (95% CI, 34.1%–40.5%) specificity. As for non-hemorrhagic ICP, both the sensitivity and negative predictive values (NPV) decreased to 75.0% (95% CI, 53.3%–90.2%) and 98.2% (95% CI, 96.1%–99.3%), respectively. The authors conclude that the OSAH rule had 100% sensitivity and NPV for diagnosing SAH and ICH with acute headache. The sensitivity and specificitywere lower for non-hemorrhagic ICP. The OSAH rule may be an effective tool to exclude acute ICH and SAH in our setting.	First, although the study contained a fair number of patients, authors collected data from a single teaching hospital; therefore, this may limit the generalizability of findings to other ED settings. Second, due to the retrospective methods of reviewing of themedical chart records, there is a possibility that patients may not have been included in the study if the symptoms/signs were not recorded. Third, authors selected patients with the chief complaint of headache based on the ICD code, hence, if the coding was not carried out accurately, some patients may have been missed. Fourth, due to the limitations of retrospective studies, in general, the authors could not exercise control over all possible confounding factors.
Xie H, Zhang Q, Huo K, et al. Association of white matter hyperintensities with migraine features and prognosis. BMC Neurol. 2018; 18(1):93.	29966519	Prospective study	Low	To examine the correlation of WMHs with migraine features and explore the relationship between WMHs and migraine prognosis.	A total of 69 migraine patients (52 females and 17 males, average age: 33.6 years old) were consecutively recruited from the Headache Clinic of the Department of Neurology, The First Affiliated Hospital of Xi'an Jiaotong University from February 2012 to November 2016. Inclusion criteria included: (1) patients with migraine who fulfilled the International Classification of Headache disorders (ICHD)-3 (β) criteria [1]), and (2) age between 12 and 55 years old. Exclusion criteria: (1) patients with major neurological diseases, (2) patients with major systemic diseases, (3) patients with thyroid diseases, (4) pregnant and/or lactating patients, and (5) patients with claustrophobia.	Patients underwent MRI scans to evaluate WMHs. Migraine features were compared between patients with and without WMHs. After an average follow-up period of 3 years, these patients were divided into two groups, according to the reduction of headache frequency: improved and non-improved groups. The percentage and degree of WMHs were compared between these two groups.	total of 24 patients (34.8%) had WMHs. Patients with WMHs were significantly older (39.0 ± 7.9 vs. 30.6 ± 10.4 years, P < 0.001) and had a longer disease duration (median: 180.0 vs. 84.0 months, P = 0.013). Furthermore, 33 patients completed the follow up period (15 patients improved and 18 patients did not improve). Patients in the non-improved group had a higher frequency of WMHs (55.6% vs. 13.3%, P = 0.027) and median WMHs score (1.0 vs. 0.0, P = 0.030). The authors conclude that WMHs can predict unfavorable migraine prognosis. Furthermore, WMHs may have a closer association with age than migraine features.	The relatively small number of enrolled patients is considered to be the main limitation. Furthermore, the absence of a control group precluded definitive conclusions about the nature of the observed alterations in WMHs or whether their degree is beyond normal aging. Age should be controlled in the design of the study. Thus, future work should focus on investigating the implication of WMHs among relatively young migraine patients. Similarly, the heterogeneity of the patient cohort such as migraine with and without aura, episodic migraine and chronic migraine, should be improved. Different migraine types possibly have different effects on the prognosis. The relatively low migraine frequency at baseline in our study is also a major limitation as prognostic information may be of greater value in high frequency migraine states.