Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Author & Year: Cull, 1995[175] **Study design:** Retrospective **Setting:** Neurology outpatient clinics, UK and Holland **Duration of follow-up:** N/A	**Patient group:** Patients with migraine with or without aura. **Inclusion criteria:** Patients presenting with 1st attacks of migraine with or without aura after the age of 40. **Exclusion criteria:** NR **All patients** **N:** 69 **Age of onset (mean, SD):** 51.6 (8.9) **F/M:** 46 (66.6%)/ 23 (33.3%) **Migraine with aura:** 59/69 (86%) **Migraine without aura:** 10/ 69 (14%) **Family history of migraine**: 15/69 (22%)	**All patients** Clinical and investigation data were collected on patients at neurology outpatients clinics between 1988 and 1994. Participating physicians were asked to record patient history clinical examination and non invasive investigations. CT or MRI was performed in all cases and where possible Doppler US. Clinical neurological examination was normal in 65 cases (94%) CT scanning carried out on 67 patients. MRI scanning in 2 patients.	**Arterio- venous malformations** (n)	0/65	**Funding:** NR **Limitations:** Only includes patients with migraine. **Additional outcomes:** Routine haematology and auto-antibodies were assessed. **Notes:** Carotid Doppler US studies carried out in 38 patients. 1 patient had MS. 1 patient had migraine related to head injury. Patients had CT or MRI.
			Tumours (n)	0/65	
			Abnormal CT (n)	5/67 (7.69%) 1 moderate atrophy (MS) 4= 1 or more cerebral infarctions	

Abbreviations: NR=not reported, NA=not applicable, M/F=male/female, N=total number of patients randomised, SD=Standard deviation, SE=Standard error, ITT=Intention to treat analysis

Study Details	Patients	Interventions	Outcome measures	Effect size	Comments
Author & Year: Demaerel et al, 1996[190] **Study design:** Retrospective **Setting:** Department of radiology, University hospital, Belgium. **Duration of follow-up:** N/A	**Patient group:** Patients complaining of headache **Inclusion criteria:** Normal clinical neurological examination **Exclusion criteria:** Patients with dizziness, vertigo, migraine and epilepsy. **All patients** **N:** 363 **Age (mean, range):** 35 (3-83) **Drop outs:** N/A **F/M:** 212 (58.4%)/ 151 (41.6%)	**Group 1** Consecutive patients with chronic headache examined by cranial CT before and after intravenous contrast enhancement. Patients divided into 3 groups: **Group 1 -** (321/ 363) normal CT findings **Group 2 -** (31/363) patients with non significant abnormalities **Group 3 -** (11/363) significant abnormality. All had a space occupying lesion. MRI undertaken in 8/11 patients in this group.	**Tumour / neoplasm**	9/363 (2.18%) **Meningioma:** 4 **Multiple metastases** (originating from an oat cell carcinoma in the lung): 1 The following patients were treated surgically and pathological findings were: **Oligodendrioma** (grade 2): 1 **Astrocytoma** (grade 3): 1 **Ganglioma**: 1 **Undifferentiated carcinoma with neuroendocrine features**: 1	**Funding:** NR **Limitations:** Patients with migraine excluded. In 2 patients a developmental venous anomaly on CT could not be confirmed. One patient had a developmental venous anomaly that could be seen on MRI but not on CT. Unclear on what basis patients in group 3 were referred for MRI. **Additional outcomes:** NR **Notes:** Intraventricular cysts recorded as significant abnormality. An additional brain MRI requested in 29/363 (8%) patients. Additional MRI carried out in 8/11 patients in group 3. CT was carried out both with and without contrast material, some patients had MRI.
			Intraventricular cyst	2/363 (0.55%)	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Author & Year: Grimaldi et al, 2009[342] **Study design:** Prospective cohort **Setting:** 8 emergency departments (ED) in northern Italy **Duration of follow-up:** 3 months after emergency department admission	**Patient group:** Adults >18 with headache **Inclusion criteria:** Patients >18 years presenting to ED with headache as the chief complaint. **Exclusion criteria:** Head trauma in previous 30 days, complaint of visual aura not followed by headache and re-admission to ED after recruitment into the study. **All patients** **N:** 120* **Age (mean):** 40 (14) **Drop outs:** 17 (14.1%) **F:** 77 (64.2%)	Detailed history and examination of the patient, ED physician assigned patient to 1 of 4 clinical scenarios to each patient. An indeterminate clinical scenario was used if the patient did not fit one of the 4 scenarios or if they met the criteria for more than 1. Once the scenario was assigned physician was suggested to follow the recommended diagnostic procedures (previously published) but physician was free to select best care for patient. Scenario 1, 2 and 3: classified as malignant headaches Adult patients admitted to ED for severe headache (acute onset, focal signs, fever/ neck stiffness, progressively worsening). Scenario 4: classified as benign headaches (previous history of headache- complaining of a headache very similar to previous in terms of intensity, duration and associated symptoms). There was also an indeterminate group, which either fitted more than one of the 4 scenarios, or did not match any of them. Head CT scan without contrast with 3mm slices through posterior fossa of brain and a follow up structured telephone interview by a neurologist expert in headache management at least 3 months after ED admission.	**Serious abnormalities**	0/103	**Funding:** NR **Limitations:** Only 80/120 patients assigned to scenario 4 were included in the analysis, stated that 17 dropped out. Discrepancy in numbers. There was an indeterminate group- unclear whether these should be included. Does not state type of primary headaches that included patients diagnosed with. **Additional outcomes:** N/A **Notes:** *256 included, but only looking at scenario 4 therefore n=120. Head CT scan assessed by a trained neuroradiologist. Interviewer was unaware of scenario assignment by ED physician at recruitment. Interview performed using a structured questionnaire.

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Author & Year: Jordan et al, 2000[406] **Study design:** Retrospective **Setting:** Long beach memorial medical centre, USA **Duration of follow-up:** N/A	**Patient group:** Patients presenting for MRI of headache at institution over a 3 year period **Inclusion criteria:** NR **Exclusion criteria:** Patients with focal findings on physical examination, prior brain surgery, head trauma or immunocompromise. **All patients** **N:** 328 **Age (mean):** 42 (6-84) **M/F:** 106 (32.3%)/ 222 (67.7%) **Drop outs:** N/A	Patients had MRI for headache. Patients categorised as: Group 0= negative study, (n-163) Group 1= positive study without any significance, (n=158) Group 2= positive study with clinically significant result. (n=5)	**Tumour / neoplasm** **Arteriovenous malformations** **Cysts**	1/ 328 (0.30%) (low grade glioma) 1/328 (0.30%) (dural) 9/328 (2.74%) (7 arachnoid, 2 pineal)*	**Funding:** NR **Limitations:** Unclear if patients previously had CT. Unclear whether study includes secondary headaches. -Does not state what type of primary headache the patient is diagnosed with. **Additional outcomes:** Referral speciality and motivation for referral for imaging. **Notes:** Discrepancy between total included in study(n=328), and group totals (n=326) *cysts were considered as group 1 as they were small and had a lack of mass effect.

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Study Details	Patients	Interventions	Outcome measures	Effect size	Comments
Author & Year: Sempere et al, 2005[712] **Study design:** Prospective **Setting:** Neurology clinics, Spain. **Duration of follow-up:** At least 3 months	**Patient group:** >15 years with non-acute headache **Inclusion criteria:** Consecutive patients >15 years attending neurology clinic with non acute headache as main symptom. Defined as any headache which began at least 4 weeks before. Referred by family physician working in the health area. **Exclusion criteria:** Patients with facial pain alone and pregnant women. **All patients** **N:** 1876 **Age (mean, range):** 38 (15-95) **F/M:** 1243 (66.3%)/ 633 (33.7%) **Drop outs:** NR **Migraine:** 919 /1876 (49%)* **TTH**: 664/1876 (35.4%)* **Cluster:** 21/1876 (1.1%)* **Indeterminate:** 203/1876 (10.8%)* **New-onset headache:** 629 (33.5%) **Headache for >1 year:** 1247 (66.5%) **Normal neurological examination:** 1857 (99.2%) **CT scan:** 1432/ 1876 (76.3%) **MRI:** 580/ 1876 (30.9%)	Every patient received CT or MRI- choice made on individual basis. MRI performed with 1.5-T imagers (sagital and axial T1 weighted and axial T2 weighted imaging with 6mm thickness. CT studies performed with high resolution scanners- slice thickness was 5mm in posterior fossa and 10mm in the supratentorial cavity. Choice of contrast medium made on individual basis by radiologist. Neuroimaging results classified as significant abnormalities, non-significant abnormalities or normal. MRI performed after a normal CT if patient's headache did not respond to treatment or in patients with abnormalities on CT to improve their diagnosis.	**Tumour / neoplasm**	7/1857 (0.37%) (3 pituitary adenomas, 1 low grade astrocytomas, 2 meningioma, 1 brain stem glioma) 1 new onset common migraine, 1 indeterminate type headache, 1 history of episodic cluster headache	**Funding:** NR **Limitations:** MRI carried out in 119 patients with normal CT and revealed 1 meningioma and 1 acoustic neurinoma. Unclear why MRI carried out in this subgroup and whether results reported with main results. Dropouts NR **Additional outcomes:** Likelihood ratios for a significant abnormality on neuroimaging. **Notes:** Radiologist who performed evaluation of CT and MRI did not access patients' clinical history. Results from patients with normal neurological examinations only.
			Hydrocephalus	2/1857 (0.11%) 1 had history of episodic migraine, 1 had chronic indeterminate type headache	
			Arteriovenous malformation	1/1857 (0.05%) Episodic migraine for previous 6 years	
			Cyst	2 /1857 (0.11%) (1 colloid, 1 arachnoid) 1 chronic indeterminate and 1 new onset migraine	
			Stroke	1 /1857 (0.05%) (acute stroke) New onset headache of indeterminate type.	

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Author & Year: Tsushima & Endo, 2005[805] **Study design:** Retrospective **Setting:** Department of radiology, Japan. **Duration of follow-up:** N/A	**Patient group:** Adults with chronic or recurrent headache **Inclusion criteria:** Chief complaint of chronic or recurrent headache with duration of 1 month or more. No other neurologic symptoms or focal findings on examination, no prior head surgery, head trauma, or seizure. **Exclusion criteria:** NR **All patients** **N:** 306 **Age (mean, SD):** 54.2 (15.2) **Drop outs:** N/A **M/F:** 136 (40%)/170 (50%)	All patients underwent examination with MR imager. Transverse T1 weighted spin echo, proton density weighted and T2 weighted fast spin echo image were obtained. Section thickness was 5mm with a gap of 2.5mm for all sequences.. Contrast material enhanced transverse T1 weighted images were obtained by using gadopentetate dimeglutamine if a more detailed examination was recommended by the patient's physician or demanded by the patient. MR imaging results were divided into 3 groups: those with no abnormality, those with minor abnormality, those with clinically important intracranial abnormality	**Tumour / neoplasm** **Subdural haematoma**	1 /306 (0.33%) (pituitary macroadenoma) 1 /306 (0.33%)	**Funding:** NR **Limitations:** 23 patients underwent repeat MRI scans due to patient demand-no abnormality found in any scan. Does not state type of headache that included patients were diagnosed with. **Additional outcomes:** N/A **Notes:** All MRI images were interpreted by one of the authors with 15 years experience as a general radiologist. The images were not reinterpreted for this study.

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Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Author & Year: Wang et al, 2001[836] **Study design:** Retrospective **Setting:** Patients referred to department of radiology, New York, USA. **Duration of follow-up:** N/A	**Patient group:** Adults referred for MRI evaluation of headache. **Inclusion criteria:** Primary complaint of headache with a duration of 3 months or more who have had an evaluation by the neurology service. **Exclusion criteria:** Other neurologic symptom **All patients** **N:** 402 **Age (range):** 18-85 **Drop outs:** N/A **M/F:** 116 (28.9%)/ 286 (71.1%) **Migraine:** 161/402 **TTH:** 71/402 **Mixed:** 27/402 **Atypical:** 64/402 **Other:** 79/402	Sagittal T1 weighted, axial proton density weighted and axial T2 weighted images were obtained. In 84 patients, iv gadolinium-based contrast material was administered and additional axial and coronal images were obtained. MRI findings categorised as negative or positive for major abnormality.	**Tumour / neoplasm**	4 /402 (1%) (1 glioma, 1 meningioma, 1 pituitary macroadenoma, 1 metastases) All had atypical headache	**Funding:** NR **Limitations:** Paper also includes patients with secondary headaches, but separates results for primary headache. **Additional outcomes:** N/A **Notes:** Abnormality defined as major if it was a mass, caused mass effect or was believed to be the likely cause of the patient's headache.
			Cyst	2 /402 (0.5%) (1 petrous apex cholesterol cyst, 1 large arachnoid cyst) 1 had migraine 1 had atypical headache	
			Arteriovenous malformation	1/402 (0.25%) Atypical headache	
			Subdural haematoma	1/402 (0.25%) Atypical headache	
			Hydrocephalus	3/402 (0.75%) 2 had atypical headache 1 tension type headache	

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