Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Author & Year: Pfaffenrath et al, 1994[626] **Study design:** RCT **Comparison:** Antidepressant vs Placebo **Setting:** NR (7 study centres in 3 countries (4 in Germany, 1 in Austria and 2 in Switzerland) **Duration of follow-up:** 24 weeks	**Patient group:** Adults meeting IHS criteria for chronic tension type headache. **Inclusion criteria:** Female and male patients aged 18–65 years; IHS criteria for tension type headache; headache present on more than 15 days/month for at least 6 months. **Exclusion criteria:** Accompanying migraine; Participation in a study in previous three months; Suspected poor compliance; Pregnant/breastfeeding women; Drug abuse and psychiatric illness; Patients taking simple analgesics, mixed analgesics, ergotamine tartrate or dihydroergotamine tartrate, acetylsalicylic acid and/or paracetamol or codeine on more than 10 days/month, other antidepressants, neuroleptics, tranquilisers, established headache prophylactics (β blockers or calcium channel blockers) less than 3 months before baseline phase, drugs for treatment of bipolar affective disorders (lithium and carbamazepine); Use of medications leading to headache as side effect; Contraindications for tricyclic antidepressants; Impaired renal function; Hepatic failure and haematological disorders. MAO inhibitors had to be discontinued within 4 weeks prior to the beginning of study. All patients on prophylactic treatment for TTH required a wash-out phase of 2 weeks before the beginning of baseline phase. **All patients** **N:** 211 (available for evaluation); 197 (received study treatments 110 F, 87 M) **Age (mean):** NR **Drop outs:** 14 (in baseline period due to non-attendance,	**Group 1 Amitriptyline** 25 mg tablets **Group 2 Placebo** **Both groups**: 4 week baseline period (no treatment medication given), 12 week treatment period and follow up period of 8 weeks. 1 tablet in weeks 5-8 2 tablets in weeks 9-12 2 or 3 tablets in weeks 13-16. Doses were increased only if the previous lower dose had been well tolerated. Patients kept a daily headache diary throughout the study to record the frequency and duration of headache.	**Change in patient-reported headache days** (Final values mean ± SD in last 4 weeks of therapy)	**Group1:** Baseline 16±8 Final 15±10 **Group 2:** Baseline 15±8 Final 16±9	**Funding:** NR **Limitations:** Unclear randomisation, allocation concealment and blinding. Patients with suspected poor compliance excluded but no reason given. **Additional outcomes:** Change in mean duration of headache per day. Response rate defined as at least 50% reduction of the product of duration x frequency of headache and at least 50% reduction in headache intensity after 16 weeks as compared to baseline. **Previous medication tried:** NR **Notes:**
			Change in patient-reported headache intensity VAS 0=no pain to 8=unbearable pain (Final values mean ± SD in last 4 weeks of therapy)	**Group1:** Baseline 3.7±1.9 Final 2.8±2.0 **Group 2:** Baseline 3.4±1.5 Final 1.7±2.0	
			Incidence of adverse events % reporting moderate to severe adverse events	**Group1:** 73.1% (48/67) **Group 2:** 57.8% (37/64)	

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	language difficulties or accompanying migraine) **Group 1 Amitryptiline** **N:** 67 (ITT) **Age (mean):** NR **Drop outs:** 18/67 (26.9%)[19.4% poor compliance, 7.5% lack of efficacy, 17.9% side effects] **Group 2 Placebo** **N:** 64 (ITT) **Age (mean):** NR **Drop outs:** 13/64 (20.3%) [17.2% poor compliance, 12.5% lack of efficacy, 10.9% side effects]				Three armed study looking at amitriptylinoxide, amitriptyline and placebo. Amitriptylinoxide data not reported here.

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, MAO=Monoamine Oxidase, TTH=Tension type headache