

# Drugs for headaches



# Drugs that cause headaches

Amitriptyline,  
imipramine  
ASA, acetaminophen  
(frequent use)  
Benzodiazepines  
Nitroglycerine  
MAOIs  
Metoclopramide  
Estrogen  
Sulphonamides  
Theophylline  
NSAIDS  
Fluoxetine

Withdrawal of:  
Benzodiazepines  
Caffeine Ergotamine  
Methysergide  
ASA, APAP ( $\pm$ codeine)  
some antihypertensives

# Aspirin for migraine

Migraine headache pain will be reduced from moderate or severe to no pain by 2 hours in approximately 25% of people taking a single dose of 1000 mg of aspirin, compared with about 10% taking placebo. CD008041

Migraine headache pain will be reduced from moderate or severe to no worse than mild pain by 2 hours in roughly 50% of people taking a single dose of 1000 mg of aspirin compared with approximately 33% taking placebo. CD008041

# ASA vs sumatriptan vs ibuprofen vs placebo for acute migraine

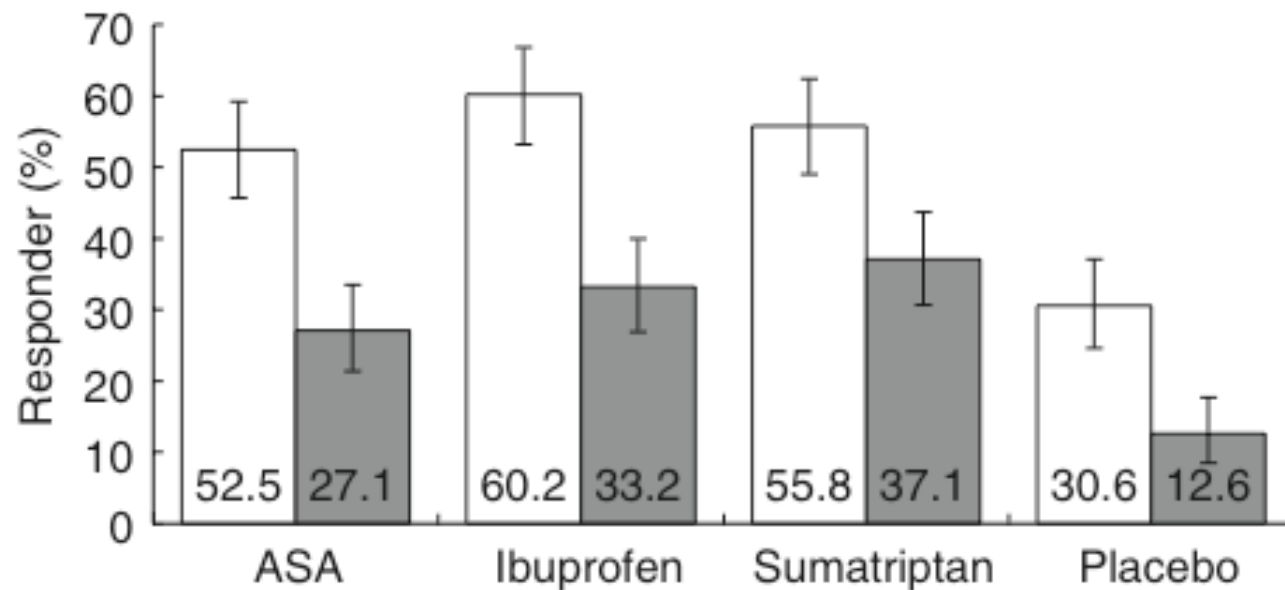
## **Patients**

312 patients - cross-over DB RCT - mean age 38, 81% women, severe headaches (45%)

## **Treatment**

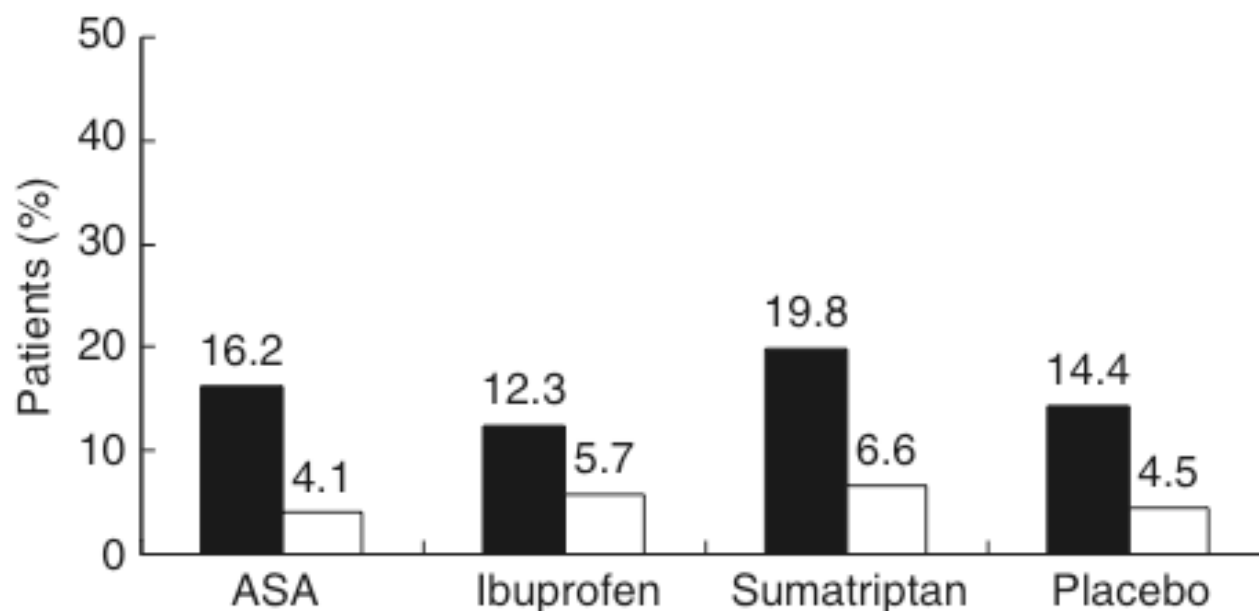
effervescent ASA (1000 mg), sumatriptan (50 mg), ibuprofen (400 mg), or placebo

Cephalalgia 2004;24: 947–54



**Figure 1** Percentage of ITT patients (responders, mean and 95% confidence intervals) with reduction in headache severity from severe or moderate to mild or no pain at 2h (□) and percentage of patients (responders) pain-free at 2h (■). All active drugs are superior to placebo.

# Adverse events



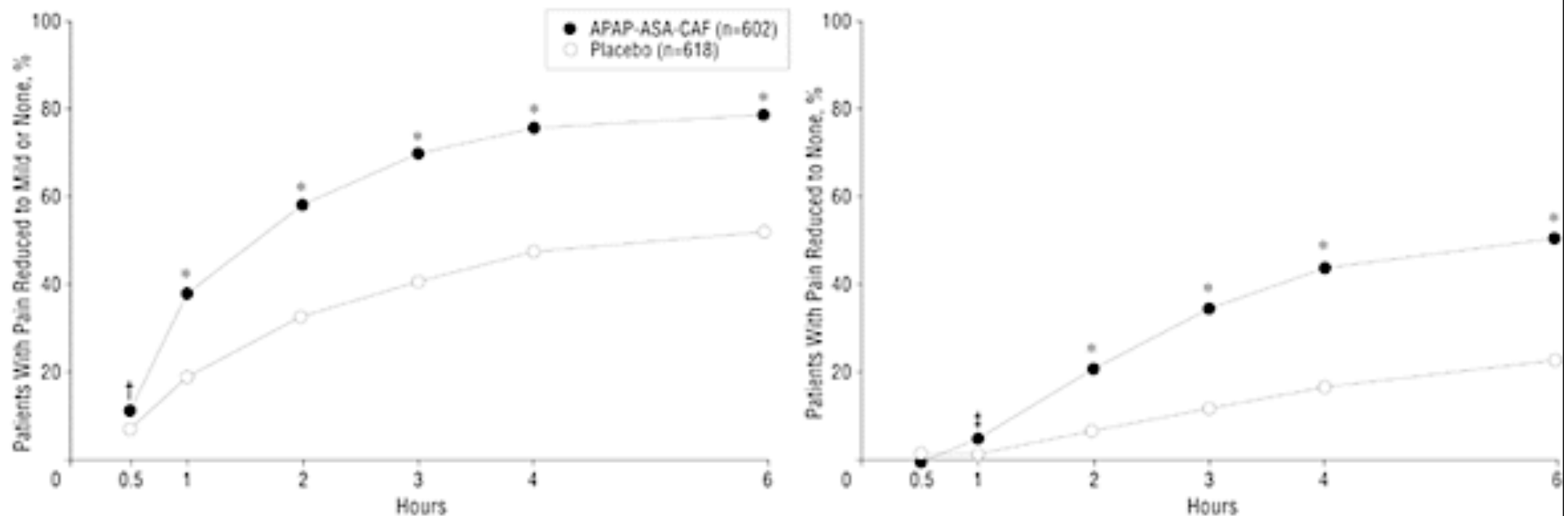
**Figure 5** Adverse events (safety population,  $n = 313$ ). Total adverse events (■); drug-related adverse events (□) were investigator attributed.

Stats and type of AE  
not reported

Cephalalgia 2004;24: 947–54

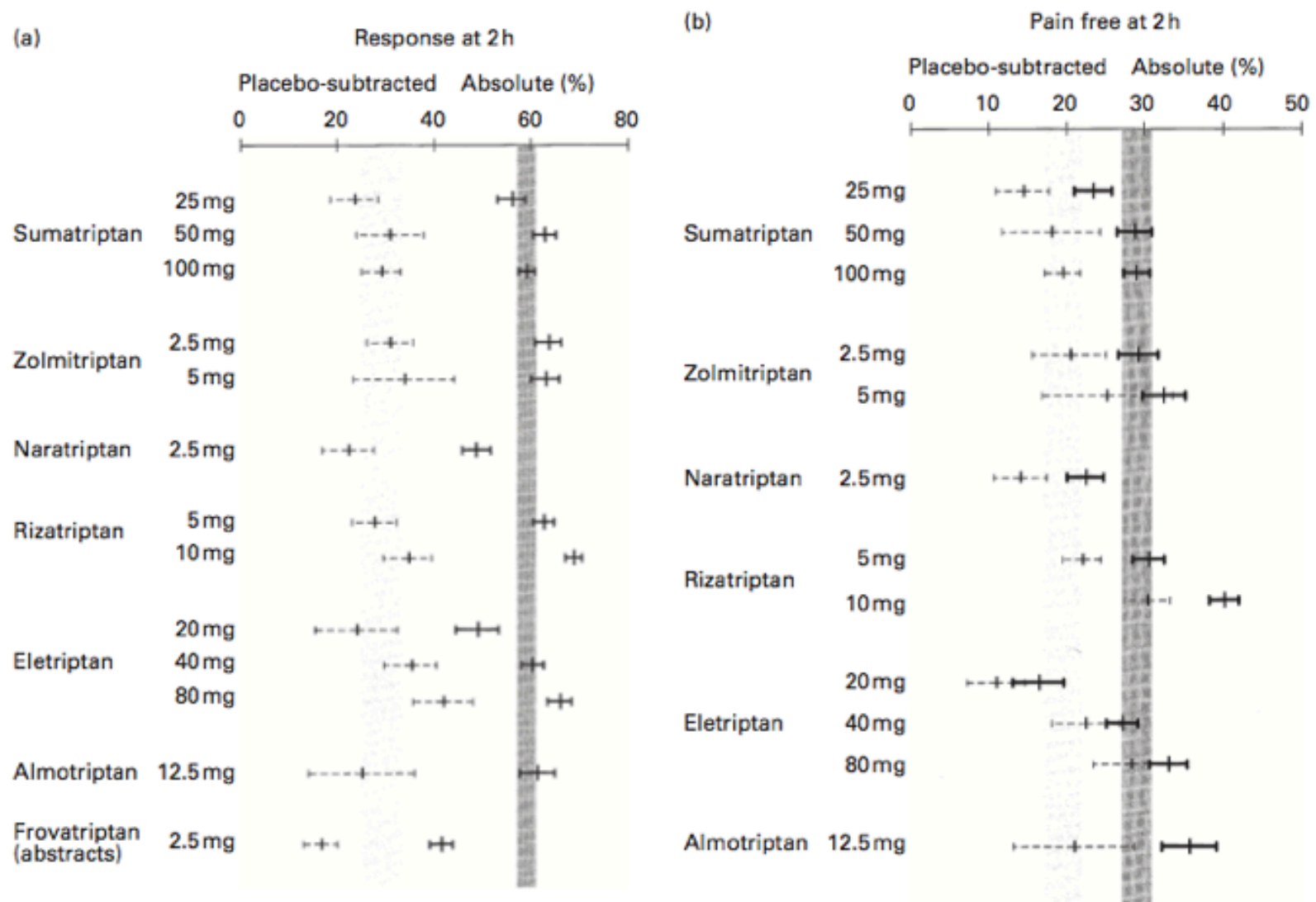
500 mg aspirin/500 mg acetaminophen/130mg caffeine  
or placebo

1220 patients with moderate “migraine”



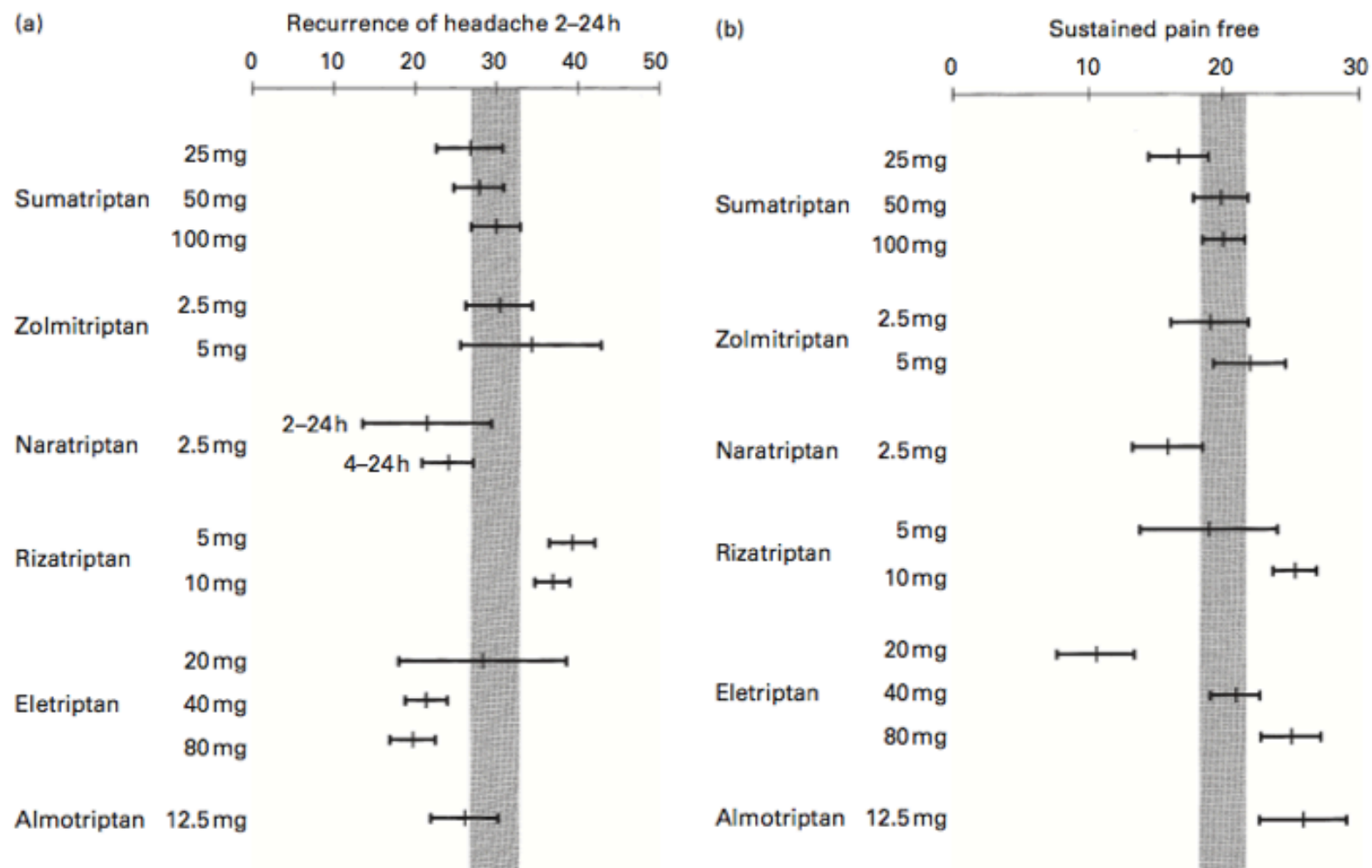
Percentage of patients with pain intensity reduced to mild or none (left) or to none (right)

Arch Neur 1998;55:210-7



**Figure 2** Data (mean and 95% confidence intervals) for headache response at 2 h (a) and pain free at 2 h (b) are shown for each triptan. Absolute and placebo subtracted outcomes are presented with the hatched region being the 95% confidence interval envelope for sumatriptan 100 mg.





**Figure 3** Data (mean and 95% confidence intervals) for headache recurrence from 2 h to 24 h (a) and sustained pain free (b) are presented with the hatched region being the 95% confidence interval envelope for sumatriptan 100 mg. For naratriptan the recurrence rate is given for the time period 4-24 h post-dose (as presented in the original publications) and for 2-24 h post-dose (after recalculating the data).

# Triptan AEs

“tingling, paraesthesias, and warm sensations in the head, neck, chest, and limbs; less frequent are dizziness, flushing, and neck pain or stiffness”

Much rarer ‘central nervous system (CNS) AEs  
“asthenia, abnormal dreams, agitation, aphasia, ataxia, confusion, dizziness, somnolence, speech disorder, thinking abnormal, tremor, vertigo, and other focal neurological symptoms) and notably the ‘chest- related AEs’ (chest pressure, chest pain, radiating pain in arm, other chest feelings, heavy arms, shortness of breath, palpitations, and anxiety)”

# Triptan dosage forms

## Oral

sumatriptan, zolmitriptan, naratriptan,  
rizatriptan, almotriptan, eletriptan,  
frovatriptan

## Nasal spray

sumatriptan, zolmitriptan

## Subcutaneous inj

sumatriptan

# Dihydroergotamine

Can be used SC, IM, IV

more nausea but less chest pain than the triptans

## An approach for migraines

Mild - NSAID/acetaminophen/caffeine  
+/- metoclopramide

If no effect in an hour - triptan

If no effect in a couple of hours -  
narcotic

# Who is a candidate for prophylaxis?

Recurring migraines which significantly interfere with daily routines, despite acute treatment

Frequent headaches

Contraindication to, failure of, or overuse of acute treatments

Adverse effects with acute treatments

Patient preference

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# Effects of starting prophylactic therapy

During 6-12 mos following initiation of prophylaxis:

Office visits ↓ 51%

ED visits ↓ 82%

CT scans ↓ 75%, MRIs ↓ 88%

21% ↓ triptan utilization

Triptan cost/month ↓ \$48 - \$132

# Principles of Prevention

Avoid trigger factors

- Oral contraceptives

Use lowest effective doses

May take 2-4 months for effect

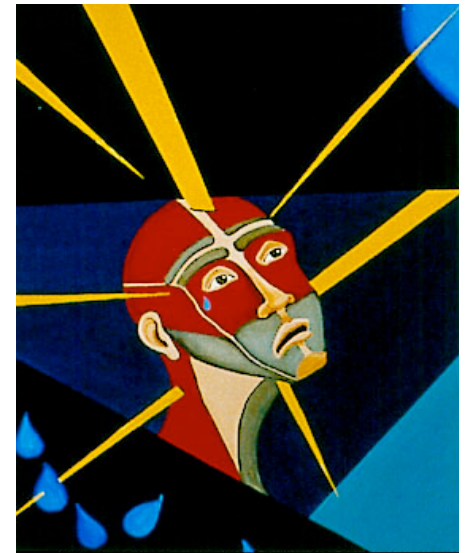
Educate (mechanism, goals, likely adverse effects)

Discuss expectations

- frequency vs. severity

Design formal management plan (including rescue plan)

Headache diaries (frequency, severity, duration, disability, treatment response, adverse effects)



Loneliness, Pain, Tears. Denise Auger

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All agents below have demonstrated efficacy superior to placebo in randomized trials of appropriate duration:

Propranolol 80-240mg/d, Nadolol 80-240mg/d, Atenolol 100mg/d, Timolol 20-30mg/d, Metoprolol 200mg/d, Bisoprolol 5mg/d

Flunarizine 10mg/d, Verapamil 240mg/d

Methysergide 6mg/d, Pizotifen 1.5-6 mg/d

Naproxen 500 mg/d, Flurbiprofen 200 mg/d, Fenoprofen 1800 mg/d, Mefenamic acid 1500 mg/d, Ketoprofen 150 mg/d, ASA 500-650mg/d

Amitriptyline 30-150mg/d, Fluoxetine 20 qOd – 40mg/d

Valproic Acid / Divalproex 500-1500 mg/d, Topiramate 25-325 mg/d, Gabapentin 900-2400 mg/d

Riboflavin (B2) 400 mg/d, Magnesium 400-600 mg (16-24mmol)/d, Feverfew 50-82 mg/d, Histamine 1mg SC 2x weekly

Lisinopril 20mg daily, Bromocriptine 2.5 mg tid (menstrual), Naratriptan 1 mg bid (menstrual), Estradiol 1.5 mg/d via gel x 7 days (menstrual), Botulinum toxin A?

# The Bottom Line on Prevention

**RESPONSE** =  $\geq 50\%$  reduction in headache severity, frequency, or duration (usually assessed at 3 mos)

Across all high-quality trials, **24%** will have response to placebo, **45%** respond to drug  
each patient's chance of response with drug:

either “**50/50**” or

“**1 in 5**” depending on whether you are comparing to doing “nothing” or giving placebo.