

# Refractory Headache: when standard management falls short?

**Bethany Hill**

Advanced Nurse Practitioner and Lead Nurse

Headache and Facial Pain

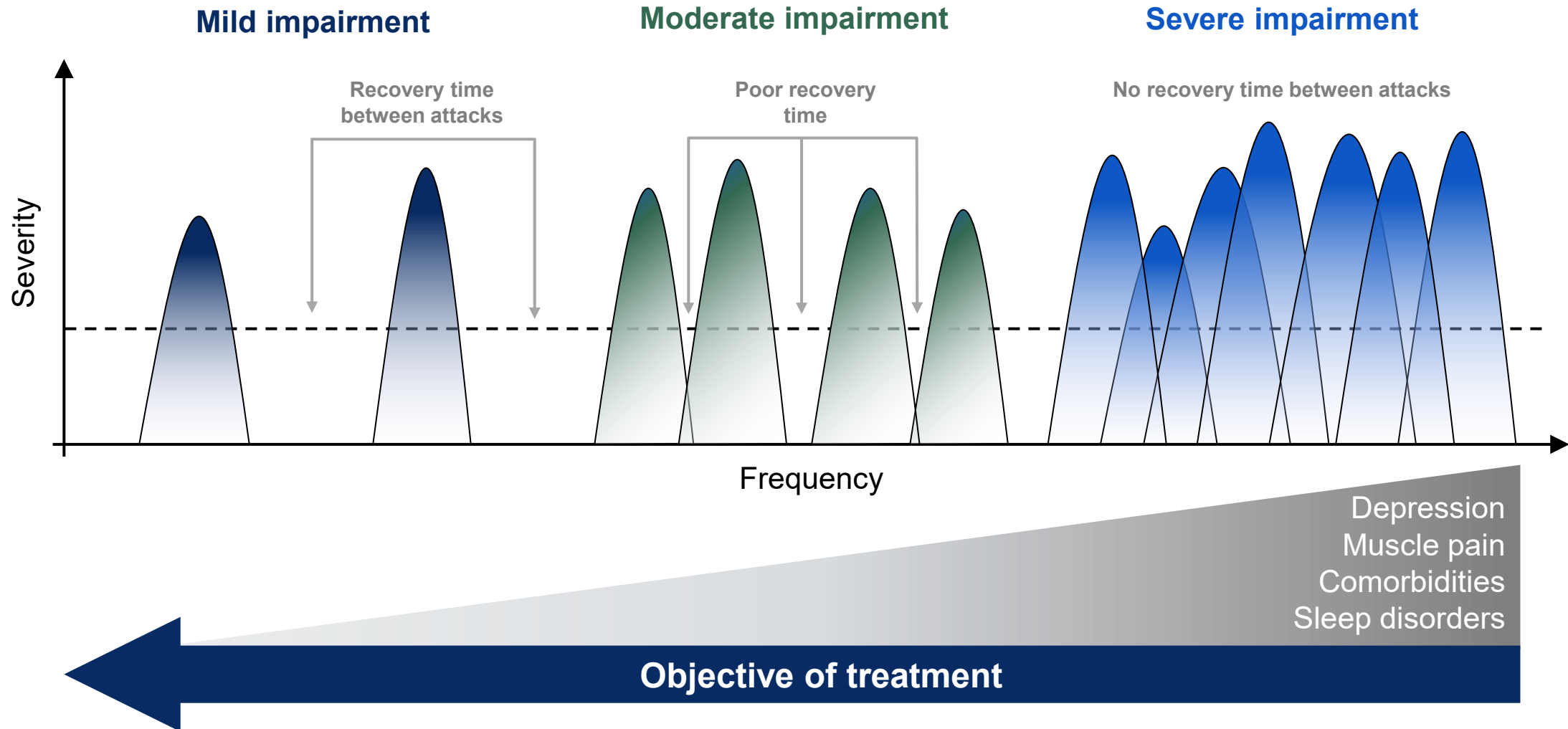
Guy's and St Thomas' NHS Foundation Trust

# Disclosures

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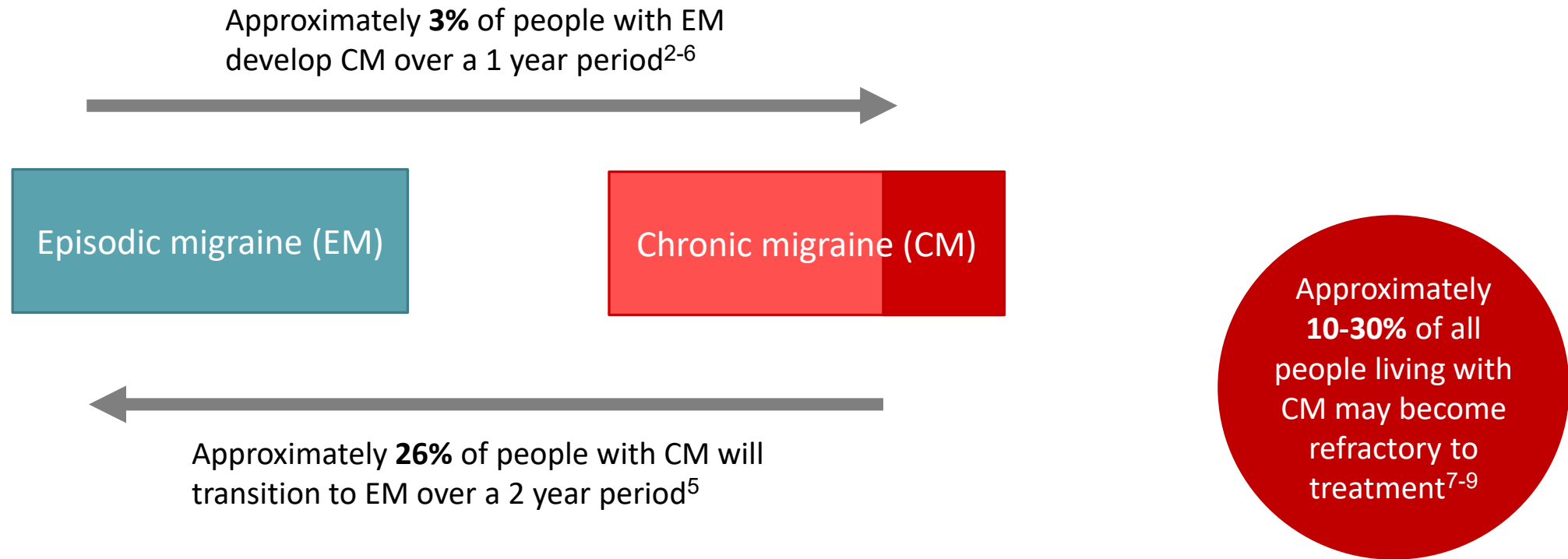
- Received honoraria for oral presentation from:
  - Teva
  - Organon
  - Lundbeck
- Advisor fees for attending a meeting:
  - Pfizer
  - Lundbeck
  - AbbVie
- Received travel fees or reimbursements from:
  - AbbVie
  - Lundbeck
  - eNeura<sup>®</sup>
- Honorary advisor to the British Association of the Study of Headache (BASH) Council (2023 – present)

# Migraine 'chronification'



# Migraine progression

Migraine progression is not linear and fluctuates with individuals<sup>1</sup>



## Potential negative predictors for response to standard management

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Medication Overuse

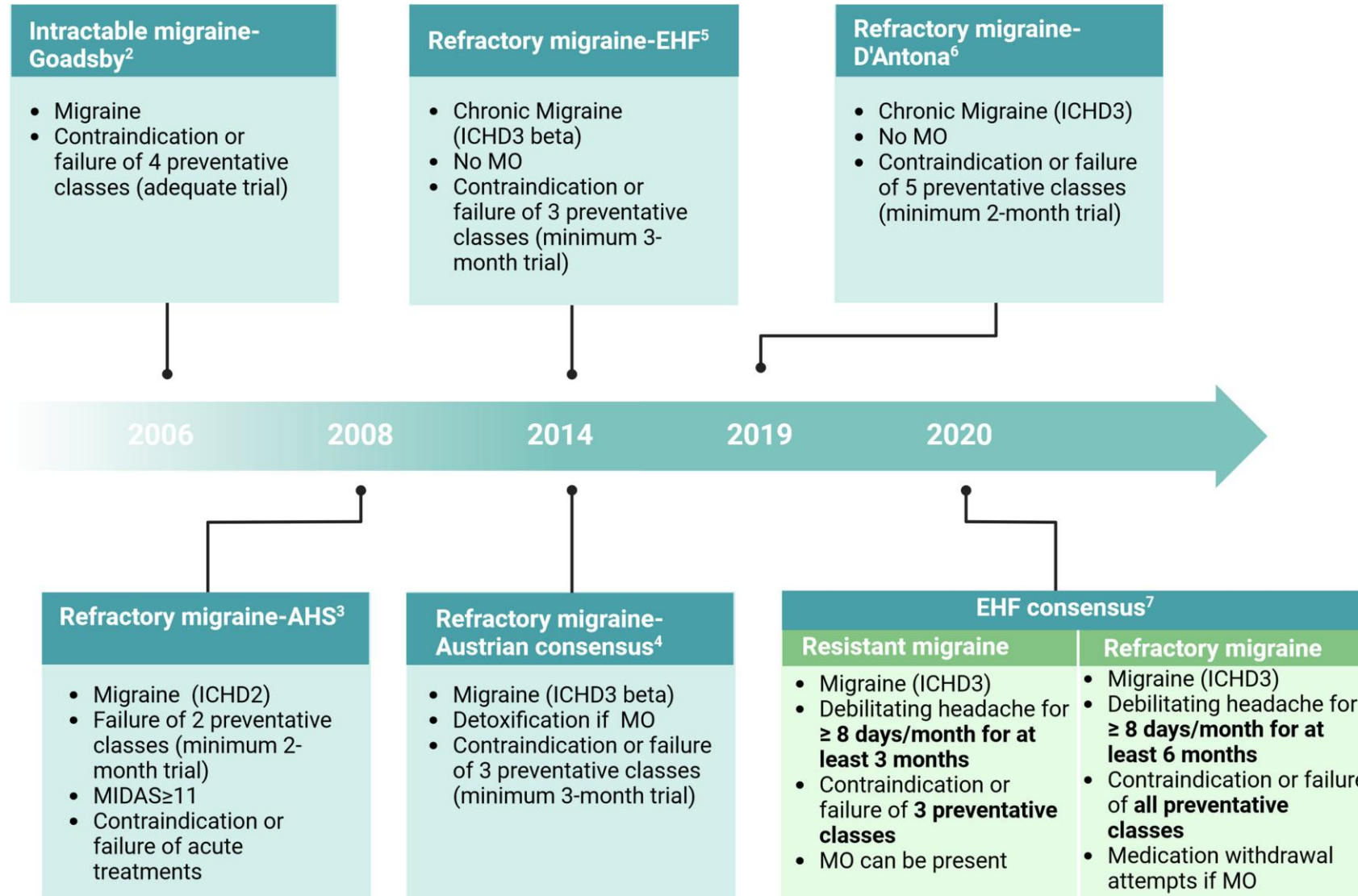
High number of attack frequency/  
lack of headache free days

Co-morbidities:  Psychiatric (e.g. anxiety, depression, PTSD)  
Other (e.g. obesity, sleep disorders, chronic pain)

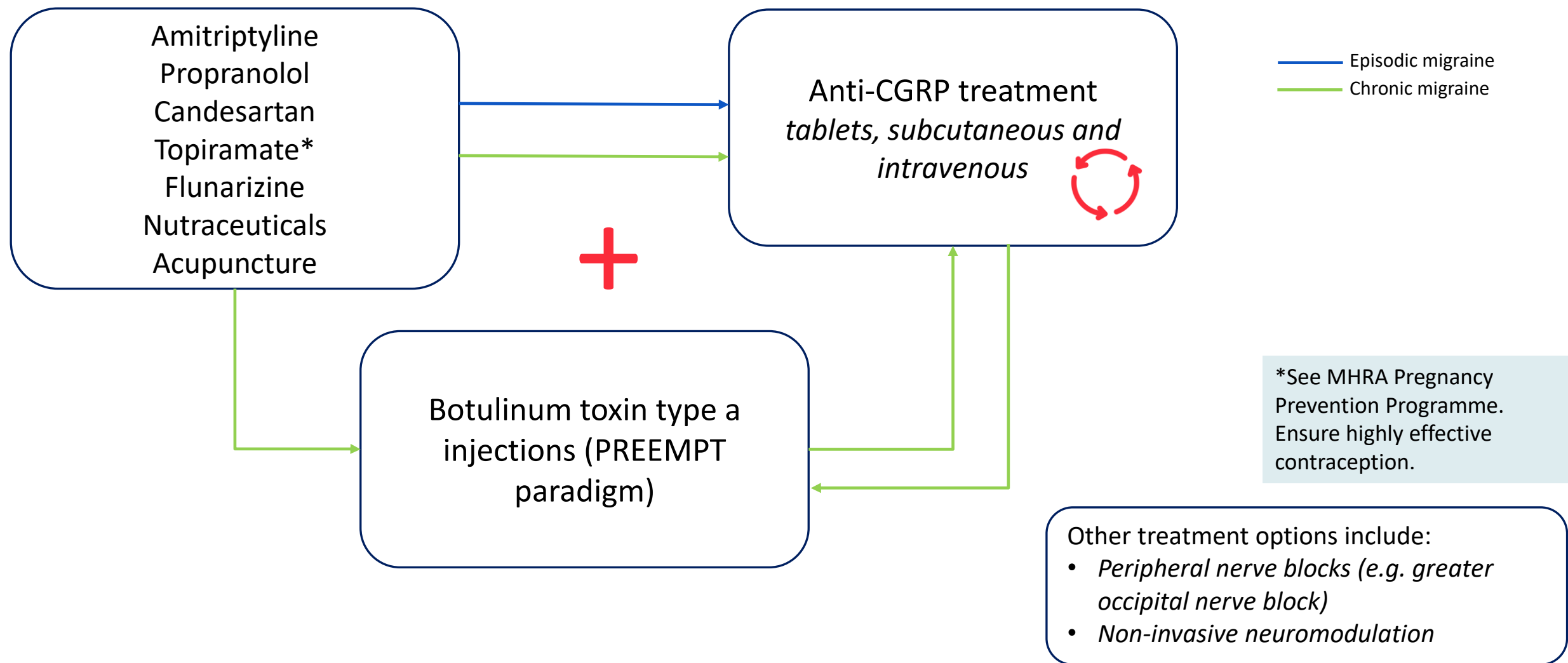
Lifestyle & Environmental factors: High stress, poor sleep hygiene, smoking,  
limited exercise, poor diet, excessive caffeine, low socioeconomic status

Disease related: Length of migraine history, mis-diagnosis, delayed or lack of  
access to medical care and treatment

# Definitions through the years<sup>1</sup>



# Preventative treatment for migraine



## 2022 EHF Consensus Statement: Definition of triptan response<sup>1</sup>

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### **Triptan responder**

A given triptan leads to effective attack treatment in  $\geq 3$  out of 4 consecutive migraine attacks

### **Triptan ineligible**

Acknowledged contraindication to triptan use, as specified in the SmPC

### **Triptan resistant**

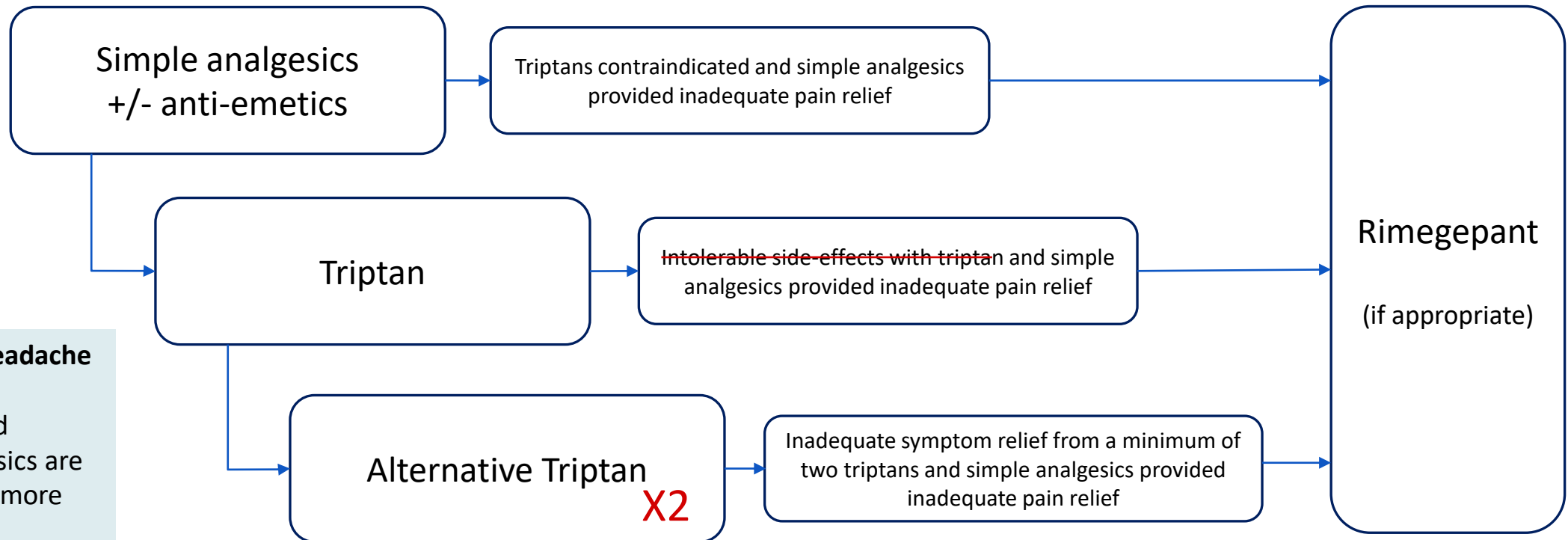
Failure of  $\geq 2$  triptans

### **Triptan refractory**

Failure of  $\geq 3$  triptans, including SC formulation

# Acute treatment for migraine

**Do not  
prescribe  
opioids.**

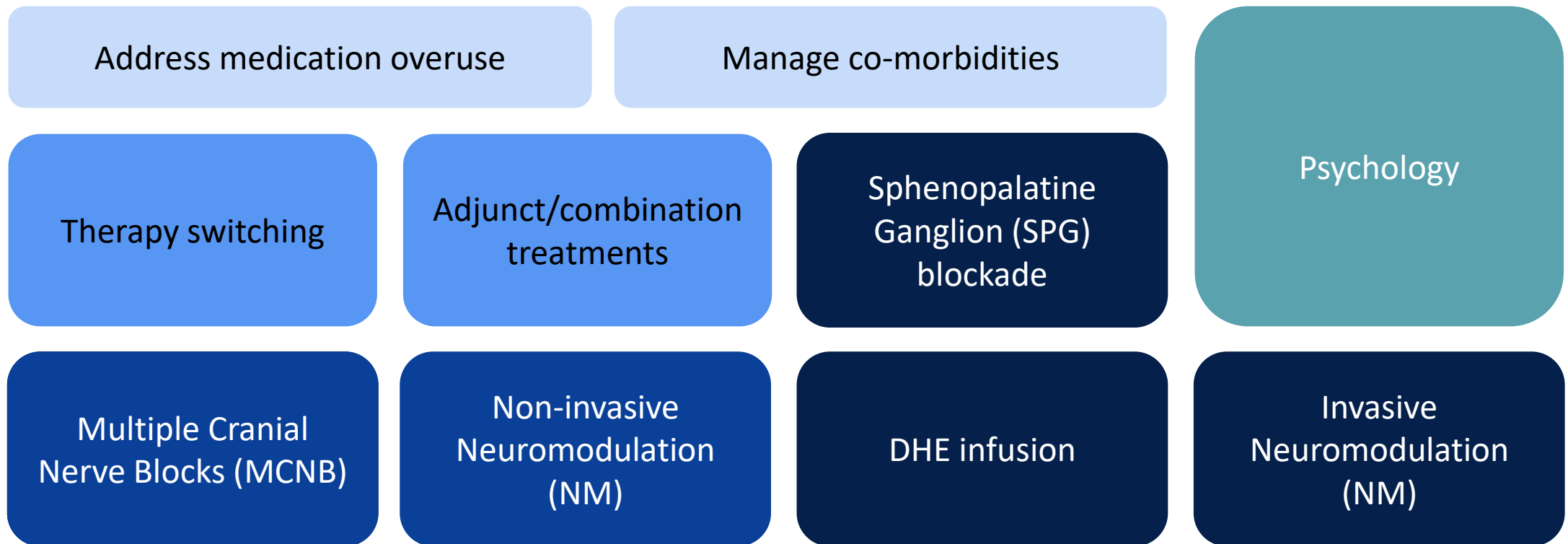


**Medication overuse headache**  
can develop when:

- Triptans, opioids and combination analgesics are taken on 10 days or more per month
- Simple analgesics such as paracetamol are taken on 15 days or more per month<sup>1</sup>

# Treatment of refractory migraine:

The treatment of resistant and refractory migraine requires careful clinical assessment of the individual, optimisation of acute and preventive treatment, management of comorbidities, and psychological support<sup>1</sup>



# Therapy switching:

From erenumab to  
fremanezumab  
(n=13/39):

*33% responders<sup>1</sup>*

Based on a long-term, prospective real-world analysis of treatment-refractory chronic migraine patients.

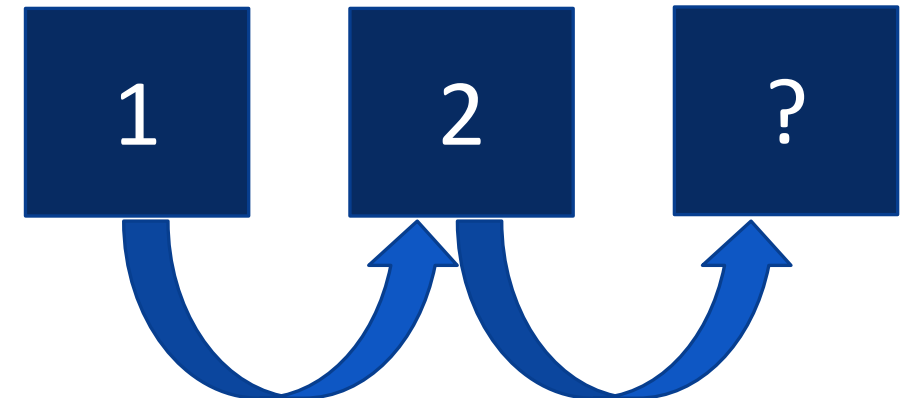
Responders defined as patients with a reduction in the mean MMD of  $\geq 30\%$  after 3 months of treatment with fremanezumab injections compared to post-erenumab baseline.

From galcanezumab  
and/or erenumab to  
fremanezumab  
(n=59/138):

*43% responders<sup>2</sup>*

Based on data from multi-centre, prospective, observational study (FINESSE) of patients treated with fremanezumab following treatment with galcanezumab and/or erenumab.

Responders defined as patients with a reduction in the mean MMD of  $\geq 50\%$  after 3 months of treatment with fremanezumab compared to baseline.



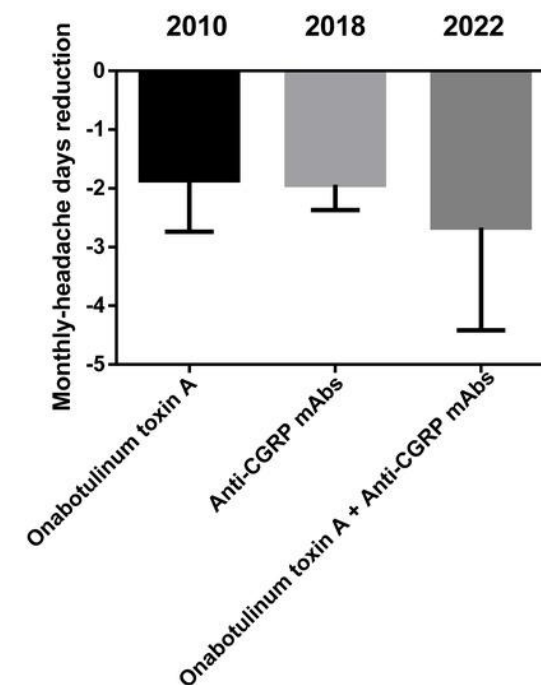
# Adjunct treatments:

- Real world evidence shows that combination treatment with onabotulinumtoxinA and anti-CGRP mAbs is well tolerated, with no new safety signals and incremental clinically meaningful benefits (reduction in MMDs and migraine-related disability)<sup>1,2,3</sup>

Meta-Analysis > Toxins (Basel). 2022 Aug 1;14(8):529. doi: 10.3390/toxins14080529.

## Pooled Analysis of Real-World Evidence Supports Anti-CGRP mAbs and OnabotulinumtoxinA Combined Trial in Chronic Migraine

Damiana Scuteri <sup>1 2</sup>, Paolo Tonin <sup>2</sup>, Pierluigi Nicotera <sup>3</sup>, Marilù Vulnera <sup>4</sup>,  
Giuseppina Cristina Altieri <sup>4</sup>, Assunta Tarsitano <sup>5</sup>, Giacinto Bagetta <sup>1</sup>, Maria Tiziana Corasaniti <sup>6</sup>



# Multiple Cranial Nerve blocks (MCNB)

**Targets:** greater and lesser occipital, supraorbital, supratrochlear, and auriculotemporal nerves

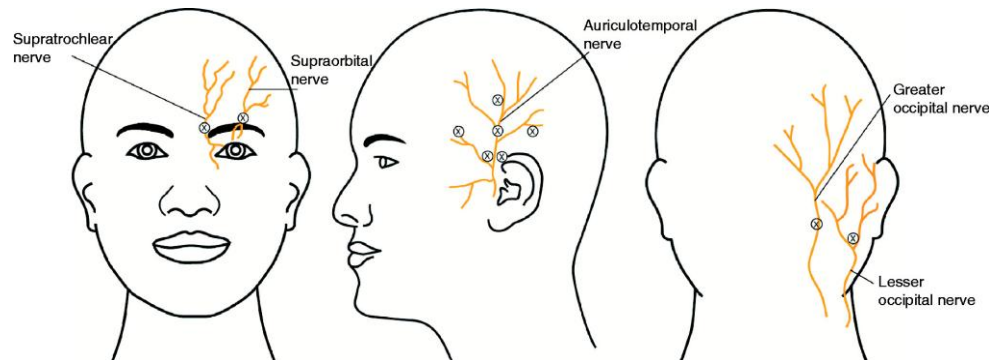
**Can provide effective transitional treatment for chronic headache disorders when greater occipital nerve blocks have been unsuccessful<sup>1</sup>**

Clinical Trial > Cephalalgia. 2019 Oct;39(12):1488-1499. doi: 10.1177/0333102419848121.

Epub 2019 May 13.

## Multiple cranial nerve blocks for the transitional treatment of chronic headaches

Sarah Miller<sup>1</sup>, Susie Lagrata<sup>1</sup>, Manjit Matharu<sup>1</sup>



### Open-label prospective study:

- 119 patients
- 41.2% with Chronic Migraine
- Previous failed treatments: 9.7
- Response rate at 2 weeks was 49.0%
- In responders MHD reduced by 10.4
- Duration of benefit: 47.1 days
- Subjective benefit: 60.0%
- Time to response: 33.6 hours

# Dihydroergotamine (DHE) infusion

IV DHE is a viable option in inpatient settings for disabling, refractory primary headache disorders, with longer treatments giving better results<sup>1</sup>

> [Neurology](#). 2011 Nov 15;77(20):1827-32. doi: 10.1212/WNL.0b013e3182377dbb. Epub 2011 Nov 2.

## Intravenous dihydroergotamine for inpatient management of refractory primary headaches

Abraham J Nagy <sup>1</sup>, Sonia Gandhi, Ria Bhola, Peter J Goadsby

Affiliations + expand

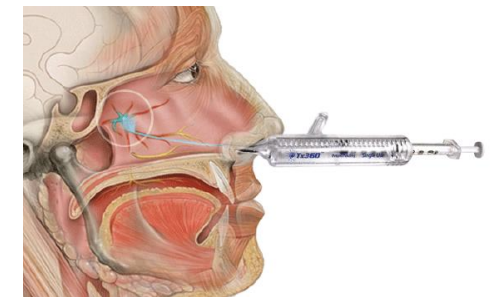
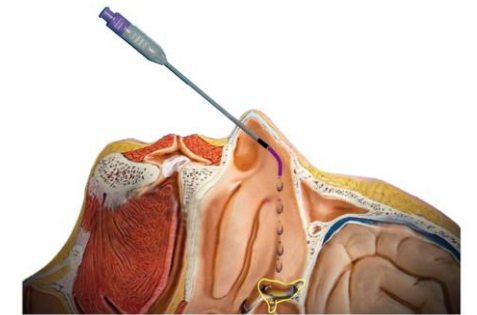
PMID: 22049203 DOI: [10.1212/WNL.0b013e3182377dbb](#)

### Retrospective audit:

- 163 patients
- 114 with refractory migraine
- 5 day repetitive infusion
- 50% reported moderate-excellent response
- Most common side-effects: nausea (n=94), leg cramps (n=46) and re-siting cannula (n=46).

# Sphenopalatine ganglion (SPG) blockade

| Device/Method                                  | Route        | Invasiveness  | Notes                                               |
|------------------------------------------------|--------------|---------------|-----------------------------------------------------|
| Cotton swab / Nasal applicator                 | Transnasal   | Low           | Traditional, simple                                 |
| Sphenocath <sup>®</sup> / Allevio <sup>®</sup> | Transnasal   | Low           | Clinic-based                                        |
| Tx360 <sup>®</sup>                             | Transnasal   | Low           | Clinic-based                                        |
| Nasal spray                                    | Transnasal   | Very low      | Variable efficacy                                   |
| Needle percutaneous injection                  | Percutaneous | Moderate      | Image-guided, precise                               |
| Radiofrequency probe                           | Percutaneous | Moderate-High | Longer-lasting, invasive (PRF or ablation)          |
| SPG neurostimulator (Pulsante <sup>®</sup> )   | Surgical     | High          | Refractory chronic cases (Chronic Cluster Headache) |



# Non-invasive NM treatments

| Device                                                | NM target        | Indication | Acute / Preventive | NHS access?                              |
|-------------------------------------------------------|------------------|------------|--------------------|------------------------------------------|
| Single-pulse Transcranial Magnetic stimulation (sTMS) | Occipital cortex | Migraine   | Both               | No<br>(Individual Funding Requests only) |



> [J Headache Pain. 2022 Jun 6;23\(1\):63. doi: 10.1186/s10194-022-01428-6.](#)

## Single-Pulse Transcranial Magnetic Stimulation for the preventive treatment of difficult-to-treat migraine: a 12-month prospective analysis

J O Lloyd <sup>1</sup>, B Hill <sup>2</sup>, M Murphy <sup>2</sup>, A Al-Kaisy <sup>2</sup>, A P Andreou <sup>1 2</sup>, G Lambru <sup>3 4</sup>

**OUTCOME:** N= 153 treated ➤ **96 (60%) patients considered responders**

# Invasive NM treatments

| Target                     | Indication      | Acute/<br>Preventive | Lead<br>placement            | Invasiveness |
|----------------------------|-----------------|----------------------|------------------------------|--------------|
| Occipital nerve            | CM, CH          | Preventive           | Subcutaneous<br>(peripheral) | +            |
| Sphenopalatine<br>ganglion | CH, SUNA        | Both                 | Intraoral                    | +            |
| Cervical spinal cord       | CM, CH,<br>SUNA | Preventive           | Epidural                     | ++           |
| Deep brain<br>stimulation  | CH              | Preventive           | Hypothalamic                 | +++          |

- At GSTT all patients are assessed by the multi-disciplinary team, including psychology
- Patients are required to attend either a whole day or two week programme to prepare them for the procedure and implications of this treatment



# Psychology

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- Stress can decrease response to acute treatments, possibly leading to medication overuse<sup>3</sup>
- Pain catastrophising, feelings of helplessness and ruminative thinking are more pronounced in individuals with migraine, mostly CM, compared with those without migraine, which might favour nocebo effect<sup>4</sup>
- There is evidence for the synergistic benefit of combination of pharmacologic and behavioural therapy<sup>1, 2</sup>
- **However current use of behavioural therapy is limited by availability in Headache Centres, due to lack of resources<sup>5</sup>**

# Conclusion

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- Early diagnosis and intervention may prevent refractoriness
- Further research and consensus statements are required for therapy switching and combining preventative treatments
- There are a number of evidence-based advanced treatments available for patients with refractory headache disorders, however protocols may vary and access to these treatments is limited
- The role of psychologists in the management of migraine and access to psychological treatment should be standardised and equitable across headache services

## Acknowledgements

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- Dr Sinan Barazi
- Ms Eleni Maratos
- Karen Sanderson

St Thomas' Hospital



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King's College London Headache research Laboratory

# Thank you

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