Quality and Safety in Practice Committee

Migraine: Diagnosis and Management from a GP Perspective

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Migraine

Diagnosis & Management

From a GP Perspective

Quick Reference Guide

Quality and Safety in Practice Committee

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This quality of care may be dependent on the appropriate allocation of resources to practices involved in its delivery. Resource allocation by the state is variable depending on geographical location and individual practice circumstances. There are constraints in following the guidelines where the resources are not available to action certain aspects of the guidelines. Therefore individual healthcare professionals will have to decide whether the standard is achievable within their resources particularly for vulnerable patient groups.

The guide does not however override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of individual patients in consultation with the patient and/or guardian or carer.

Guidelines are not policy documents. Feedback from local faculty and individual members on ease of implementation of these guidelines is welcomed.

Evidence-Based Medicine

Evidence-based medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.

In this document you will see that evidence and recommendations are graded according to levels of evidence (Level 1 – 5) and grades of recommendations (Grades A-C) respectively. This grading system is an adaptation of the revised Oxford Centre 2011 Levels of Evidence.

Levels of Evidence

Level 1: Evidence obtained from systematic review of randomised trials
Level 2: Evidence obtained from at least one randomised trial
Level 3: Evidence obtained from at least one non-randomised controlled cohort/follow-up study
Level 4: Evidence obtained from at least one case-series, case-control or historically controlled study
Level 5: Evidence obtained from mechanism-based reasoning

Grades of Recommendations

A Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence levels 1, 2).

B Requires the availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation (evidence levels 3, 4).

C Requires evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates an absence of directly applicable clinical studies of good quality (evidence level 5).

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Section 1: Introduction

1.1 Background

Migraine is the most common headache disorder seen by doctors. The WHO (World Health Organization) Global Burden of Disease (GBD) Studies have recently ranked migraine as the second highest cause worldwide of years lost due to disability (YLD)[1]. Migraine is the leading cause of YLD in the age group 15-49 years. YLD is considered to be the most appropriate measure of disability in non-fatal medical conditions. It is estimated that there are currently more than a billion people with migraine on the planet and there are approximately 600,000 to 700,000 people in the republic of Ireland with this condition. The WHO estimates that 10% - 14% of global population have migraine. Migraine patients may experience episodic[2] or chronic symptoms, and the latter is usually associated with the most significant disability[3]. There is often a component of overuse of painkillers or analgesics (medication overuse) in patients with more chronic symptoms. Furthermore, there is an increased risk of certain medical comorbidities in patients with chronic migraine including depression, anxiety, fibromyalgia[4] and obesity.

1.2 Aims of this Document

The main aims of this guide are to illustrate the clinical spectrum of migraine and to give recommendations on the most appropriate treatments for people suffering with this disabling neurological condition.

The European Commission Executive Agency for health and Consumers commissioned a study on the medical care of people with migraine[5]. It found that even in wealthy European countries, too few people with suspected migraine consult doctors. Furthermore, migraine specific medications were used inadequately. It recommended that health-care providers and the public need to be further educated regarding migraine.

Section 2: Migraine - Summary

Diagnosis of Migraine

- Unilateral or bilateral, typically lasts 4 to 72 hours
- Pulsating or throbbing pain, moderate or severe
- Associated with other symptoms such as sensitivity to light/sound, nausea, vomiting, diarrhoea disequilibrium, neck pain.
- Aura can occur with or without headache - Typical aura symptoms include visual, sensory, speech disturbance and occasionally motor symptoms which are reversible
- Frequency < 15 days per month = EPISODIC MIGRAINE +/- aura ≥ 15 days per month = CHRONIC MIGRAINE +/- aura

Acute Treatment

- Combination therapy with an oral triptan, NSAID, paracetamol and anti-emetic even in the absence of nausea and vomiting
- If monotherapy preferred, oral triptan or NSAID or aspirin 900mg or paracetamol
- Do NOT use ergots or opioids
- If oral preparations are not an option due to nausea + vomiting, consider adding a rectal NSAID, anti-emetic (prochlorperazine) and intranasal or subcutaneous triptan

Menstrual migraine: offer longer acting triptans e.g. Frovatriptan or naratriptan 2.5mg BD on the days -2 to +3 with NSAIDs' and paracetamol

General Management and Prophylaxis

Emphasise the importance of regular lifestyle, diet, exercise, avoidance of stress, alcohol, smoking and other stimulants.

Offer topiramate, amitriptyline, propranolol, candesartan or nortriptyline, having evaluated each patient individually before deciding on which therapy to use. Be aware that topiramate is associated with teratogenicity and can potentially impair the effectiveness of hormonal contraceptives at higher doses. Some patients lose significant amounts of weight on topiramate, this needs monitoring (in the US, topiramate has a licensed preparation to aid weight loss). Give patients an adequate trial of at least three of the above medications in general practice before referral to a specialist, hospital based, headache clinic.

Progesterone only pill desogestrel, progesterone 3/12 injection, progesterone implant can be prescribed even in the presence of migraine with aura.

Acupuncture, 10 sessions over 5 to 8 weeks combined with symptomatic treatments reduces the frequency of migraine attack. If receiving another form of prophylaxis (e.g. amitriptyline) and migraine is well controlled, continue current treatment as required. Advise patients that riboflavin (vitamin B2), 400mg daily, magnesium and CoQ10 may be effective in reducing migraine frequency but the evidence is relatively weak.

Physiotherapy may be effective for those with migraine associated with neck pain. Some people find other forms of alternative medicine very helpful including reflexology, biofeedback.

Section 3: Prevalence and Associated Disability

Migraine is a significant cause of disability worldwide. The peak prevalence is for women between the ages of 15-49 years. The life-time prevalence is 42% in females[6]. Some patients experience relatively infrequent attacks during their lifetime, while the average patient gets one to two attacks per month. Approximately 10% of all patients get weekly attacks.

The Global Burden of Disease (GBD) studies provide the most comprehensive estimates of disability with respect to headache disorders worldwide. These studies have been undertaken by the World Health Organisation (WHO) since 1990. The measurements used include "Years lived with Disability" (YLD) and "Disability-adjusted life years" (DALYs). Disabilities are subdivided into six different levels. At level four, which includes non-fatal disease, in 2016, migraine was ranked as the 2nd cause of YLD worldwide[1] (see table 1).

It was responsible for 5.6% of total YLD, second only to low back pain (7.2%).

Low back pain
Migraine
Age-related hearing loss
Iron-deficiency anaemia
Major depression
Neck pain
Other musculoskeletal disorders
Diabetes
Anxiety disorders
Falls

Figure 1: Top 10 diseases which affect morbidity
Showing YLD in GDB 2016 (Global, all sexes and ages)

Section 4: Pathophysiology

Migraine is considered to be a primary disorder of the brain. It is a complex neurovascular condition that involves activation and sensitisation of neuronal pathways within the peripheral and central nervous systems. This involves sensory information passing from the periphery to more central areas such as the trigeminovascular complex. Neuronal activation, cortical spreading depression (CSD) and vascular changes are present during the migraine attack. However, blood vessel dilatation and constriction are not necessary or sufficient to induce an attack.

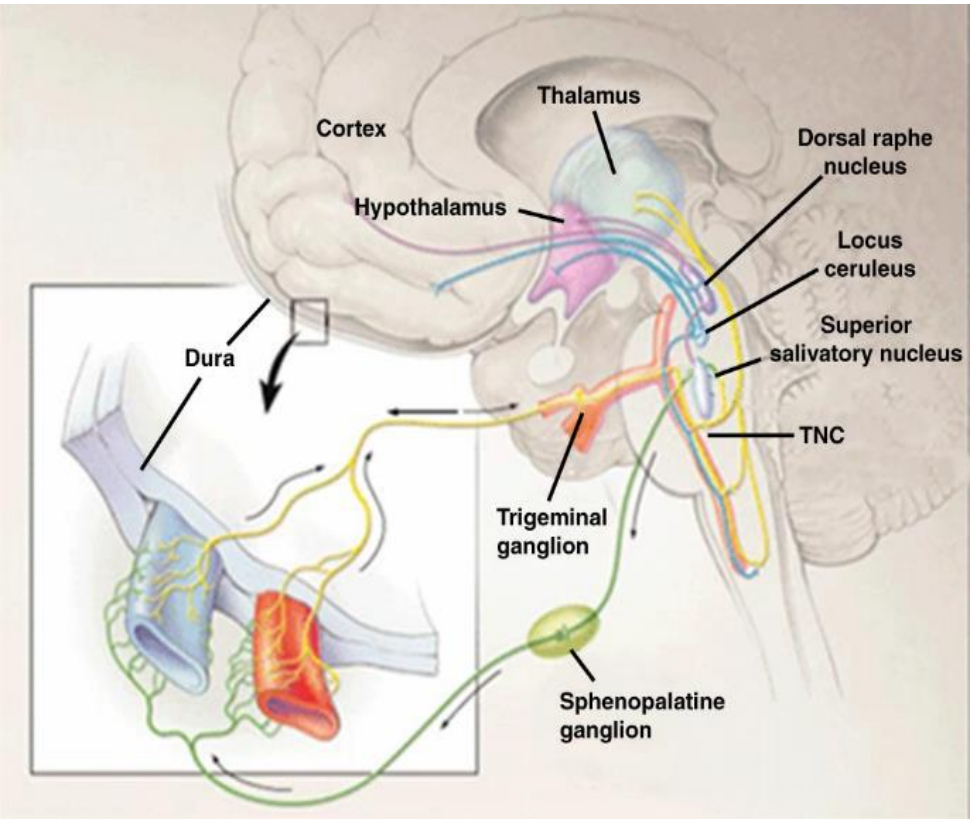

Figure 2: Pathophysiology of migraine[7]. With kind permission from N Eng J of Med

Section 5: Classification and Diagnostic Criteria

Migraine classification is the remit of the International Headache Society (IHS) and their most recent recommendations are contained in the International Classification of Headache Disorders (ICHD-3)[8].

Types of Migraine
1.1 Migraine without aura
1.2 Migraine with aura
I. Typical aura
II. Brainstem aura
III. Hemiplegic migraine
IV. Retinal migraine
1.3 Chronic migraine
1.4 Complications of migraine
I. Status migrainosus
II. Persistent aura without infarction
III. Migrainous infraction
IV. Migraine aura-triggered seizures
1.5 Probable migraine
1.6 Episodic syndromes that may be associated with migraine

Table 1: ICHD-3 2018 classification of migraine[8]

These recommendations have been incorporated into the World Health Organization's International Classification of Diseases (ICD-111) which was published in summer 2018.

In addition to the above main classification of migraine, the ICHD-3 includes an appendix which contains a number of additional migraine subtypes and associated variants, many of which are well known to General Practitioners (see table 2 below) and are not included in the formal classification of migraine

Additional Migraine Subtypes and Variants
A1.1 Migraine without aura
A1.1.1 Pure menstrual migraine without aura
A1.1.2 Menstrually related migraine without aura
A1.1.3 Non-menstrual migraine without aura
A1.3 Chronic migraine (alternative criteria)
A1.3.1 Chronic migraine with pain free periods
A1.3.2 Chronic migraine with continuous pain
A1.4 Complications of migraine
A1.6 Episodic syndromes that may be associated with migraine
A1.6.4 Infantile colic
A1.6.5 Alternating hemiplegia of childhood
A1.6.6 Vestibular migraine

Table 2: ICHD-3 2018 migraine subtypes and variants from the appendix[8]

As migraine is most often seen in females of childbearing ages, most general practitioners will have seen women who relate their migraine to their menstrual cycle. Most general practitioners will also have many children with infantile colic. In such cases, it is now considered important to ask if there is a family history of migraine.

Migraine without aura is the most common migraine headache and has specific diagnostic criteria.

Diagnostic Criteria for Migraine Headache without an Aura
A. Five attacks or more B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated) C. Headache has at least two of the following four characteristics: I. Unilateral location II. Pulsating quality III. Moderate or severe pain intensity IV. Aggravation by or causing avoidance of routine physical activity for example walking or climbing stairs. D. During the headache at least one of the following: I. Nausea and/or vomiting II. Photophobia and phonophobia (noise sensitivity) E. Not better accounted for by another ICHD-3 diagnosis

Table 3: ICHD-3 2018 criteria 1.1[8]

Early in their migraine history, many patients are initially worried about the migraine symptoms that they experience. Often, patients are concerned that they may be suffering from a sinister medical condition, such as a "brain tumour". Confirmation of the diagnosis of migraine is a very important part of the consultation. In some cases, neuroimaging with an MRI scan of the brain is not clinically indicated, but may be requested by the patient for further reassurance. MRI Scans and other investigations may be required when "red flag" symptoms are present[9] (see appendix 1). It is obviously very important not to miss a secondary cause for the patients' symptoms.

In children and adolescents, migraine attacks are generally of shorter duration than those seen in adults. Children often give a history of travel sickness and recurrent abdominal pain or cyclical vomiting syndrome, prior to the development of headaches in their late teens or adulthood.

As general practitioners', we often underestimate how migraine affects the family unit, for example, disruption of family events, time with children, and weekend activities. Migraine sufferers often feel guilty that they did something which may have brought on the attack.

Section 6: Stages of a Migraine Attack

The migraine attack is typically depicted as four separate, but overlapping, phases (figure 2). Migraine patients may not experience all phases and symptoms shown below and not all possible symptoms are listed.

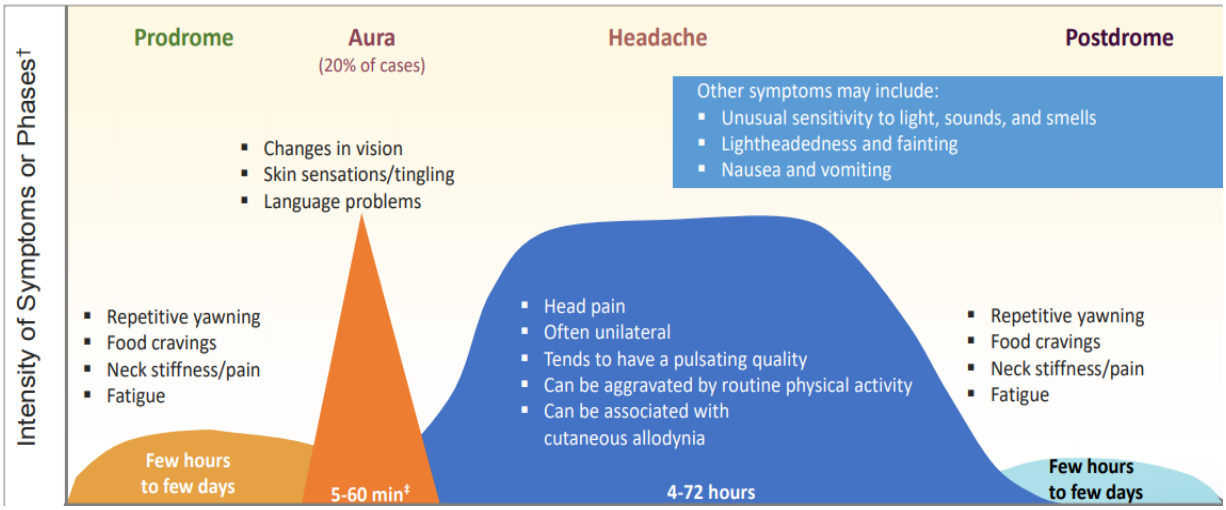

Figure 3: Stages in a migraine attack adapted from Blau JN Lancet 1992[10].
Information adopted from International Headache Classification[8]

Prodrome

Patients are frequently not familiar with the idea that there is a prodrome phase of a migraine attack. However, once these prodromal symptoms are described to them, they readily recognise them from their own experiences. Identification of these prodrome symptoms in a given patient will frequently facilitate early treatment of an acute attack, and this typically results in a significantly better response to acute treatment. The prodrome precedes the headache phase and may last from 4 to 48 hours. The symptoms may be psychological, neurological or constitutional, and they include change in mood (euphoria or feeling low), irritability, tiredness, yawning, photophobia, neck stiffness/soreness, food cravings, and an altered perception of heat and cold.

Aura

Aura occurs in approximately 20%-30% of patients. The aura can be very frightening for people, especially when it happens initially. There are several different types of aura in migraine as outlined below.

Diagnostic Criteria for Migraine Headache without an Aura
A. Two attacks or more B. One or more of the following reversible symptoms: I. Visual II. Sensory III. Speech and/or language IV. Motor V. Brainstem VI. Retinal C. At least three of the following six characteristics: I. At least one aura symptom spreads gradually over 5 minutes II. Two or more aura symptoms occur in quick succession (if 3 symptoms occur, the acceptable maximum duration is 3 by 60 minutes, motor symptoms may last up to 72 hours) III. Each individual aura symptom last 5-60 minutes IV. At least one symptom is unilateral (aphasia is always regarded as unilateral; dysartharia may or may not be) V. At least one aura symptom is positive (scintillations, pins and needles are positive symptoms) VI. The aura is accompanied, or followed, within 60 minutes by headache D. Not better accounted for by another ICHD-3 diagnosis

Table 4: ICHD-3 diagnostic criteria for migraine with an aura 1.2[8]

Many patients with migraines experience attacks both with and without auras. Furthermore, they may experience aura without significant headache or head pain. The aura typically consists of transient, focal neurological symptoms, usually lasting from 5 to 60 minutes. Visual symptoms lasting seconds to 1-2 minutes are not normally considered to be visual aura. Aura typically precedes the headache, but it may coincide with and persist into the headache phase. The most common aura symptoms are visual. These include zig-zag lines, shimmering, tunnel vision, enlarging blind spot (scotoma) or undulating images**.**

Figure 4: Representation of a visual aura courtesy of Shutterstock

Other aura symptoms that are commonly described by migraine patients include sensory changes in limbs and face, speech disturbance (word finding difficulties, dysarthria), vertigo (see Appendix 2), ataxia, clumsiness, limb weakness and infrequently loss of consciousness.

Migraine with brainstem aura symptoms, mentioned above in Table 5, has replaced the older term basilar migraine. These brainstem aura symptoms (in particular limb weakness), can easily be confused with the onset of a transient ischaemic attack or cerebrovascular accident. Table 6 below is often helpful for doctors as they try clinically to distinguish between these two conditions.

	Migraine with aura	Transient ischaemic attack (TIA)
Features of attack		
Onset of symptoms	Gradual	Abrupt
Effect on vision	Positive visual symptoms	Visual loss
	Unusual to get visual loss	
Headache present	Follows in 80%	Seldom present
Duration	Up to 60 minutes	less than 24 hours
Pattern of events	Repeated stereotyped	May recur
Age profile of patient	Young adult	Usually > 50 years
Vascular risk factors	none	present

Table 5: Features of migraine with aura VERSUS TIAs'.
Adapted from Fisher 1986, Stroke[11]

It is not uncommon that a patient may self-refer to the hospital emergency department or they may be referred by their general practitioner when they develop migraine aura symptoms (for example, limb weakness or speech disturbance), as there may be concern that the symptoms represent a vascular event. It is important to distinguish between these two conditions as misdiagnosis could have serious repercussions going forward. For example, it can affect premiums for life insurance. Furthermore, it happens occasionally that migraine patients are thrombolised during the aura phase. Imaging of the brain with an MRI scan is generally indicated in migraine with aura[12].

Headache

Headache is commonly the most disabling feature of a migraine attack and severe headache is the most frequent reason for consultation with primary care physicians. The pain can begin abruptly or it can be gradual in onset.

It usually lasts 4-72 hours, the average being 12-24 hours. The headache is classically described as pounding, throbbing or pulsating at worst. It is often exacerbated by routine physical activity or movement. Patients usually prefer to be still, and they may sit or lie down. In 60%-70% of migraine attacks, the headache is unilateral, but it may be bilateral. The pain can move around the head and face during or between attacks.

Facial pain (neuropathic facial pain) is very common in migraine patients and is often misdiagnosed as sinus pain, dental issues, trigeminal neuralgia, or temporomandibular joint (TMJ) problems.

There are often a number of associated non-headache symptoms during a migraine attack and these clinical features can be very useful when making the diagnosis. Nausea can be present in up to 80% of patients, which occasionally leads to vomiting. The other common associated features are photophobia, phonophobia, osmophobia (intolerance of odours), vertigo/disequilibrium, fatigue/exhaustion, neck stiffness, sinus congestion, cutaneous allodynia (heightened sensitivity to normal stimuli), the latter being a marker of chronic migraine.

Postdrome

Most migraine attacks gradually subside over 1-2 days, but patients often feel “washed-out” for a further 24-72 hours. A common complaint from migraine sufferers is that they feel “delicate or hungover” for a further 1-2 days, without having consumed any alcohol. Patients may lose their appetite at the beginning of the attack and may be very hungry during the postdrome. If the person eats at this stage it may help them to feel better. Others find that vomiting gives them relief and this can herald the end of the attack. Sleep seems to help many sufferers, who find that even an hour or two can be enough to help. This sleep period may even be shorter (as little as 15 minutes) in children.

Section 7: Trigger Factors

The identification of migraine trigger factors is an important part of the clinical history and headache consultation. Approximately three quarters of patients with migraine can recognise individual trigger factors, some of which they may be able to avoid[13].

Trigger Factors in Migraine	
I.	Stress is implicated in up to 80% of migraine attacks. It can occur particularly in the period of relaxation after stress (let down), hence the term weekend migraine.
II.	Menstrual cycle is implicated 65% of the time, particularly if the migraine happens on the days prior to and during menstruation (-2 to +3) and at ovulation
III.	Change in the lifestyle or routine. For example, skipping meals, lack of sleep, too much sleep or over tiredness. In children, too much excitement of lack of activity.
IV.	Strong odours: perfumes, paints and petrol
V.	Environmental factors: bright lights, sunlight, weather or noise
VI.	Change in caffeine intake (withdrawal or excessive intake or more then 3-4 coffees daily), or (excessive) alcohol.

Table 2: Trigger factors listed in order of their relevance in migraine

There is often an accumulation of factors in provoking a migraine attack. It was previously believed that cheese and/or chocolate were triggers for a migraine attack. However, it is now understood that craving sweet or savoury foods may be part of the prodrome phase of migraine. Specifically, food cravings may represent hypothalamic activation prior to the onset of migraine headache.

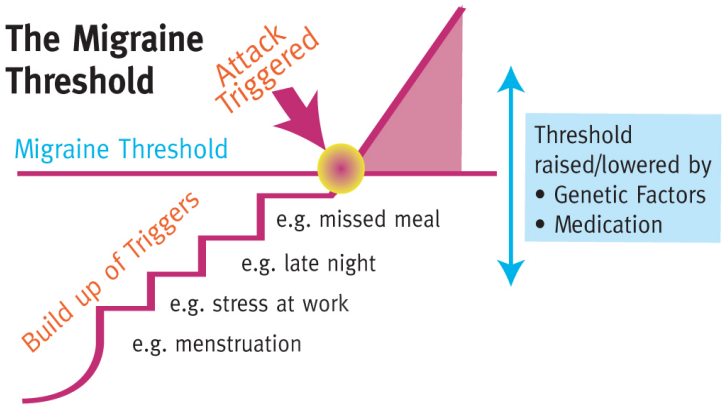

Figure 5: Migraine triggers, picture by kind permission of Migraine Association of Ireland

Section 8: Episodic Migraine

Migraine is defined as episodic if it occurs less than 15 days[2] per month. Headache experts generally refer to low (1-4 days/month), moderate (5-9 days/month) and high (10-14 days/month) frequency episodic migraine. When a patient presents to a general practitioner with recurrent headaches, they should be advised to keep a detailed daily diary. This should include details about the severity of the headaches, associated features, acute treatments used, effect on lifestyle and possible triggers. This provides very useful clinical information and can help confirm the diagnosis. In addition, the diary often demonstrates the benefits of acute and/or other therapies.

8.1 Management of Acute Episodic Migraine Attacks by the Patient

Patients should take acute treatments as early as possible during an attack, preferably before the headache is well established.
However, it may be difficult for patients to predict whether they will have a mild, moderate or severe attack. It therefore follows that it may be difficult for healthcare professionals to be very specific about when patients should self-medicate. Many patients will learn from their own experiences when to and when not to treat an attack. Detailed diaries and personal awareness are very important in this regard. Acute migraine treatments, including painkillers/analgesia, non-steroidal anti-inflammatories drugs (NSAID's) and triptans should be used no more than 4-6 days per month in order to avoid medication overuse in the context of migraine. The number of days per month that acute medication is taken determines if medication overuse is present. In addition, it is generally advised that patients should avoid codeine, tramadol or other opiate derivatives.

The acute treatment of migraine changed significantly in the early 1990s'with the advent of the triptans. Many patients report that triptans are the single most useful drug for the treatment of acute attacks. Combination treatment (paracetamol, an NSAID and a triptan) may provide further benefit for some patients.

Medication for acute migraine attack

Analgesia	NSAIDs'	Triptans
Paracetamol 500mg Max dose-2 tabs every 6 hours	**Naproxen** Max dose - 500mg 12 hourly	**Sumatriptan 50-100mg** Max dose 300mg daily
	Ibuprofen Max dose - 600mg 8 hourly	**Zolmitriptan 2.5mg** Max 10mg daily
	Diclofenac Max dose - 75mg 12 hourly	**Frovatriptan 2.5mg** Max dose 5mg daily
	Aspirin Max dose - 900mg 6 hourly	**Almotriptan12.5mg** Max dose 12.5 daily
	Mefenamic acid Max dose - 500mg 8 hourly	**Eletriptan 40mg** Max dose 80mg daily
		Naratriptan 2.5mg Max dose 5 mg daily

Table 7 – Adopted from how to acutely treat your headache - unpublished work[14]

The current recommendations for treating acute migraine attacks are to consider a combination of:

1) Paracetamol
2) NSAIDs'[15] (level of evidence – 1, grade of recommendation - A)
3) triptan[15] (level 1, grade A). Triptans are recommended early in the attack. If migraine recurs in patients who respond, repeat the dose at a minimum of a two hour interval being careful not to exceed the maximum daily dose and frequency

Individual patients may respond effectively to simple analgesia combinations, such as paracetamol and ibuprofen taken together. Alternatively, some patients may need a combination of medications from all three categories, for example, paracetamol, naproxen and frovatriptan. These medications can all be taken at the same time. Anti-emetics (such as domperidone or prochlorperazine, ondansetron) can often improve the response to acute treatment by mechanisms that are not clearly understood. It is believed that these latter agents may be prokinetic.

If the initial combination of acute medication does not work after the timely treatment of two or three migraine attacks, it is important to change the medication combination. Pain freedom at two hours is considered to be a good response to treatment and is the standard measure used for efficacy in clinical trials. For example, if paracetamol, naproxen and sumatriptan are not effective for repeated attacks, one could try paracetamol ibuprofen, and frovatriptan. General Practitioners tend to have considerable experience in the use of paracetamol and NSAIDs. However, they are less accustomed to using different triptans.

8.2 Commonly Prescribed Triptans

Sumatriptan, zolmitriptan and almotriptan have a quicker time of onset as compared to frovatriptan and naratriptan. However, frovatriptan and naratriptan have longer half-lives with longer clinical effect. Sumatriptan is currently the most versatile of the triptans with an oral, nasal and subcutaneous (SC) formulation.

Sumatriptan in SC injection form is the most rapidly absorbed, but has the most severe side effects. There may be a transient increase in headache ("head rush") for 10-20 minutes after the use of the SC formulation. Nevertheless, it is particularly useful in patients who have significant vomiting early in an attack. These patients also benefit from a rapid onset to peak concentration of triptan. When prescribing triphan in any formulations, if there is any concern about the person's cardiac status, a stress ECG and echocardiogram should be carried out to out rule ischaemic heart disease or a cardiomyopathy.

Sumatriptan SC is not licenced in Ireland. It is only available on a "named patient basis" so this may lead a delay in getting it from the pharmacy. The traditional nasal sumatriptan spray is relatively poorly absorbed nasally and also may have some gastro-intestinal absorption. It often gives a significant bitter after taste in the person's mouth, which may make any pre-existing nausea worse. However, many patients find this sumatriptan preparation useful.

Zolmitriptan also has a nasal formulation and it is well absorbed through the nasopharynx (40%), with the remainder being absorbed through the gastrointestinal tract. Zolmitriptan is also available as a rapimelt tablet, which dissolves quickly under the tongue.

In practice, the choice of acute therapy for episodic migraine will depend on the;

(1) efficacy of previously tried therapies
(2) severity, impact and disability associated with a typical attack
(3) patient's pre-existing history

Previous concerns about the use of triptans in patients with complex aura, such as brainstem and hemiplegic migraine, have not been substantiated[16]. Triptans should be used with caution in those with established moderate to severe coronary heart disease (see section 13, Migraine in Sport for further details)

8.3 Management in General Practice & Hospital Emergency Department

It is not uncommon for patients to attend their general practitioner or the emergency department when:

- The headache is severe
- The attack is associated with persistent vomiting
- There are new associated neurological symptoms
- The patient is unsure as to the cause of the headache

Initial assessment usually includes exclusion of secondary causes of headache (see Appendix 1). This is followed by a detailed history of the characteristics of the headache (see Appendix 3). The history should include documentation of all the medications the patient is taking, the timing of acute medication and whether or not it has been helpful. Treatment failure of acute attacks may be caused by inadequate dosing or not using appropriate combinations.

For patients with regular, rapid and persistent vomiting, consider non-oral routes of administration of acute medications. For example:

- Rectal diclofenac and paracetamol
- Nasal or subcutaneous sumatriptan (can be very useful as they can be administered at home).

Sometimes intravenous (IV) fluids, IV paracetamol, IV/intramuscular (IM) anti-emetics, and/or IV/IM injections of NSAIDs are also required.

Morphine and opiate based preparations should be avoided due to the risk of medication overuse, dependency, associated co-morbidities and side-effects. Regular use of steroids should be avoided.

Routine follow-up with the general practitioner should be encouraged after an acute episode where the patient attended hospital casualty or the emergency GP, out of hours, service. Patients with more regular headache and migraine symptoms should keep a detailed headache diary (appendix 4). In patients with an average of more than 8-10 days per month of headache/migraines, patients should be advised that preventative or prophylactic treatment (see section 10.1) is indicated. Their own general practitioner is well placed to initiate such treatment, particularly if the patient attends with a headache diary. The diary should include, at the least, symptoms, duration, severity, medication taken and its effect for each attack.

Nerve Blocks

Greater occipital nerve (GON) blocks can be used as an acute treatment in migraine injecting a mixture of steroid (depomedrone) and local anaesthetic (lidocaine). Currently, in Ireland, patients can be treated with them in some emergency departments. It may also be done in general practice, but to date, no research on its usage in general practice has been undertaken. This therapeutic procedure gives short term relief of two to three months. Rare side effects (less than 1%) include lipoatrophy at the injection site with loss of hair growth.

Figure 6: Site of greater occipital nerve block. Photo by kind permission of BM Kearney

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The greater occipital nerve can be found superficially, approximately 2.5-5cm infero-lateral to the occipital prominence. The patient is positioned sitting with the head either vertical or slightly flexed. The nerve is located and felt along the superior nuchal line. Depo-mederone 40mg/ml is used. The 2ml amp is diluted with 3ml sterile water and injected into the tender GON.

GON blocks may improve the headaches and associated symptoms in the short to medium term, usually weeks to months. They also form part of a preventative treatment strategy (see section 10.2 - Other treatment strategies for migraine prevention) in some specialised headache centres for short to medium term relief of primary headache disorders (including migraine and cluster headache). Many patients will improve significantly for a number of months after a single GON block. Other patients may require a number of GON blocks for sustained improvement.

Sphenopalatine ganglion (see figure 1) blocks can also help migraine attacks can be done in the emergency department. The spenopalatine ganglion is located deep in the nasal mucousa. A SphenoCath which is a soft flexible catheter can deliver local anaesthetic deep into the mucosa. This treatment is not routinely available in Ireland.

Section 9: Chronic Migraine

Chronic migraine was first defined in 2004. It is distinguished from episodic migraine by its clinical, epidemiological, sociodemographic and co-morbidity profiles. It has specific diagnostic criteria.

Diagnostic Criteria for Chronic Migraine
A. Headache (migraine like or tension-type-like) on 15 days/month for > 3 months and fulfilling criteria B and C B. Occurring in a patient who has had at least five attacks fulfilling criteria B-D for 1.1 Migraine without aura and /or criteria B and C for 1.2 migraine with aura C. On 8 days/month for > 3 months fulfilling any of the following: I. Criteria C and D for 1.1 migraine without aura II. Criteria B and C for 1.2 migraine III. Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative D. Not better accounted for by another ICHD-3 diagnosis

Table 8 – ICHD-3 criteria for chronic migraine headaches[8].
For 1.1 & 1.2 mentioned above - See tables 4 and 5

Chronic Daily Headache is an umbrella term and it includes four primary headache disorders, the most common being chronic migraine. The other three conditions listed under this heading are new daily persistent headache, hemicrania continua and chronic tension type headache. These relatively rare primary headache disorders will be discussed in detail in ICGP Quick reference guide on "Headaches" due to be published in 2019.

Chronic migraine is associated with significant disability. For example, it has been reported that chronic migraine patients have more difficulty with work related activities than patients with epilepsy[3] (see figure 8). In addition, chronic migraine is generally more disabling than episodic migraine[3]. This high level of disability has a significant impact on quality of life and behaviour in those with more chronic migraine. Furthermore, stigma (a culturally embedded process through which individuals experience stereotyping, devaluation and discrimination) is greater for chronic migraine, than for episodic migraine.

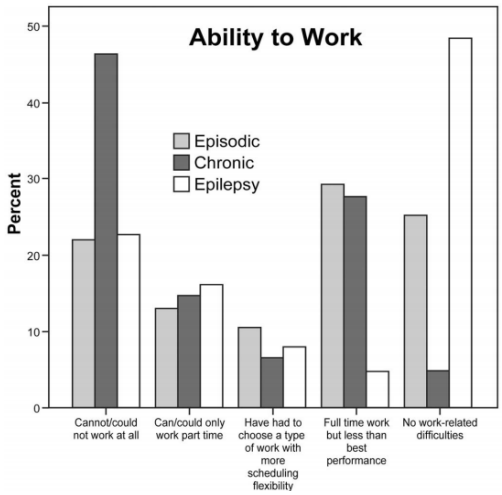

Figure 7: Effect of migraine – episodic and chronic on work[3].
By kind permission Dr Young & PLoS

Section 10: Prophylactic Therapies for Migraine

Prophylactic oral therapies are usually indicated for the treatment of migraine when migraine symptoms occur on at least 8-10 days per month and are of moderate to severe intensity. As noted in section 2.4, acute medications can be taken on average 4-6 days per month, but preferably not more often due to the risk of medication overuse. A pragmatic management approach needs to be taken with patients who experience an intermediate frequency of migraine symptoms (on average 6-8 days per month).

Prophylactic therapies should be started after the patient has been assessed to determine an appropriate agent. Patients should be advised that most preventative medications do not work effectively in the presence of medication overuse[17]. Furthermore, it is important to emphasise to patients the value of conservative management strategies in conjunction with preventative medication. These strategies include a healthy lifestyle, daily exercise (moderate intensity for a minimum of 20-30 minutes at least five days a week), a balanced diet, good hydration, moderate caffeine intake (which should not exceed two or three 300ml cups daily)[18], good sleep hygiene and appropriate stress management. Lifestyle factors may improve headaches and severity in some cases. Each patient therefore, plays a vital role in helping themselves. The Irish patient organisation, Migraine Association of Ireland (MAI), provides very helpful information and support in this regard, and it is often useful to inform patients of this resource. The MAI website www.migraine.ie also has a section specifically for Health professionals and organises training and research days for health care professional on an annual or twice annual basis.

For optimal efficacy, it is recommended[19] that for each preventative agent:

1) Start at a low dose
2) Increase the dose in small increments every 2-8 weeks
3) Give an adequate trial for 2-3 months at the maximum tolerated dose
4) Avoid overuse of analgesics or painkillers
5) Discuss contraception with women of child-bearing age and the potential risk of these preventative medications, primarily during pregnancy and breastfeeding
6) Consider co-morbid medical conditions and aim to use a single medication that may treat multiple disorders if possible (for example, candesartan for hypertension and migraine)
7) Revaluate therapy at a reasonable interval of 3-6 months preferably with the help of a migraine diary

A realistic goal is that a preventative drug should give at least 30% - 50% improvement in headache disability overall, without having significant side effects[19]. If this level of improvement is not achieved at the maximum tolerated dose, strong consideration should be given to weaning the medication, after a 3-6 month period (see appendix 5 for pro forma for follow-up of the patient with migraine). It is recommended that patients should be involved in the decision regarding the choice of preventative treatment as it often aids medication compliance. This discussion should include the realistic benefits and possible side-effects in the hope of improving compliance.

The headache impact test (HIT-6) is a patient questionnaire which could be used at the 3-6 monthly review. It gives the patient an opportunity to describe and communicate the way they feel and what they cannot do because of the headaches. It was developed from SF-36 health assessment tool. It can be accessed here.

All of the current preventative agents have been identified by chance, after being used to treat other medical conditions including epilepsy, depression and hypertension.

First Line Prophylactic Therapies for Migraine in Ireland

- Topiramate (25-400mg daily), beware of teratogenicity, can be used in the presence of medication overuse
- Amitripyline (2.5-150mg daily) or less sedating, nortriptyline
- Propanolol (20-160mg daily)
- Candesartan (4-32mg daily)

The most frequently prescribed preventative agents in Ireland are outlined above. Medications used may vary from country to country, and are strongly influenced by personal experience.

Second Line Prophylactic Therapies for Migraine

- Sodium valproate (200-2000mg daily) beware of teratogenicity
- Pizotifen (3-4.5mg daily)
- Metoprolol (50-100mg daily); bisoprolol, atenolol
- Venlafaxine (37.5-225mg daily)
- Physiotherapy
- Acupuncture
- Menstrual related migraine – offer long acting triptan on days -2 to +3

A number of second line therapies are also available, see above. All of these therapies are detailed in this chapter. It would be very helpful if patients could be given a trial of at least **three** of the above, 1st or 2nd line prophylactic medications in general practice before considering referral to a specialist, hospital based, headache clinic.

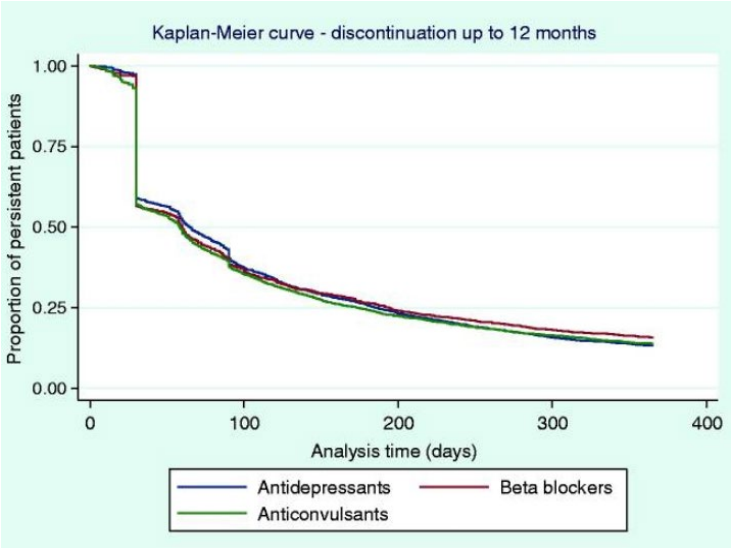

Figure 8: Time to discontinuation up to 12 months' follow-up from starting the prophylactic[20].
By kind permission Dr Z Hepp & SAGE, open access pages

More than 80% of chronic migraine patients discontinued prophylactic treatment within one year of starting it. A sizeable decrease in adherence was observed after the first month (see figure 8).

10.1 Oral Preventative Medication

Epilepsy Medication

Topiramate (25-400mg daily) is widely used for migraine prophylaxis (level 1, grade A). A randomized controlled trial was initially done in 2004[21]. The usual starting dose is 25mg once daily, titrated upwards in 25mg increments every 2-8 weeks up to a maintenance dose of somewhere between 25mg-200mg BD. The dose of topiramate used in epilepsy can be as high 700-800mg daily. However, the maximum dose routinely used in migraine is 400mg daily. The maintenance dose achieved depends on tolerability and efficacy. Common side-effects of topiramate include weight loss, tingling of fingers and toes, cognitive dysfunction, worsening of depression/anxiety and insomnia. As migraine is most common in women of childbearing years, female patients should be strongly advised to avoid pregnancy while taking topiramate[22] due to the risk of foetal abnormalities.

The combined oestrogen contraceptive (which should usually only be prescribed for migraine patients without aura) may be rendered less effective (and may cause breakthrough bleeding and result in pregnancy) when the dose of topiramate is increased above 200mg daily.

Sodium valproate[23] (200-2000mg daily) may be effective (level 1, grade A) for migraine prophylaxis and is reasonably well tolerated in both episodic and chronic migraine patients. However, valproate can cause birth defects and should not be used[24] in female patients of child bearing age. Studies have shown that patients were more than twice as likely to have their headache frequency reduced by 50% or more with sodium valproate than they were with placebo. The most common starting dose is 200mg once or twice daily. The typical maximum maintenance dose for migraine is 1000mg twice daily. Potential side effects include tremor, weight gain and hair loss. Side effects are normally dose dependant.

Gabapentin(900-3,00mg)[25] has been generally found not to be effective for prophylaxis of migraine in adults (level 1 grade C). However, it may be used in clinical practice. Side effects include dizziness, weight gain and somnolence.

Pregabalin[25] does not have strong evidence for prophylactic use in migraine, although it is frequently prescribed (level 1, grade C). Common side effects include dizziness and weight gain. It should be prescribed with caution, due to its current '*street value*'. Zonisamide (100-200mg daily) has showed benefit in an open label study[26] (level 3, grade B) in refractory patients. It was mainly used in patients who responded to topiramate, but could not tolerate the side effects. Like topiramate, zonisamide used at a dose greater than 200mg daily may cause breakthrough bleeding and result in pregnancy.

Anti-epileptics other than those mentioned above[27] have been used in migraine prophylaxis. They include acetazolamide, carbamazepine, clonazepam, lamotrigine, oxcarbazepine and vigabatrin. Overall, they were no more effective than placebo in reducing headache frequency (level 1, grade C).

Anti-Depressant Medication

Amitriptyline (2.5-150mg nocte) is widely used for migraine prophylaxis. It is a first line agent in many international headache clinics[18]. However, the evidence in episodic migraine is relatively weak, where it was found to be no more effective than placebo[28] (level 2, grade A). The evidence in chronic migraine is more robust. As it may also be an appropriate medication for central pain conditions, fibromyalgia, insomnia and depression, it may be helpful in those patients where these conditions co-exist with migraine. The most common side effects include drowsiness (often in the morning), dry mouth, constipation, weight gain and vivid dreams. If side effects are a significant problem, a trial of nortriptyline is worthwhile.

Amitriptyline is not available in an elixir form in Ireland and the dose of the smallest tablet available is 10mg. However, the tablet can be halved or further divided.

Nortriptyline (2.5mg – 150mg) has been found to be effective for migraine prevention by a concensus of headache experts[18] (level 4, grade C). There are no randomised controlled trials of nortriptyline in migraine prophylaxis. It appears to have fewer anticholinergic adverse effects than amitriptyline. Patients who experience side effects may tolerate smaller doses of nortriptyline (or amitriptyline). Nortriptyline is not available in an elixir form in Ireland and the dose of the smallest tablet available is 10mg. Again, the tablet can be halved. It is available as an elixir in some countries.

Venlafaxine (37.5-225mg daily) is a serotonin-norepinephrine reuptake inhibitor (SNRI) that is sometimes prescribed for migraine prophylaxis. The evidence is not robust. In one trial, it was found to be no better than placebo or amitriptyline[29] (level 1, grade A) for reducing migraine frequency, intensity and duration over two to three months of treatment. The participants treated with venlafaxine suffered fewer side effects than those who took amitriptyline. However, the number of people who stopped taking one or the other drug due to side effects was approximately equal.

Selective serotonin reuptake inhibitors[30] (SSRIs) may be used for migraine prophylaxis. However, the evidence is weak. Fluoxetine and paroxetine have been shown (level 1, grade A) to be no more effective than placebo or amitriptyline in reducing migraine frequency and intensity. However, there may be clinical benefit in some patients who have co-morbid anxiety, depression or other chronic pain symptoms including fibromyalgia.

Hypertensive Medication

Candesartan (4-32mg daily), an angiotension 2 receptor blocker, is commonly used for hypertension and was found to be an effective migraine preventative agent in Norway in 2003[31]. More recently, candesartan 16mg daily has been shown to be as effective as propranolol 160mg daily in migraine prevention[32] (level 1, grade A) with somewhat different side-effects. Side effects include dry cough, respiratory tract infections, dizziness/vertigo and headache. It does not usually cause weight gain, drowsiness or mood disturbance.

Propranolol (80- 160mg daily, long acting formula) has been shown to be more effective than placebo in the prevention of migraine attacks[33] (level 1, grade A). It is one of the most commonly used migraine agents in Ireland. Multiple studies of beta-blockers in migraine have been reported since 1984[34]. The ideal beta-blocker should be cardioselective to reduce side effects (such as cold extremities) and hydrophilic (therefore less likely to provoke nightmares and hallucinations). Propranolol is not cardioselective, but it is still commonly used as many patients find it helpful.

Metoprolol (50-100mg daily) is cardioselective and has been shown to be as effective as propranolol in migraine prevention[34] (level 3, grade A).

Atenolol (25-100mg daily) is cardioselective and hydrophilic, but is unlicensed in Ireland for migraine.

Bisoprolol (5-10mg daily) has been used for migraine prophylaxis, but there is limited data[35] (Level 3 grade B).

Flunarizine (5-15mg daily) is a calcium channel blocker and has been shown to reduce migraine frequency more than placebo and to a similar degree to the active comparators propranolol and topiramate[36] (level 3, grade B). It is often helpful in children, adolescents and those with hemiplegic migraine. It may cause weight gain, low mood and anxiety. It is contraindicated in people with recent or current depression, and pre-existing Parkinsonism and other extra-pyramidal disorders. It should not be used in patients with second or third degree atrioventricular block and left ventricular failure.

Verapamil (80-480mg daily) is another calcium channel blocking agent and is sometimes used for migraine prevention[37] (level 2 grade B). It is relatively safe and well tolerated. The typical side effects include constipation, dizziness, nervousness or headache.

Other Oral Medications

Pizotifen has been used in migraine prophylaxis since 1977[38]. It is a potent 5-HT2 antagonist with antihistaminic effects. It was not found to be as effective as propranolol in a study carried out in India in 2006-2007, but the study was not published until 2013[39](Level 3, grade C). Currently, pizotifen is licensed in Ireland, but not in the USA[18]. It is frequently used in children. Common side effects include weight gain and sedation.

Dietary management of migraine should include a regular eating pattern. Patients should be advised to avoid skipping meals. Vitamin and mineral supplementation: riboflavin (vitamin B2, 400mg daily), magnesium and CoQ10, may be effective in reducing migraine frequency but evidence has not been substantiated by randomized double blind clinical trials A review of magnesium trials using high levels of magnesium dicitrate (600mg) seems to be a safe but results are anecdotal (level 4 grade C)[40] .

Mini-prophylaxis has been recommended for episodic migraine predominantly associated with menstruation[41]. This is where triptans are used prophylactically in those with predictable menstrual related migraine that does not respond adequately to standard acute treatment (see section 12 under mini-prophylaxis for more detail).

Memantine and Mexiletine are other preventatives used in tertiary referral clinics for headaches in refractory cases.

10.2 Other Preventative Strategies

Physiotherapy may be helpful for those migraine patients with significant vestibular features and/or neck pain[42]. Disequilibrium or vertigo symptoms are often experienced by migraine sufferers (see Appendix 2). Manual mobilisation therapy and trigger point treatments of the cervical spine and scalp may be helpful.

Acupuncture had been shown in a Cochrane review[43] to help some patients with migraine (level I grade A). The available trials suggest that acupuncture may be at least as effective as prophylactic treatment with oral sodium valproate or metoprolol.

Greater occipital nerve (GON) blocks are sometimes used in the outpatient setting to treat more chronic migraine sufferers. In our practice, we use a combination of steroids and lidocaine. In the USA and other hospitals, they are usually performed with lidocaine alone[18]. GON blocks using steroids should not be performed more frequently that every 4-6 months on each side due to the risk of local tissue damage. Furthermore, there is a limit as to the total number of GON blocks in an individual patient, due to the risk of systemic side effects. GON blocks have been shown to reduce pain severity and frequency as well as the use of analgesia up to two months after intervention[44].

Botulinum Neurotoxin (BoNT) or “Botox” is a protein complex produced by the anaerobic bacterium clostridium botulinum. There at least seven different BoNT serotypes, of which only two are currently in clinical use: Botox type A[45] and Botox type B. Botox type A was shown to be effective in prophylaxis of chronic migraine in an international, multi-centre, double blind, randomized, placebo-controlled trial (RCT) in 2010[46].

In this study, known as **P**hase 111 **Re**search **E**valuating **M**igraine **P**rophylaxis **T**herapy (PREEMPT), a protocol was agreed in advance where a minimum of 31 specific injections sites were used (see figure 9).
These studies showed that there was significant improvement compared to placebo in multiple headache measures and this resulted in reduced headache disability.

In Ireland, access to Botox is very limited via the public hospital system and private health insurers do not usually reimburse patients for this treatment. In the UK, the National Institute for Health and Care Excellence (NICE) will recommend its use in patients with chronic migraine who have not responded to at least three prior pharmacological[41] prophylactic therapies and whose condition is appropriately managed for medication overuse. Ireland uses this protocol when assessing patients for Botox. In addition, it recommends that they have had a therapeutic trial of three GON block injections in advance of being listed for Botox.

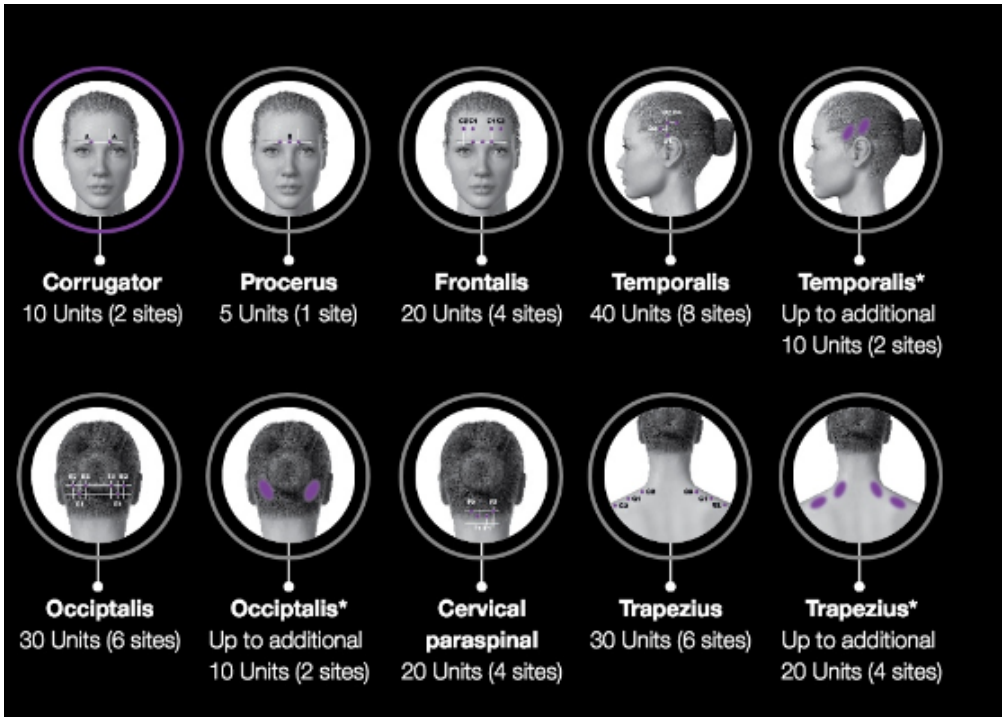

Figure 9: Picture by kind permission Allergan Pharmaceuticals

Patients with chronic migraine may respond to inpatient treatment with intravenous dihydroergotamine (DHE) or lidocaine. This type of treatment is reserved for migraine patients with at least 20 headache days per month. It is only available in a limited number of hospitals in Ireland. DHE may be helpful in 40-50% of chronic migraine patients, typically for a number of months.

Neuromodulation is a novel treatment approach for patients with episodic and chronic migraine. There are several different devices available and the evidence for their use is very variable. However, some patients respond very well and there are usually limited side effects. The exact mechanism of action is unclear for many of these treatments. The most simple and non-invasive devices are handheld. They are used by the patient every day for short periods of time (typically less than an hour each day). The best evidence in migraine prophylaxis is for transcranial magnetic stimulation (TCMS) with the SpringTMS product. Alternatively, the supraorbital transcutaneous stimulator (Cefaly) has been shown to be effective and safe as a preventative treatment for migraine[47]. Vagal nerve stimulation (VNS) with the nVNS hand held device appears to be helpful for the acute treatment of migraine attacks.

More invasive neuromodulation approaches include hypothalamic deep brain stimulation, occipital nerve stimulation, sphenopalatine ganglion and cervical spinal cord stimulation. . In general, these are very specialised treatments and they should only be considered for the most refractory patients in specialised headache clinics. Many of these more invasive treatments are not available in Ireland and patients need to be referred overseas.

Alternative migraine therapies including biofeedback, mindfulness, reflexology, and TENS machines may be helpful for some migraine patients. Many of these approaches are used in the Danish Headache Centre, with variable outcomes. It is difficult to do a double blind trial with these interventions and anecdotal reports are mixed.

Section 11: Episodic Syndromes & Migraine in Children

Episodic syndromes that are associated with migraine, or are believed to be precursors of migraine, The are classified in the ICHD-3.

Classification of Episodic syndromes
1.6.1 Episodic syndromes that may be associated with migraine: I. Recurrent gastrointestinal syndromes II. Cyclical vomiting syndrome III. Abdominal migraine 1.6.2 Benign paroxysmal vertigo 1.6.3 Benign paroxysmal torticollis

Table 9: ICHD-3 detail of episodic syndromes

Previously, episodic syndromes were called childhood periodic syndromes. Episodic syndromes most commonly occur in children, but can occur in adults as well. Most general practitioners will have seen children with recurrent gastrointestinal disturbance, such as cyclical vomiting or abdominal pain, who subsequently go on to develop migraine in their teens or adulthood. The diagnosis is clinical but the ICHD-3 have suggested the following criteria should be fulfilled.

Diagnostic Criteria for Recurrent Gastrointestinal Disturbance
A. At least 5 attacks with distinct episodes of abdominal pain and/or discomfort and/or nausea and/or vomiting B. Normal gastrointestinal examination and evaluation C. Not attributed to any disorder

Table 10: ICHD-3 criteria for diagnosis of recurrent gastrointestinal disturbance [8]

Cyclical vomiting syndrome was first described by Heberden in 1806 and it is typified by recurrent episodes of intense nausea and vomiting that may last hours to days. Following the ictal (active vomiting) phase, children may fall asleep for several hours and wake up later with les symptoms. Attacks may be associated with pallor, lethargy, light and/or noise sensitivity. There is complete resolution of symptoms between attacks[48]. It is more common in children between 4-5 years[18] old, but it may occur in older children and adults[49].

Abdominal migraine was first described by Buchanan in 1921 and is typified by recurrent attacks of moderate to severe midline abdominal pain associated with nausea and vomiting. Attacks usually last hours to days, and the child is generally well in between episodes. Headache is an uncommon symptom during these episodes. Physical examination should be performed, and in addition vital signs, temperature and urine analysis need to be checked. Urine analysis is critical to exclude ketoacidosis or urinary tract infection which may present with recurrent abdominal pain[50]. In the presence of a classical history and normal examination/investigations, imaging is not usually recommended. If a child with previously diagnosed abdominal migraine presents again with abdominal pain, doctors should not be complacent and the above evaluation should be completed to exclude a secondary diagnosis.

Benign Paroxysmal Vertigo was first described by Basser in 1964. It characterised by the abrupt loss of balance, with associated vertigo. It is equally common in boys and girls. Onset is usually in primary school or early childhood. At the beginning of an episode, children may appear frightened while trying to hold on to furniture. They may refuse to walk and want to lie still. Attacks are usually brief, lasting 5 minutes in most cases, although persistent episodes have been described for up to 48 hours. Young children may not be able to describe their symptoms. Activities that stimulate the labyrinth, such as swings and roundabouts, may trigger the episodes. It is a diagnosis of exclusion and is most often made in a hospital setting after appropriate clinical evaluation and investigations. Differential diagnosis includes posterior fossa pathology and episodic ataxia.

Benign Paroxysmal Torticollis was first described by Snyder in 1969 and is characterised by sudden onset of recurrent abnormal movements involving the neck. There is characteristic rotation of the head and neck towards the affected side, which is often accompanied by ataxia and vomiting. Episodes usually last hours to days, and resolve spontaneously. Patients typically develop symptoms between two and eight months of age that resolve by 3-5 years.

Migraine in Children

According to epidemiological studies, migraine may start earlier in males[18], its incidence peaks at five years of age, while in females it peaks between 10-14 years. Between the ages of 5-11 years, migraine is more common in boys. With the onset of puberty, the prevalence of migraine increases in females significantly and continues to do so until the fourth decade of life (For section 12 for more details, figure 11).

Migraine in childhood may go undiagnosed as nausea, vomiting and pallor[8] are the most obvious presenting symptoms. Headache may be relatively mild. In children, migraine headaches differ from those experienced by adults in a number of ways:

- The headache is often of shorter duration (2-4 hours). The duration is important to keep in mind when treatment options are being considered. Ideally medications should have a rapid onset of action and a relatively short half-life to prevent lingering side effects once the headache has resolved
- Gastrointestinal symptoms often predominate in children
- The headache may be relieved by vomiting or a short period of rest or sleep.

Children often find it difficult to describe the headache or how they are feeling during a migraine attack. It may be helpful to ask them to point to where the pain is most severe or to draw a picture[51] of the headache or their symptoms. This can be particularly helpful when trying to make a diagnosis.

The triggers for these episodic syndromes and migraine in children are often similar to those of adults (see section 7). Late nights, skipping meals, excitement (birthday parties and school trips), excessive exercise, monosodium glutamate, screen use and artificial lightening are particularly common trigger factors in children.

The use of preventative medication in children and adolescents is still a matter for debate, because of concerns by parents regarding potential side effects and long term consequences of daily oral medication. Furthermore, the benefit of prophylaxis appears to be less clear in children. In January 2017, a randomised controlled trial[52] showed that there were no significant differences in terms of reduction in headache frequency or headache related disability in childhood and adolescent migraine with amitriptyline, topiramate or placebo over a 24 week period (level 2 grade A). Many of these prophylactic medications may be associated with side effects. For example, Topiramate may interfere with concentration which could affect the child's education. In many cases, discussion of the diagnosis and explanation of the symptoms with the child and their parents is all that is required. For acute attacks, an adequate dose of paracetamol and/or ibuprofen is all that is required.

Section 12: Female Hormones and the Migrainous Brain

Migraine is three times more common in women than in men in the 15-49 year old age group. These sex differences are generally attributed to the differential effects of male and female sex hormones on migraine pathophysiology. The migraine pattern may evolve over a woman's reproductive lifetime.

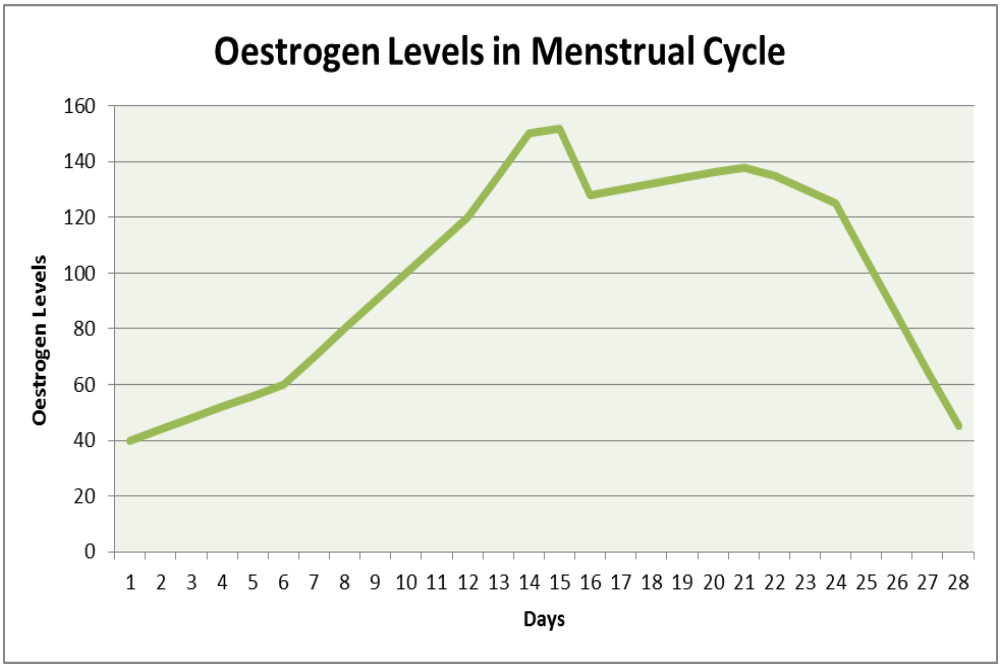

Figure 10: Oestrogen levels in menstrual cycle.
Based on 28 day menstrual cycle

As shown above, oestrogen levels rise mid-cycle at ovulation, usually at day 14 and then reduce slightly, but remain relatively static until the 2-3 days before menstruation. It is not an absolute fall, but a relative decrease in oestrogen. Menstrual migraine attacks are mostly without aura[8] (see table 3 for detailed classification). In some cases, female patients may also develop migraine at ovulation on a regular basis. In this scenario, a woman may be sensitive to the small drop in oestrogen that occurs, about 12 days before menstruation starts.

Pure menstrual migraine (PMM) is present in 7-14% of migraneurs[18] and its occurrence is wholly confined to a strict period around menstruation, and very rarely at other times. It is important that diary-documented evidence, over a minimum of three cycles, is present to confirm the diagnosis of PMM as you can see from the ICHD-3 criteria listed below.

Criteria for Pure Menstrual Migraine (PMM)
A. Attacks in a menstruating woman, fulfilling criteria for 1.1 migraine without aura and criterion B below
B. Occuring exclusively on day 1+2 (ie -2 to +3) of menstruation in at least two out of 3 menstrual cycles and at no other time of the cycle

Table 11: ICHD-3 Criteria for diagnosis of Pure Menstrual Migraine (PMM)
Note: The first day of menstruation is day 1, the preceding day is -1, and there is no day 0.

Menstrual related migraine (MRM) occurs in two thirds of female patients. This is where attacks occur during menstruation two thirds of the time and at other times.

Menstruation is considered to be endometrial bleeding resulting from either:

- Normal menstrual cycle
- Withdrawal of exogenous progesterone when using the combined oral contraceptive pill
- Withdrawal of cyclical hormone replacement therapy.

The predictability of MRM makes these headaches more amenable to planned treatment. The importance of distinguishing between PMM and MRM is that hormone prophylaxis is more likely to be effective for the former.

12.1 Mini-Prophylaxis for Menstrual Migraine

In many women, migraine around the time of menstruation is more difficult to treat. The attacks are usually of longer duration and are more severe than migraine at other times in the cycle. In general, treatment is the same for menstrual migraine as non-menstrual migraine. If migraine is infrequent, NSAIDs alone (or with paracetamol) or in combination with a triptan, may be particularly helpful. NSAIDs are also beneficial for treating menstrual cramps. If migraine is frequent, predictable, prolonged or poorly responsive to therapy, consideration should be given to what is known as mini-prophylactic treatment[41]. In this situation, the long acting triptans, frovatriptan or naratriptan 2.5mg twice a day, are recommended for continuous use over 3-5 days. This should not significantly contribute to medication overuse as long as these latter agents are limited to no more than 6-8 days per month. The triptan may be started in combination with a NSAIDs two days before the expected date of menstruation (in patients with regular cycles) or during the prodrome.

Another approach is to increase the dose of their regular preventative medication, such as topiramate or amitriptyline five days before menstruation (level 4, grade C)[18]. Adding magnesium 500mg starting at ovulation and continuing until after menstruation may prevent or decrease the severity of migraine attacks[18] (level 4, grade c).

MRM with aura, in the age group 15-49 years, usually has a different hormonal response than those who get PMM or MRM without aura. MRM with aura is most often seen in high oestrogen states such as combined hormonal contraception or hormonal replacement therapy.

12.2 Other Prophylactic Options for Menstrual Migraine

For those with PMM and MRM, a possible approach is to supress ovulation using the following:

- Progesterone only pill (POP) desogestrel[53]. Other POP's act primarily through their effects on cervical mucosa and are unlikely to supress ovulation. The POP is safe in those with migraine with aura.
- Progesterone injection i.e. depo-provera which is given 12 weekly
- Progesterone implant i.e. implanon, which is a and lasts three years

The MIRENA coil also contains progesterone. It acts at a local level on cervical mucosa and results in thinning of the uterus. It usually does not supress ovulation, so it may not prevent PMM or MRM for some women.

A further approach is to supplement oestrogen during the days when oestrogen levels drop significantly with an oestrogen containing gel[54]. It is possible to partly or completely supress the menstrual cycle by using the combined oral contraceptive pill (COCP) without a break for 63-84 days (three or four 21 day packs without a break). It is acceptable to continue this 63-84 day cycle for a number of years. Women need to be mindful of weight gain when taking hormonal contraception as it is a risk factor for headaches.

12.3 Oral Contraceptive Options

There are three different types of oral contraceptives: fixed dose, triphasic and progesterone only pill. The use of triphasic oral contraception may increase migraine due to repeated hormone changes and should be avoided where possible. If using combined oral contraceptive pill (COCP), use a low dose oestrogen product. There are generally fewer side effects and the incidence of migraine is lower than with higher dose pills. Many women may have their first migraine when using the COCP. In one-third of women, there COCP will have no effect on their migraine, one-third will get worse, one-third will get better. In female migraineurs with aura who also smoke, their COCP is absolutely contraindicated, as there is a considerable risk of stroke.

Migraine with aura, but not migraine without aura is associated with a 2 fold increased risk of ischaemic stroke[55], although the absolute risk in young women is low. For those with migraine with aura and smoke, there is a 5 fold increase[56] in the risk of ischaemic stroke in women.

One should stop the COCP in migraineurs when:

- Migraine frequency and/or severity increases
- New-onset aura occurs
- In unusual or prolonged migraine

POP is often the contraceptive of choice in migraine. As mentioned above, desogestrel is particularly helpful in PMM. However, there may be side effects including bleeding and weight gain. The bleeding can be helped by increasing the dose of progesterone to two tablets daily[53]. This in turn may further help the migraine.

12.4 Migraine and Pregnancy

Approximately 41% of all Irish pregnancies are unplanned[57], so inadvertent foetal exposure to medication is likely in those who have migraine. It is therefore important to counsel all women of child bearing age about this possibility when prescribing medication. Topiramate and valproate are particularly of concern as there are significant risks to a pregnancy. It is important to discontinue almost all medication prior to conception in women who are considering starting a family. For most women, their migraine improves in pregnancy, especially in the second and third trimester. However, 4-8% of women worsen during pregnancy[18]. 5-10% of migraine begins in pregnancy. Pre-pregnancy headaches almost invariably return following childbirth.

Management of migraine in pregnancy should focus on maximising life style measures initially. Low dose propranolol or amitriptyline may be used for prophylaxis in pregnancy if the migraine is particularly troublesome[18]. The use of triptans or NSAIDs in pregnancy is not recommended. They have been shown to cause decreased foetal body weight, increased miscarriage and an increase in foetal abnormalities in animals. They should be avoided if at all possible, but can very occasionally be used after discussing the need for treatment and the associated risks[41]. Oral steroids are not recommended. Women may benefit from greater occipital nerve (GON) blocks or use of the cephaly stimulator[45]. When theses therapies are not available, it is recommended that they should be offered paracetamol for the acute treatment of migraine[41]. They should take the lowest dose possible for the shortest time. If persistent vomiting is present with the migraine attacks, intravenous fluids with metoclopramide or ondansetron may help.

Post-partum, approximately half of the women with migraine have a recurrence within one month of giving birth. This may be delayed by breastfeeding. Most of the medications that are routinely used in migraine are excreted in breast milk. In general, medications deemed safe to be used in pregnancy are safe for breastfeeding, with the exception of diphenhydramine (present in Benylin). The prescribing information for sumatriptan says to “pump and dump” the breast milk.

12.5 Menopause

Menopause is defined at the absence of menstruation for one year. The average age for menopause is 53 years old. Peri-menopause is described as the decade preceding menopause. An increase in migraine during this period (see figure 11 below) is most likely due to fluctuating hormones and more frequent menstruation.

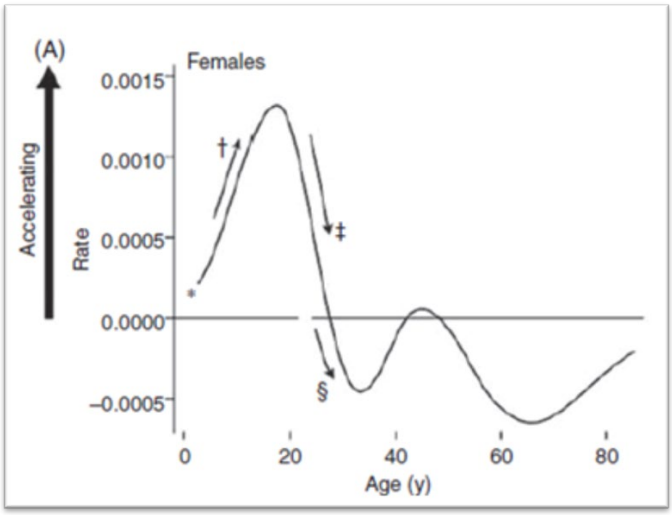

Figure 21: The rate of change in prevalence over age continuum in females. By kind permission Cephalalgia[56]

*The horizontal line at 0 on the Y axis indicates no change (i.e. acceleration or deceleration) †During childhood and early adolescence, the rate is accelerating quickly.‡ Rate begins to slow its acceleration. § Rate is decelerating.

Maintenance of a stable hormonal milieu is typically associated with fewer migraine attacks. This could be achieved during the peri-menopausal period by supressing ovarian activity using: estrogen supplements, estradiol implants, continuous combined hormonal contraceptive or the progesterone only contraceptive, desogrestel[59]. Trans-dermal estradiol administration (using the lowest effective dose that controls vasomotor symptoms) may be particularly helpful as absorption is less variable.

Following natural menopause, migraine improves in 60-70% of women. After surgical menopause, migraine symptoms worsen in 40-70%[18]. No recent study has been undertaken in this area. The increase in symptoms before menopause and the decline after spontaneous menopause tends to occur only in women with a history of menstrual associated migraine[18].

Hormone replacement therapy (HRT) is not contra-indicated in those with migraine with aura as HRT contains natural estrogen[59]. If using HRT, the dose of oestrogen is as important as the route of delivery. Too high a dose, coupled with surges in natural oestrogen, can trigger migraine with aura as well as causing symptoms of oestrogen excess including nausea, fluid retention, breast tenderness and leg cramps. As in the peri-menopausal period, transdermal low dose oestrogen is recommended[54]. Some post-menopausal women continue to produce significant amounts of oestrone and estradiol in extra-ovarian tissue, including the brain. Women with migraine and vasomotor symptoms in whom oestrogens are contraindicated may benefit from escitalopram or venlafaxine[60].

Section 13: Migraine in Sport

While physical activity and exercise is very often recommended for people with migraine, it can also be a trigger for migraine, especially in combination with other triggers (poor sleep hygiene, missed meals, dehydration, stress and changes in routine). Furthermore, if the patient does not follow proper warm-up procedure when partaking in sport, a migraine can be triggered.

Therefore, the advice to those who partake in sport is:

- Be well rested prior to planned sporting activities
- Eat a meal high in slow release carbohydrate a few hours earlier
- Always remain well hydrated
- Rest following exercise[61]

The first choice for acute treatment of migraine for the amateur sportsperson is an NSAID together with an anti-emetic. If triptans are needed, their potential impact on performance needs to be considered, particularly from a cognitive perspective. There are also theoretical concerns regarding the potential for coronary vasoconstriction. This is not a problem typically encountered in clinical practice. Triptan formulations such as sublingual ("melts") that are rapidly dissolved in the mouth and have rapid absorption. They are not faster acting but may be more convenient in the sporting context. A subcutaneous injection of sumatriptan does act faster than oral formulations (see section 8.2 Triptans).

Preventative treatment for people who participate in sport is complex, as certain medications may be unsuitable for several reasons. For example, beta blockers are banned in many professional sports and have obvious implications for limitations of performance as they reduce the heart rate and blood pressure. Topiramate, sodium valproate or pizotifen are reasonable alternative choices with appropriate monitoring for potential side effects[62].

Section 14: What the Future Holds?

There is a clear clinical need for specific acute and preventative migraine treatments. The most promising new preventative treatments are the Calcitonin gene-related peptide (CGRP) monoclonal antibodies, which have been developed after significant research which started in 1985 in Sweden. It is known that CGRP levels are raised in migraine patients, and it is believed that the CGRP system plays a fundamental role in the migraine attack. CGRP is one of the most potent naturally occurring vasodilators.

Four different CGRP agents have been developed by five pharmaceutical companies. They bind to CGRP molecule or its receptor. The first commercially available CGRP drug (erenumab) has recently been licenced in the US and Europe, These new anti-CGRP treatments are mainly for prophylaxis and are delivered by IM or IV injection once every 4-12 weeks. They appear to block the CGRP pathway and results in clinical trials are very promising[63,64]. Long term safety and durability testing is ongoing at present, and results are expected later in 2018 and 2019. Cost and access to these new treatments in Ireland are going to be the most significant going forwards. Never the less, the future for those with migraine is brighter now than ever.

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Appendix 1: Red Flags in Headache

When a person presents with a symptom of a headache, on initial patient assessment, one needs to out-rule a serious life threatening headache which needs immediate hospital referral or medical treatment. The mnemonic "SNOOP" is in common usage as a screening tool when a doctor assesses a patient with a headache. It is important to ask specifically about these symptoms as patients often do not volunteer them. They have been designed to help out rule potentially lifesaving headache, commonly referred to as red flags in headaches.

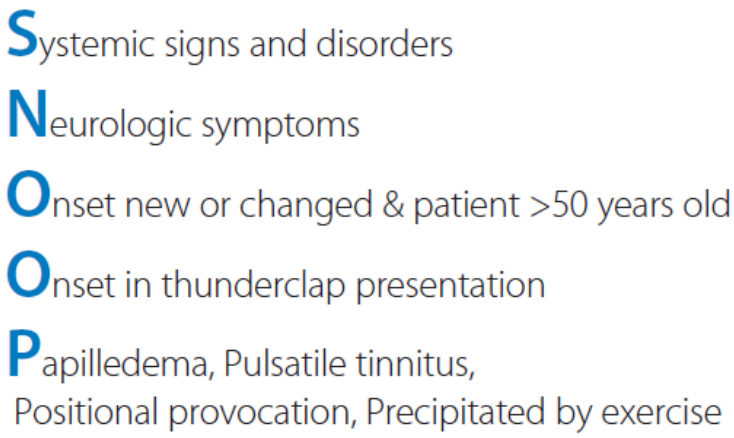

Figure 12: Red flags in headaches

A full clinical examination is always advised but clinical signs that would trigger immediate hospital referral are:

- Tenderness of temporal artery -suggestive of giant cell **arteritis**
- Misty vision or haloes suggestive of acute **glaucoma** (headache with painful red eye)
- Papilledema in optic fundus suggesting raised intracranial pressure

Appendix 2: Vertigo

Vertigo can be caused by both peripheral and central vestibular deficits. It can be described in several different ways[8] by patients :

1. Internal vertigo – a false sensation of self motion
2. External vertigo a false sensation that the visual surround is spinning or flowing
3. Position vertigo – occuring after a change in head position
4. Visually induces vertigo, tiggered by a large moving stimulus
5. Head motion-induced vertigo, occuring during head motion
6. Head motion induced dizziness with nausea

Vertigo is reported in 60% of those with migraine and may be any of the six different formats mentioned above. When vertigo occurs in migraine with brainstem aura, it is one of two brainstem symptoms which last 5-60 minutes before the headache starts. The other possible brainstem symptoms are dysartharia, tinnitus, hyperaccusis, diplopia, ataxia and a loss of conscious.

The vertigo which occurs in vestibular migraine:

- Lasts between 5 minutes to 72 hours
- Is not associated with any other brains stem symptom
- And is not present before the headache starts

The appendix of the ICHD-3 have diagnostic criteria for vestibular migraine.

Diagnostic criteria for vestibular migraine headache
A. At least five attacks fulfilling criteria C and D B. A current or past history of migraine with or without aura C. Vestibular symptoms of moderate or severe intensity lasting between 5 minutes- 72 hours D. At least 50% of episodes are associated with at least one of the following migrainosus features I. Headache has at least two of the following four characteristics a. unilateral location b. pulsating quality c. moderate or severe pain intensity d. Aggravation by routine physical II. Photophobia and phonophobia (noise sensitivity) III. Visual aura E. Not better accounted for by another ICHD-3 diagnosis

Table 3: ICHD–3 criteria for vestibular migraine headache A1.6.6[8]

Vestibular symptoms may be present for hours, days, or even months in those with more chronic migraine. They can be intermittent in nature, but may recur many times each day. The vertigo symptoms that occur in "migraine with brainstem aura" lasting between 5-60 minutes should not be confused with vestibular migraine as described above. Vestibular migraine was previously known as migraine-associated with vertigo/dizziness / migraine-related vestibulopathy / migrainous vertigo.

Appendix 3 Characteristics of Different Headaches

The chart outlines the main presenting features for the common headaches seen in general practice.

	Primary Headache Characteristics Comparison						
			Migraine	**Tension type headache**	**Trigeminal automonic cephalagias (TAC) e.g. cluster headache**	**Hypnic Headache**	**Medication overuse headache (MOH) with or without migranous features**
L	LOCATION		Unilateral	Bi-frontal; Band-like	Unilateral; Orbitotemporal	Unilateral but generally bilateral	Central, frontal, occipital
I	INTENSITY		Moderate - Severe	Mild - Moderate	Severe	generally moderate but can be severe	Mild, moderate or severe
Q	QUALITY		Pulsating/throbbing	Squeezing/pressing	Boring/penetrating	Dull, waken you from sleep	Squeezing/pressing/ pulsating
D	DURATION		4-72 hours	<4 hours	<4 hours	15mins - 3 hours	at least 4 hours over at least a 6 month period
F	FREQUENCY		Episodic (average 1 attach per month)	Episodic	≥ 1 per day for up to 8 weeks	≥15 per month	> 15 days/month
O	OTHER FEATURES						
	Aura		yes	No	No	No	Variable
	Photophobia/ Phonophobia/ other		visual,sensory or motor symptoms in 30% of people	No	Never	Only in 11%	Intermittently
	Nausea /vomiting		Yes	No		Relieved by caffeine	Variable
	Aggravated by Movement		Yes	No	No	No	No
	typical behaviour when headache is present		retreat to dark room	Little effect	Pacing, inability to remain still	lying aggravates the pain, wakens person from sleep	Variable
E	EFFECTS on activities of daily living		Variable	Mild - Moderate	moderate to severe	moderate	severe
	female to male		3:1	3:2	1:5	2:1	3:2

Figure 13: Characteristics of migraine compared to other headaches.
Adopted by kind permission Migraine Association of Ireland

The interview with the patient should ideally be a series of open-ended queries regarding headaches. So often, one finds people not able to give a detailed history as they want to forget the detail of the headache and just get something for the pain. This chart helps give structure to history taking to a parson who has a headache. If this chart is presented to the patient during the consultation, it can often reassure them about their diagnosis. It also helps the patient understand why you, the general practitioner, need such a detailed history.

Appendix 4: Headache Diary

There are several headache diary formats in smartphone and regular diary format. Migraine Buddy – American based headache diary which is available as an app on your smartphone. It can be send to your headache specialist by email or you can print it out in advance of your visit to your doctor.

Time Period: **8/25/16 - 9/13/17**
Attack Type: **All**

Number of Attacks	Attack Days	Attack-Free Days	Avg Attack Duration
93	143	243	19h:31m

#	Started	Lasted	Pain Level	Affected Activities	Potential Triggers	Symptoms	Auras	Pain Positions		Medication	Non Drug Relief Methods
								Left	Right		
1	06-Sep 15h:10m Location: Work	39h:51m	6	Hard to concentrate	Stress, Florescent lights	Can't concentrate, Constant pain, Moody	No	Left Front Head	Right Front Head	**Unsure** - 1x Solpadine Oral	
Notes: 2 hours explaining what needs to be done to Mathew on his 3rd day											
2	04-Sep 09h:42m Location: Work	06h:47m	4	Hard to concentrate	Florescent lights	Confusion/Light headed, Constant pain	No	Left Front Head, Left Eye		**Unsure** - No medication	**Unsure** - No relief
Notes:											
3	02-Sep 11h:52m Location: Social event	08h:13m	6	Slower [social]	Continued migraine, Florescent lights	Confusion/Light headed, Constant pain	Headache	Left Front Head, Left Back of Head (Upper)	Right Back of Head (Upper), Right Front Head	**Unsure** - 1x Solpadine Oral	**Unsure** - Dark room rest, Sleep
Notes: stress over FB posting issues											
4	01-Sep 17h:48m Location: Social event	06h:00m	6	Slower [social]	Travel	Constant pain	No	Left Eye	Right Front Head	**Unsure** - No medication	**Unsure** - No relief

Figure 14: Reproduced with permission from the patient

The Migraine Association of Ireland has produced this regular diary and is happy to send it to patients when requested. The diary can also be download from www.migraine.ie.

Month: ______________ The Migraine Association of Ireland

Day	Headache Pain Score (1-10)	Symptoms	Acute Medications	Time to Headache Relief (if any)	Possible triggers
Monday					
Tuesday					
Wednesday					
Thursday					
Friday					
Saturday					
Sunday					
Monday					
Tuesday					
Wednesday					
Thursday					
Friday					
Saturday					
Sunday					
Monday					
Tuesday					
Wednesday					
Thursday					
Friday					
Saturday					
Sunday					
Monday					
Tuesday					
Wednesday					
Thursday					
Friday					
Saturday					
Sunday					

Figure 15: Sample of migraine diary by kind permission of Migraine Association of Ireland

Appendix 5

3-6 Monthly follow-up appointment

1. Review headache diary – empowers patient to help themselves
2. Ask how many headache days per month and how many "crystal clear days" per month the patient has
3. Check severity of headaches
4. Any change in headaches or associated symptoms i.e. neck, facial pain
5. Review mood, lifestyle (school/employment), encourage exercise,
6. Check weight

Medication:

7. Check prophylactic medication consumption watch for MOH
8. Check if taking medication for other reasons
9. Advise when to come off prophylactic meds – need to be 6-12 months headache free

10. Give patient realistic expectations when starting treatment, as many chronic headaches are difficult to treat
11. Additional support may be available from the Migraine Association of Ireland www.migraine.ie Information & support 1850 200 378

If well – review in 6/12

- Persistent symptoms despite max tolerated prophylactic meds for 2-3 months – consider change in preventative therapy

- Remind patients that a regular lifestyle may well improve their migraine

Contribution of the Authors

Dr Mary Kearney has developed a special interest in primary headache disorders and she identified the need for a Quick Reference Guide (QRG) for primary care physicians. As a member of the Irish College of General Practitioners (ICGP), she submitted a proposal for a QRG on Headache to the ICGP Quality in Practice committee. The committee felt that the subject material was very extensive and therefore suggested that there should be two separate documents, one for migraine and one for other primary headache disorders.

Dr Kearney has collaborated with Esther Tomkins (Clinical Nurse Specialist, Beaumont Hospital) and Dr Martin Ruttledge (Consultant Neurologist), to produce this educational material. Dr Kearney has also visited a number of specialist headache clinics throughout the country and she is grateful for the support and advice received. In addition, she has received helpful advice from the Migraine Association of Ireland (MAI).

Education in Practice

If a patient has recurrent headaches:

Do you check how many days a month they have headaches?
Do you check if they have medication overuse?
Do you ask them to keep a headache diary?

Do you consider co-morbid conditions when prescribing prophylactic medication for migraine?

Do you ask parents/gaurdians of children with recurrent abdominal pain if there is a family history of migraine?

Audits on Aspects of Migraine Relevant to Clinical Practice

Suggested audit topics include:

1. Review all those patients who have been prescribed triptans – review the history taken and reaudit the patients in 3/12 where appropriate
2. Review headache patients who also have hypertension. Consider changing medication to propranolol or candesartan.
3. When reviewing those on the contraceptive pill, ask about headache and smoking.

How Patients were involved in the Creation of this Guide

This document was reviewed by the MAI, and five different patients including two patients who are also health care professionals and a member of the International Headache Society (IHS).