The State of the Migraine Nation

Migraine care

Rapid research review
Foreword

This is the last in a three-part series of evidence reviews that The Migraine Trust is releasing to inform our larger ‘State of the Migraine Nation’ project.

As our charity celebrates our 55th anniversary this year, our ‘State of the Migraine Nation’ project seeks to take stock of all the progress our community has made, identify the issues that matter most to our community and draw together priorities for future policy change to improve the lives of people affected by migraine.

This review series is just one of the many ways we’re collecting new evidence as part of this programme of work, all leading up to the publication of a final report at our 18th Migraine Trust International Symposium (MTIS) Public Day in London on 13 September 2020. The recommendations in the final report will form the basis of our charity’s campaigning agenda for the next decade.

The first two rapid reviews in this series looked at migraine in a broad sense, exploring the characteristics of the migraine population and the impact that migraine has across individuals and UK society.

This review switches focus to look at migraine care. Based on surveys, workshops and interviews we’ve recently held with people affected by migraine, we know that many people feel let down by the care and treatment they receive and are struggling to manage their migraine effectively.

We’ve also heard from migraine and headache professionals that while the NHS is doing a lot of things right when it comes to migraine, there continue to be significant organisational and system level barriers to effective migraine management. This review is part of our attempt to understand these issues in more detail, so that we can start to consider how to overcome them.

We hope you enjoy reading the findings from this review. Please let us know what you think by emailing policy@migrainetrust.org or tweeting us using the hashtag #MigraineNation.

Gus Baldwin
Chief Executive
Main messages

Setting the scene
Migraine is a serious neurological condition which can have debilitating effects such as pain, nausea and visual disturbances. With around 10 million people in the UK affected and migraine having such significant impacts, The Migraine Trust wanted to explore research about migraine prevention and care. This rapid review draws on 250 studies about migraine care in the UK and elsewhere. It sought to summarise trends in research about a wide range of care, rather than examining the clinical effectiveness of specific medications. International research was included because the goal was to explore the range of evidence, not solely what has been researched in the UK.

Treating migraine attacks
During a migraine attack, people can experience significant pain and disability. The aim of ‘acute treatment’ is to reduce the intensity and/or duration of symptoms during a migraine attack such as pain and nausea. A variety of medications have been researched. Simple pain killers, triptans and anti nausea medicines have been found to be effective, though most do not completely alleviate pain for most people, and some have side effects.

Other treatments for relieving symptoms during migraine attacks include portable machines that send magnetic impulses to the nerves, cognitive behavioural therapy and hypnotherapy. These have been less extensively researched but there are some favourable findings.

Preventing migraine attacks with medication
Preventive medications are available to reduce the number and duration of migraine attacks amongst people living with migraine. These medications may be prescribed when people experience migraines regularly. Some antiepileptic drugs, botox, and some beta blockers and ACE inhibitors have been found to be effective. These medications do not ‘prevent’ migraine completely, as people usually still experience attacks, but they may help to reduce the number of attacks, the length of attacks and the severity of pain or disability.

A new class of medication known as CGRP receptor antagonists has recently been introduced. These have been found to be useful for both acute and preventive treatment, though as with most medications, there may be side effects.
Preventing migraine attacks with other initiatives
Other initiatives researched to reduce the number or severity of migraine attacks include avoiding factors that may trigger migraine, behavioural therapy, acupuncture, spinal stimulation and others. The evidence for these initiatives varies, but they can be helpful for some people, particularly for increasing people’s confidence in managing migraine and their quality of life.

Digital interventions such as smartphone apps and online resources are available but there is minimal research about their effectiveness. Tools such as digital diaries or reminder prompts have been found to increase self care and help people see patterns in their condition to support better care.

Educational interventions in the workplace have been tested in some countries. Such interventions have been found to improve people’s understanding of migraine so they can avoid triggers. However these programmes generally have not educated people’s work colleagues or employers about providing supportive work environments. This may be an important area of future study.

Enablers and barriers
Research has identified a number of factors that help and hinder effective care for people with migraine. Some of the most commonly identified enablers include involving people in coproducing their care; supporting self care; empathetic and well informed health professionals; appropriate diagnosis; and a pathway which provides holistic support in primary care with access to specialists where needed. Some of the most commonly identified barriers include lack of awareness about migraine amongst the public, health professionals and employers; delayed diagnosis; inadequate use of preventive medications; lack of adherence to treatment; and not trying treatments other than medications.

Knowledge gaps
Most research does not compare treatments with one another or explore the effectiveness for people with different types of migraine or various demographic characteristics. Therefore it is not possible to set out the ‘best types’ of care. There is little research about public health or environmental strategies to prevent migraine, what could be done to develop supportive workplaces or the cost effectiveness of care. Much of the research focuses on medications rather than strategies for identifying and educating people with migraine, their families and health professionals. There is a real opportunity in the UK to strengthen the evidence available about the best care for people with migraine, focusing on much broader approaches than just medications.
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Acknowledgements
This rapid review was produced for The Migraine Trust by an independent organisation, The Evidence Centre, in January 2020. To maintain the independence of the review, it has not been edited by The Migraine Trust. The review summarises the findings from published research. That research does not necessarily reflect the views of The Migraine Trust or The Evidence Centre.
Background

Scope

More than 10 million people in the UK live with migraine and this can have significant impacts, affecting people’s health, functioning, home life, work, quality of life and self confidence. It may also cost the UK economy around £10 billion per year in healthcare costs and lost productivity. Therefore it is essential that effective and accessible care and support is available.

Migraine is the third most common health condition in the world, after dental caries and tension type headache. It is more common than diabetes, asthma and epilepsy combined. About one in five working age adults in the UK live with migraine (23% of those aged 15 to 69 years).

Migraine is a complex condition with a wide variety of symptoms, often including painful headaches, vomiting, disturbed vision and sensitivity to light, sound and smells. The symptoms vary from person to person and between migraine attacks. Migraine can be chronic (symptoms present on at least 15 days per month) or episodic (symptoms present less than 15 days per month), and change over time.

Given the complexity of the condition and the varied symptoms and impacts, The Migraine Trust wanted to understand what is known about approaches to prevent and treat migraine.

This rapid review addresses the questions:

- What types of treatments have been researched for people living with migraine and what is their impact?
- What public health and self care approaches have been researched to help prevent migraine?
- What does research suggest are the barriers and enablers to care?

This review forms a part of The Migraine Trust’s ‘State of the Migraine Nation’ project which seeks to identify the issues that matter most to people with migraine and draw the migraine community together around shared priorities for change.
**Approach**

The Migraine Trust wanted to get a sense of what is known about migraine prevention and care and where there may be gaps in existing knowledge. To identify relevant research, an independent team searched 18 bibliographic databases. Studies were eligible for inclusion if they:

- were published in a journal
- were published between January 2000 and December 2019
- were a research study including empirical data
- focused on prevention or treatment of migraine in the UK or internationally. The Migraine Trust was interested in the best possible care for people in the UK, but recognised that important research about prevention and care has also been published internationally.

Studies of any research design could be included. Randomised controlled trials (hereafter referred to as ‘trials’) and systematic reviews (hereafter ‘reviews’) compiling other research were prioritised most highly to make sure there was a focus on high quality evidence. Where no such studies were available other designs were included. This is because the aim was to show the range of approaches, not to systematically assess the effectiveness of each approach.

More than 2,500 studies about migraine care were identified and read. Themes from the research were summarised narratively, using a sample of about 10% of identified studies as examples (250 studies). Systematic reviews summarising research and studies from the UK were prioritised as examples.

A systematic process was used to identify studies, but the rapid review did not aim to include all available research or focus on the effectiveness of individual treatments. The Migraine Trust is carrying forward a varied programme of evidence gathering, including by holding workshops and running surveys, to better understand the state of the nation related to migraine care and treatment in the UK. This rapid review is one step in that journey.

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1 The databases were Ageline, Academic Search, Cumulative Index of Nursing and Allied Health Literature, the Cochrane Library and Controlled Trials Register, Current Contents, EMBASE, Global Health, Google Scholar, IngentaConnect, PMC, PsycINFO, Pubmed, PubPsych, NHS Evidence, ScienceDirect, Scopus, Web of Science and WorldWideScience.
Treating migraine attacks

Medications

Broad themes
There are many types of migraine care. Broadly speaking, care can be divided into acute management and preventive strategies. The aim of acute management is to help people cope with symptoms during a migraine attack, seeking to restore function and reduce side effects (adverse events). Research about acute management focuses mainly on medications, of which there are many. The choice of treatment may be based on the characteristics of migraine, other conditions that people have, treatment preferences and availability.\(^4\)

In contrast, preventive strategies aim to reduce the likelihood that people will experience a migraine attack and to reduce the pain and disability experienced during an attack. These strategies can include medication, but may also involve other types of medical and psychological care as well as self care.

This rapid review first explores approaches for treating migraine attacks (acute management) and then summarises research themes about preventive strategies. The aim is to illustrate the range of approaches that have been researched rather than to systematically assess the effectiveness or potential harms of each approach. The review does not seek to identify the ‘most effective’ medications, for example, nor does it attempt to summarise all of the evidence about particular medications or other interventions.

Acute treatment has traditionally focused on analgesics, combinations of analgesics with caffeine, ergotamines and triptans. Newer approaches target calcitonin gene related peptide (CGRP) and serotonin receptors, some of which are not yet widely available in the UK. Approaches targeting other receptors have been investigated, but generally have not been found to be effective in most trials to date.\(^5\)

Appendix 1 summarises themes in research about some of the main medications used when people have a migraine attack. This is not meant to be an exhaustive list of medications and not all of them may be available or highly used in the UK.
Acute care for adults

It is difficult to suggest that one treatment is more effective or safer than others because there is much variation in the treatment approaches, doses, participant types and study designs used. The outcome of treatment may depend on migraine characteristics, demographics, dosing, medications people take at the same time, the length of treatment and how treatment is administered.⁶,⁷

Some reviews have compared different medications for adults experiencing a migraine attack, but overall there is no consensus about which medications are most effective. As an example, a review of 44 studies of migraine pain relief in the emergency department recommended prochlorperazine based on high certainty evidence; lysine acetylsalicylic acid, etoclopramide and sumatriptan based on moderate certainty evidence, and ketorolac based on a low level of evidence. The reviewers recommended strongly against the use of dexamethasone, based on moderate certainty evidence, and granisetron, haloperidol and trimethobenzamide based on a low level of evidence.⁸

A review included 11 articles about acute treatment of migraine during women’s menstrual periods, and 25 studies about preventive treatment. Acute treatment included triptans, combination therapy, prostaglandin synthesis inhibitor and ergot alkaloids. Preventive treatment included triptans, combined therapy, oral contraceptives, oestrogen, non steroidal anti inflammatory drugs, phytoestrogen, gonadotropin releasing hormone agonist, dopamine agonist, vitamin, mineral and non pharmacological therapy. There was evidence that triptans were effective for acute treatment and short term prevention of menstrual migraine.⁹

For the purposes of this rapid review, the exact medications are perhaps less important than the key messages:

- a number of medications have been tested for treating pain and nausea during migraine attacks
- each medication has advantages and limitations
- some medications have been found to be more effective than others but there is no one medication that has been found to be universally effective
- the dose, the way the treatment is administered, people’s previous and current medications and characteristics of the migraine attack all likely influence effectiveness and safety
- having a variety of options to try and expert advice about when and how to use different medications is likely important
- people may experience painful medication overuse headache if some medications are used for too long or at too high a dose
There does not appear to be a lot of research comparing the costs of different classes of medication, but a small number of examples exist. For instance a study using data from Brazil compared the cost of providing the lowest level of medication when someone was experiencing a migraine attack (general pain killers) versus ‘stratified management’ whereby a triptan was used immediately. Data modelling suggested that a stratified approach would reduce overall costs by 6%, equating to more than US$7m per annum.¹⁰

Acute care for children

Some studies have specifically explored medications for migraine attacks in children and adolescents. A review of 31 studies of treatment for migraine in children in the emergency department examined IV fluids (1 study), non specific analgesic use (2 studies), dopamine receptor antagonists (5 studies), valproic acid (2 studies), propofol (1 study), magnesium (1 study), bupivacaine (1 study), triptan medications (13 studies), and dihydroergotamine (3 studies). Effective analgesic treatments included ibuprofen and to a lesser degree acetaminophen. Ketorolac was found to be less effective than prochlorperazine. Of the phenothiazines, prochlorperazine was found to be most effective. Of the triptan medications, almotriptan, rizatriptan, zolmitriptan nasal spray, sumatriptan nasal spray, and combined sumatriptan / naproxen were effective. The reviewers concluded that ibuprofen, prochlorperazine and certain triptan medications are the most effective and safe agents for acute management of migraine in children.¹¹

Another review included 27 trials, most of which focused on triptans. Ibuprofen relieved pain in children. Triptans were effective for pain relief in children and adolescents but had higher rates of minor adverse events.¹²

Research amongst children with migraine in the USA found that triptans benefited 65% of those with chronic migraine and 88% with episodic migraine.¹³

Other reviews reinforced that ibuprofen, aspirin (in children and adolescents) and triptans (mainly in adolescents) were effective for relieving migraine pain. For adolescents, oral sumatriptan / naproxen and zolmitriptan nasal spray relieved migraine pain within two hours. No acute treatments were found to be effective for migraine related nausea or vomiting in children. Some triptans were effective for migraine related sight and hearing disturbances.¹⁴,¹⁵,¹⁶
Other interventions for acute care

Medications are the most commonly researched treatment for use during migraine attacks, but there is research available about some other interventions.

Neuromodulation

Non invasive brain stimulation has been tested for both managing migraine attacks and seeking to reduce new attacks. This approach involves sending magnetic or electrical impulses to nerves, seeking to reduce pain. A review of eight studies found that direct current stimulation, but not transcranial magnetic stimulation, may reduce migraine pain and lower the amount of painkillers people take. The evidence available was of low quality. The reviewers concluded that direct current stimulation could be explored further for pain control to reduce the intake of painkillers.17

Other studies have suggested that single pulse transcranial magnetic stimulation may be effective and well tolerated during migraine attacks. A study in the UK examined transcranial magnetic stimulation in routine clinical practice in people living with migraine with and without aura. A device was available in people’s homes for a three month period. Six out of ten people reported that the device was effective for reducing or alleviating migraine pain (62%). Half said the device helped to reduce nausea (52%), light sensitivity (55%) and noise sensitivity (53%). There was a reduction in reported monthly days with headache amongst people with episodic migraine and chronic migraine. There were no serious or unanticipated adverse events.18

In the USA a non invasive portable vagal nerve stimulator has been tested for treating migraine attacks. In a small study, 30 people with migraine with or without aura received two 90 second doses at 15 minute intervals delivered to the right cervical branch of the vagus nerve. This could be repeated for up to four migraines within a six week period. Participants administered the treatment to themselves when they experienced moderate or severe pain or after 20 minutes of mild pain. One out of five of those with moderate or severe headache were pain free within two hours (22%). There were no unanticipated or serious adverse events. Around half of participants experienced minor adverse events such as neck twitching, raspy voice or redness at the device site. The researchers suggested that for some people, a portable vagal nerve stimulator may be an effective and well tolerated treatment for acute migraine.19

More research may be needed to understand for whom these approaches are most effective.20
Cryotherapy

Cryotherapy is a common non pharmacological approach to pain relief, but not much evidence is available about its effectiveness for treating migraine attacks. A small UK study of intranasal evaporative cooling found that nine out of ten participants had pain relief within two hours that was sustained for 24 hours (87%). This was a very small pilot study and there was no comparison group so the results were not meant to be generalisable, but the researchers concluded that further research in this area may be worthwhile.21

Behavioural and psychological therapies

Cognitive behavioural therapy (CBT) focuses on developing coping strategies and restructuring how people think about things, including the pain experience in migraine. A number of studies have examined cognitive behavioural therapy as a preventive strategy for migraine and these studies are described overleaf. However a small number have specifically examined whether this approach has impacts on acute migraine attacks.

For instance a review of 14 studies found that cognitive behavioural therapy reduced acute migraine headache pain in children and was more effective than standard pain relief medication. Some of the studies found that the benefits remained one year after children had taken part in cognitive behavioural therapy.22

A review of eight studies examined hypnotherapy techniques alone or in combination with other non pharmaceutical techniques such as visualisation, relaxation and pain displacement techniques. Hypnotherapy and relaxation techniques were reported to be effective in pain management in people with migraine, including during acute attacks.23
Other interventions

Hyperbaric oxygen therapy is the administration of 100% oxygen at high pressure. A review of five trials suggested that hyperbaric oxygen therapy relieved pain during migraine attacks. There was no evidence that it prevented migraine episodes, reduced the incidence of nausea and vomiting or reduced the need for rescue medication.\(^{24}\)

Researchers in the USA examined the impact of inhaling cannabis on migraine attacks in adults. Data were self reported via a smartphone app and there was no comparison group. People reported that cannabis reduced migraine pain by about 50%. Men reported larger reductions than women. The effect appeared to diminish across time and people needed to use larger doses to achieve the same effects.\(^{25}\)

Summary

The majority of research available about treating migraine attacks focuses on reducing pain and/or nausea through medications. Various medications are available and have been researched in some depth. A number of these have been found to be safe and effective in children and adults. A smaller number of studies have explored non pharmaceutical treatments such as devices targeting nerve cells. Whilst there have been some positive trends in safety and effectiveness, the evidence base is sparse about non pharmacological alternatives and this may be an area worth considering further.

Narrative descriptions and clinical practice guidelines for treating migraine attacks emphasise the importance of early treatment, choosing a route of administration based on the individual migraine attack and providing education about lifestyle factors that can exacerbate migraine, including trigger avoidance and medication overuse.\(^{26}\) Thus it may be important for medications to be seen as one part of a broader care strategy for managing migraine attacks. Just as important as addressing the pain during attacks is concentrating on reducing the number and severity of those attacks. It is to such approaches that the review now turns.
Preventing migraine attacks

Approaches for the prevention and long term management of migraine include strategies to raise awareness about migraine causes and symptoms, self management, medications and medical devices, acupuncture and psychological therapies amongst others. This section describes examples of each of these approaches in turn.

Preventing the condition from developing

Researchers have explored ways to support people living with migraine to self care, avoid triggers and lead healthy lifestyles (see overleaf). These strategies are about reducing the number of migraine attacks that people experience, not preventing the condition from developing in the first place (primary prevention). A number of studies have examined how to prevent the development of conditions such as cancer or diabetes,27,28,29,30,31,32 for instance, but the reviewers identified no such studies about preventing someone from ever experiencing a migraine.

The lack of research about primary prevention is perhaps surprising given that the World Health Organization classifies migraine as one of the most disabling conditions, comparable in impact to psychosis, dementia and quadriplegia.33 Migraine is the seventh most disabling health condition across the world,34 yet there appears to be a lack of research about ways to stop the onset of migraine in the first place.

This may be because the exact cause of migraine is unknown. Migraine attacks are thought to be the result of unusual brain activity temporarily affecting nerve signals, chemicals and blood vessels in the brain. It is not clear what causes these changes in brain activity. It is possible that genetics influences whether people are more susceptible to experiencing a migraine attack due to a specific trigger, such as hormones, emotions, dietary factors, medications and environmental factors.
As migraine may be triggered by certain factors, it is conceivable that public health campaigns could educate people, workplaces and educational institutions about potential risk factors and put steps in place to avoid common triggers. There could be changes to the physical environment such as lighting, and policy changes to reduce access to certain food triggers. These interventions could be undertaken at a population level to see whether regions that implemented them then had a lower proportion of people living with migraine.

The reviewers searched 18 databases across a 20 year period for research about public health interventions that may prevent migraine from ever developing, but identified no studies about this. The preventive approaches researched all focused on ways to identify people with migraine and/or support them to reduce the number of migraine attacks they have or manage their migraine symptoms and impacts. Throughout this review ‘prevention’ therefore means minimising and managing migraine, not preventing it from ever occurring.

**Educational interventions**

A mainstay of approaches to help people live well with migraine is providing education about the condition, but there are differences in how and when this is done. A review of 14 trials found that migraine education may help to reduce headache frequency and disability and improve quality of life in the medium term.35

A number of different types of education have been tested, including recruiting community members to learn about migraine and perhaps thus identifying people in need of support; education provided by charities, lay people and health professionals for those diagnosed with migraine; education in workplaces; and educational programmes available online for people to participate in at home. This section provides examples of research about some of these. Only selected examples are provided as the aim is to give a flavour of the material, not to summarise every study available.
Education in the community

Migraine may be underdiagnosed and this can be a barrier to receiving appropriate care. A number of people living with migraine may not consult healthcare professionals about their condition or they may lapse from care. Several tools are available to help screen to see whether people are living with migraine and the impact of migraine on their lives.\textsuperscript{36,37} Such tools have been tested in the community and in work places to help identify people who may benefit from preventive care.\textsuperscript{38}

For instance, researchers in Italy sent a letter with a migraine identification test to all households in one region and placed posters in general practitioner (GP) waiting rooms. The letter described the impact of headache on quality of life and included a three item migraine screening test with questions about disability, nausea and light sensitivity. If people experienced headaches, they were invited to contact their GP and to have a free consultation with a headache expert.\textsuperscript{39} Nine out of ten of those who came forward for screening had migraine and seven out of ten had never consulted a health professional about headache. Follow up over time found that two thirds reported an improvement in their health status. This included reduced average pain intensity, reduced average number of days with headache per month and reduced headache duration. The researchers concluded that a ‘single shot’ educational campaign had short and longer term benefits for identifying people with migraine and ensuring they received preventive care.\textsuperscript{40}

In France free conferences were held in six large towns following a wide public information campaign. The aim was to provide education about migraine and migraine care. People provided feedback at the end of the conferences and after three months. This approach recruited mainly people who said that their migraine pain was ‘severe’, most of whom had already consulted health professionals about their condition. However most were not receiving preventive treatment. After three months, more than half of the participants had visited a professional about migraine and there was a significant improvement in reported migraine related disability.\textsuperscript{41} The programme did not achieve its aim of identifying people without a diagnosis, but found that there was significant unmet need for education and support amongst those already diagnosed.
Education in healthcare

Self management education programmes are common for long term conditions such as diabetes and arthritis, but they may be less readily available for people with migraine in the UK. Migraine education programmes have been tested with positive results in other countries, but the research available is usually not high quality. For instance, in the USA a small study tested an eight week migraine self management education programme which included verbal sessions and written, video and online materials. There was a reduction in disability, acute medication use and frequency of migraine.\textsuperscript{42}

Elsewhere in the USA, almost 300 people with migraine took part in an education programme. About half (46\%) reported a 50\% or greater reduction in the number of headaches. Over a year, participants reported fewer headaches and improved quality of life. These improvements were greater amongst those who were more worried about their headaches at the outset. There were also improvements in people’s self confidence in managing migraine and their satisfaction with care. This study did not have a control group so it is difficult to conclude that the results are due to the education programme.\textsuperscript{43}

Other researchers in the USA tested adding patient education to routine medical management of adults with migraine. In a randomised trial, 100 people attending a specialist headache clinic were allocated to receive or not receive lecture style education about migraine causes and management. The course comprised three classes taught by trained lay people with migraine. At six month follow up the education group had a greater reduction in migraine disability, average headache days per month, medication overuse and need for acute therapy. They were more likely to be taking their preventive medication and had fewer unscheduled healthcare visits.\textsuperscript{44}

A review found that such self management support interventions could improve outcomes over usual care, but the impact was small. Interventions were more effective than usual care in reducing pain intensity, mood and headache related disability, but had no effect on the number of migraine headaches. The most effective interventions had explicit educational components, mindfulness components and were delivered in groups.\textsuperscript{45}
Online education

Various educational courses are available online. An online intervention to increase self confidence in migraine self management was tested in the USA. Compared with a control group, those using the online system reported improved self confidence, increased use of relaxation, increased use of social support, decreased depression and decreased stress.\(^{46}\)

Online education need not be long. In the USA, an hour long online education video was tested amongst people with migraine experiencing significant depressive symptoms. Follow up to 12 weeks found improvements in average pain level, depression and migraine related disability. The researchers concluded that brief online education is practical and effective for enhancing self management skills.\(^{47}\)

Other examples of online initiatives are provided overleaf in a section about behavioural therapies.

Workplace interventions

Research has begun to examine the benefits of workplace interventions to provide migraine education and support. The research available to date focuses on organisations providing screening to identify people with migraine and/or educational sessions to affected employees. Examples are provided in Box 1. No examples were identified of programmes where workplaces sought to make environmental changes, sought to educate employers and employees without migraine or took other steps to create a supportive work environment.

Other educational initiatives

Even simple information leaflets may be appreciated and impactful. In Spain, researchers found that educational brochures for people attending neurology clinics for migraine were well read (81%). Three quarters of people said that the brochures increased their knowledge about migraine and half said the brochures helped them be more active in migraine self management.\(^{48}\) This study did not follow up to see whether there were any changes in self management behaviours as a result of reading the leaflets or whether leaflets were associated with fewer migraine attacks or reduced pain severity.

In the USA people with migraine received verbal advice from a pharmacist and written educational materials. Two thirds of people who had not consulted a doctor about their migraines went on to do so or said they intended to do so after the pharmacist advice.\(^ {49}\)
Box 1: Examples of workplace based interventions

**Identifying people with migraine**

ID Migraine is a validated migraine screening tool. A study in Turkey found that this tool could be used in the workplace to identify people with migraine and explore the impact on their productivity. Employees from four companies used the tool which was found to have a good level of accuracy. The researchers did not report any intervention set up to support people with migraine once they were identified.

A similar study in Brazil used a translated version of a well known MIDAS tool. This helped to identify people working in the oil industry with migraine of different levels of severity. The tool was easy to administer in the workplace. The researchers did not set up a support intervention after identifying people with migraine.

**Education for employees with migraine**

In the USA, a migraine education programme was implemented in three companies. Employees who completed a screening questionnaire and were identified with migraine received three lots of printed materials and six emailed newsletters about migraine management. Six months after the last mailing, employees were surveyed. After the programme, participants reported less migraine related disability and less productive time lost. The total costs associated with migraine decreased 15%. The researchers concluded that simple workplace programmes which screen employees for migraine and provide them with written materials can improve people’s wellbeing whilst reducing lost productivity.

Elsewhere in the USA a work based migraine education programme was tested at a large financial services organisation. The programme included webinars, emailed educational tips and resources on the company intranet. 243 employees were surveyed at the start of the programme and after six months. There were no reductions in the number of migraines but there were reported improvements in migraine severity, workdays missed and effectiveness at work during migraine. Participants reported taking action to identify and reduce migraine triggers.

Another study in the USA delivered a 45 minute standardised educational programme to 492 participants at eight companies. One month after the session there was improved quality of life, increased use of self management techniques and decreased headache related disability. This included migraine and other headaches.
Computer assisted education
Another study in the USA tested an employee education programme in six locations. A multimedia computer based programme was set up at a kiosk. Through the kiosk, employees were questioned about the type, severity and number of headaches, the impact of headaches on their daily activities and lost workdays as a result of headache. This included migraine and other headaches. Participants then received personalised reports about their headaches. Most participants were given access to an onsite neurologist and additional educational information. One in five people reported they saw a doctor about headache after their first kiosk session. After three months, half of the participants said they had better understanding of headache and improved symptoms. There was a reduction in use of the emergency department and fewer days off work.55

Education plus medication
Another study in the USA examined a workplace educational and support programme. The intervention included education to identify and avoid migraine triggers, coaching on dietary and lifestyle changes and prescriptions for medications to prevent and treat headaches. The number of participants providing follow up feedback was small, but the number and severity of headaches reduced as did people’s perceived disability.56

In Spain, a workplace migraine intervention was tested for 436 postal service employees. The intervention consisted of advice from occupational health doctors and rizatriptan 10mg for symptomatic treatment of two subsequent migraine headaches. Doctors also prescribed medications for migraine prevention. Compared to before the intervention, people had fewer days disabled by migraine. Total migraine related productivity costs to the company per migraine headache were 34 Euros per person before the intervention. This decreased to 14 Euros per person during the first headache and 5 Euros per person during the second headache following the intervention.57

Relaxation / exercise
In Italy a workplace relaxation exercise programme was tested for people with migraine or other headache and neck pain. Employees of government departments took part in relaxation exercises and received feedback about their posture for six months. Compared to people who did not take part in the programme, participants reported reduced headache, neck and shoulder pain. The programme was able to be delivered at low cost.58
Self care initiatives

In a small UK study people with migraine described five different types of preventive care that they used: healthcare services, medication, complementary therapies, social support, and lifestyle and self help initiatives. People wanted to have a central role in their own care and they adapted headache management approaches to suit their needs and preferences.⁵⁹

There are a number of things that people living with migraine can do to manage their condition, including avoiding common triggers, leading an active lifestyle and considering their dietary intake. This section provides examples of themes in research about self care.

Dietary interventions and supplements

Food may be a trigger for migraine attacks. Various studies have explored avoiding foods or supplementing with vitamins to reduce migraine, with mixed results.

Some believe that intolerance to certain foods may trigger migraine. A trial in the UK tested the value of testing for food intolerance amongst adults with migraine and advising them to avoid specific foods for 12 weeks. There was no difference in the number of migraine headaches or disability.⁶⁰

A review of 13 trials found that taking omega fatty acids (fish oil supplements) had no effect on the number and severity of migraine attacks but did reduce the duration of attacks (average reduction 3.5 hours).⁶¹

A review of 14 trials examined dietary supplements and herbs for preventing migraine. The reviewers concluded that whilst some dietary supplements and herbs have positive trends, the studies had methodological shortcomings so it was not possible to draw firm conclusions or differentiate between types of supplements.⁶²

Another review of 18 trials about vitamins and/or minerals for preventing migraine found that most research focused on coenzyme Q10 and magnesium. Neither coenzyme Q10 nor magnesium appeared to reduce migraine frequency, duration or severity in adults.⁶³ However a review of four trials found that coenzyme Q10 supplements (an antioxidant) reduced the frequency of migraine attacks by about two per month. These supplements had no effect on migraine severity or the duration of migraine attacks.⁶⁴
A review of 11 trials found mixed evidence about riboflavin, a B vitamin. Five trials found a preventive benefit in adults. Four trials found a mixed effect in children and adolescents. Two trials of combination therapy found no benefit. Adverse reactions with riboflavin were generally mild. The reviewers concluded that riboflavin is well tolerated, inexpensive and effective for reducing migraine headache frequency in adults, but more research is needed.

A trial in the USA examined the efficacy and tolerability of simvastatin plus vitamin D for adults with episodic migraine. Compared to placebo, simvastatin plus vitamin D was associated with a greater decrease in the number of days with migraine per month. Adverse events were similar in both groups.

It has been suggested that gut microorganisms may influence disease outcomes, including in neurological conditions such as migraine. A review examined whether probiotics to improve gut health may help prevent migraine. Two trials were identified with conflicting results. One trial found no significant change in the number or severity of migraine attacks. The other reported significant improvements.

Some researchers hypothesise that not drinking enough water might trigger migraines. A study encouraged people with migraine and other recurrent headaches who did not drink a lot of fluids to drink 1.5 litres water per day. In addition they were given suggestions for stress control and good sleep habits. A control group received stress and sleep advice alone. At three months, drinking more water was associated with improved migraine specific quality of life. There was no reduction in days with headache.

In Italy, a weight loss programme for obese adolescents with migraine was associated with reduced headache frequency and intensity, less use of acute medications and reduced disability.
Avoidance of other triggers

Sometimes people with migraine are advised to avoid all possible trigger factors, but a randomised trial from Australia suggests that this may not be the best advice. One group of people with recurrent headaches, including migraine, was advised to avoid all triggers. Another group had gradual exposure to selected triggers to desensitise them. Avoiding triggers did not reduce the number of headaches or medication consumption, but the graduated exposure programme was associated with significant improvements. The researchers concluded that avoiding all triggers is not an effective prevention strategy and that graduated exposure to triggers is promising and could be explored further.\textsuperscript{70}

Some people with migraine may be hypersensitive to visual stimuli. A small UK trial suggested that individually prescribed coloured filters for eye glasses might help to reduce symptoms.\textsuperscript{71}

In the USA, people with chronic migraine also tested filter coatings for eye glasses. One group tested a therapeutic filter that blocked bright light. A comparison group used a filter that was less strong. Participants wore lenses with one of the filters for two weeks, went without any lenses for two weeks then swapped and wore lenses with the other filter for two weeks. Wearing either lenses resulted in improved migraine symptoms. There was no significant difference in outcomes between lenses. The researchers suggested that the filter designed as a control intervention helped to block photosensitivity and was therefore also effective.\textsuperscript{72}

Exercise

There is mixed evidence about whether exercise may reduce migraine. A review of six studies found that aerobic exercise was associated with a reduction in the number of days per month that people have migraine attacks. There were also reductions in the duration of attacks and pain intensity after aerobic exercise, but the data about this were limited. The type and intensity of exercise varied.\textsuperscript{73}

A study in Canada found that people living with migraine who were more physically active had better overall health. The researchers suggested that by changing their behaviours, people living with migraine can improve their general health status, but they did not report the impact on migraine frequency or severity.\textsuperscript{74}

On the other hand, a review of five trials found that yoga had no effect on the number, duration or pain intensity of migraine headaches.\textsuperscript{75}
Smartphone apps

Increasingly, self management support is available through digital tools such as online courses, email and smartphones applications (apps). This section describes examples of smartphone apps and similar tools to provide medication reminders or help people collect information about migraine triggers. Examples of psychological or behavioural interventions delivered digitally are covered in a section overleaf.

In Germany a survey of 1,464 people using a migraine smartphone app found that 71% provided aggregated data from the app to their doctor at consultations. Three quarters said the app helped them to adhere to their treatment plan. People reported reduced headache days per month and reduced use of acute medication compared to before using the app.76

In the USA researchers tested an electronic diary tool to help people with migraine collect data about the patterns of migraine headache onset and progression. The tool comprised a digitised map with 44 colour coded segments to illustrate migraine pain which was overlaid on a diagram of the face, head and neck nerves. Thirty six people with episodic migraine for at least three years identified regions where pain typically started and how pain spread. The tool was able to capture patterns of pain distribution for throbbing and pressure headache. The researchers suggested that it may also be useful for assessing changes over time.77

An important barrier to migraine prevention is that people may not always take preventive medications. Mobile phone apps have been tested to provide reminders. In the USA researchers used a mobile phone app and reminder system to improve adherence to preventive migraine treatment amongst young people. Adherence to preventive medications significantly improved during the first month of the intervention, particularly amongst those in their late teens and early twenties with lower baseline adherence. The app was reported to be acceptable and easy to use.78

A review of mobile apps for the management of headache disorders, including migraine, included six studies. Apps were found to be feasible and acceptable. They helped people identify trigger factors for migraine and provided data that people could share with health professionals.79 However a study of 29 apps for migraine (14 diary apps, 15 relaxation apps) found that apps often shared information with third parties. This may pose privacy risks in countries where there are few legal protections against the sale or disclosure of data from medical apps to third parties.80
Psychological initiatives

A range of psychological interventions have been developed to help manage migraine. These are different from the educational programmes described earlier because education initiatives aim to give people information about migraine whereas psychological initiatives aim to help people change what they think or how they behave. There is not always a distinct line between these types of interventions but this section provides examples of research with a specific psychological or behavioural focus.

Cognitive behavioural therapy

Cognitive behavioural therapy aims to help people adjust their ways of thinking. There is mixed evidence about whether cognitive behavioural therapy can reduce the physical symptoms of migraines in adults.81 A review of 27 trials found that psychological treatments such as this reduced the number of days per month with migraine and the number of headache attacks. The reviewers did not indicate whether some therapies were more effective than others.82

A review of 21 trials found that psychological interventions did not appear to reduce the number of migraines, days with migraine, migraine intensity or migraine medication use. There was no effect on mood, quality of life or migraine related disability. There were no significant adverse events. Most interventions were a form of behavioural therapy. Interventions varied from one 20 minute session to 14 hours of intervention, but most were brief. There were limitations in the study quality and follow up data were sparse. The reviewers concluded that there was too little high quality evidence to judge whether psychological interventions are effective in managing migraine in adults.83

Some examples are provided here to illustrate the types of initiatives researched. A small UK study explored a behavioural intervention with relaxation and cognitive behavioural therapy components to supplement medication. The programme was delivered in three individual therapist sessions to people who had migraine headaches at least four days per month. Most participants said they valued contact with the therapist and continued to use the techniques in their daily lives after the sessions ended. Relaxation training (deep breathing) was easily adopted and often used. The cognitive behavioural therapy components were thought to be more challenging to learn and implement. The researchers concluded that people selectively employed the techniques that suited them best and that there may be merit in developing minimal contact behavioural therapy further.84 Other studies have drawn similar conclusions.85
Researchers from Germany tested approaches for preventing medication overuse in people living with migraine. A brochure about preventing medication overuse headache was compared to the brochure plus a cognitive behavioural programme with minimal contact. Participants were people who frequently took triptans or analgesics for pain relief during migraine attacks. Both interventions were associated with fewer migraine days and medication intake days per month immediately and over one year follow up. None of the participants developed a medication overuse headache.\(^{86}\)

In the Netherlands behavioural management training was provided in people’s homes by other people with migraine. Follow up at two to four years found that improvements in migraine attack frequency and self efficacy were maintained long term. Quality of life and migraine related disability improved gradually over time. There was no follow up control group so the results need to be treated with caution.\(^{87}\)

Digital psychological interventions
A lot of research is available about delivering psychological interventions digitally, via the internet, smartphone apps and similar. A review of 23 trials explored behavioural initiatives delivered via the internet, personal digital assistants or CD Rom for people with migraine and other headache disorders. The behavioural interventions included cognitive behavioural therapy, biofeedback and relaxation. Most studies used more than one type of therapy and the duration of therapy varied widely. The reviewers concluded that, although the initiatives were acceptable to participants, there was insufficient evidence about impacts. No studies in this review used smartphones or wearable technology.\(^{88}\)

Another review of internet based interventions for people with chronic pain included five studies with people with migraine or chronic headache. Online interventions with cognitive behavioural therapy elements were associated with reduced disability, pain intensity and depression. Most of the studies were of low quality and had high dropout rates.\(^{89}\)

In the Netherlands researchers tested online digital assistance to support behavioural training in migraine.\(^{90}\) A small study found that online assistance in addition to behavioural therapy in small groups was acceptable but did not result in greater reductions in migraine or improvements in quality of life compared to those that took part in group sessions only.\(^{91}\) Effects were greater in those who had more migraine headaches per month.\(^{92}\)
Researchers in the USA tested a self guided CD Rom programme containing cognitive behavioural self management strategies for children with migraine. Compared with a CD Rom containing migraine education, the self management programme was associated with lower migraine pain severity and disability. There was no difference in headache frequency or quality of life.93

**Relaxation and stress reduction**

Another type of psychological therapy involves relaxation, deep breathing and stress reduction. Here research is more limited. A review identified one trial of mindfulness based stress reduction which did not appear to prevent migraine or reduce the intensity of pain.94

A small trial in the USA examined an eight week mindfulness meditation / yoga stress reduction course for adults with migraine. There was no reduction in the number of migraines per month or their severity, but the study may have been too small to detect a difference. There was an improvement in people’s confidence in self care. There were no adverse events or dropout. 95

In the USA a smartphone app has been tested to support progressive muscle relaxation. In a small study, those who used the app frequently reported fewer days with headache per month. There was a decline in using the app over time.96

**Sleep interventions**

Poor sleep quality and insufficient or excessive sleep may trigger migraine. It has been hypothesised that improving sleep may reduce migraine headaches. A review of four studies found that psychological sleep interventions (and in one study, combined with drug therapy) significantly reduced the number of migraines. There was mixed evidence about the impact on migraine intensity. Three studies showed improved sleep duration and quality. The reviewers concluded that this is a promising area where more research is needed.97
Acceptance therapy

In the USA, military veterans returning from Iraq or Afghanistan have been found to be two to four times more likely than those in the general population to live with migraine. Veterans with migraine are more than twice as likely to have psychiatric conditions compared to veterans without migraine, including depression and post traumatic stress disorder. A one day programme for people with migraine and depression and/or anxiety included acceptance and commitment therapy plus migraine education. At follow up after three months, veterans had significantly improved depression and anxiety symptoms, general functioning, headache related disability and pain acceptance.

Participants said that migraine education helped them feel more knowledgeable about their condition so they were more empowered to better manage their headaches. This included talking to their health professional about medication adjustments. The acceptance therapy component was reported to increase awareness of the role of stress in exacerbating pain and ways to manage stress. A well regarded element of the programme was being in a group with other people with similar health difficulties. This was a small study but the researchers suggested that the short programme was acceptable, feasible and worthwhile, particularly for people who may not be able to attend weekly sessions due to their conditions.98

Preventive medications

Preventive medication is often considered for people who routinely have migraine headaches each month. Complete cessation of headaches is uncommon, so the aim is a reduction in the number of headaches and the intensity of symptoms.99

Appendix 2 summarises themes from research about different types of preventive medications. This is not an exhaustive list of the preventive medications available. Not all of the medications may be available or highly used in the UK.

As with medications for treating migraine attacks, the safety and effectiveness of preventive medications depends on people’s preferences, migraine characteristics, administration methods, adherence and other factors. This means that a preventive medication that works for one person may not be equally effective for another.
Research suggests that preventive treatment with antiepileptic medications, antidepressants, beta blockers or calcium channel antagonists may reduce the use of acute migraine medications (triptans) and visits to GPs and emergency departments. These benefits may occur without any increase in overall migraine related costs.\textsuperscript{100}

A review of 245 trials and 76 other studies explored medications to prevent chronic or episodic migraine in adults. Effective preventive medications for chronic migraine included botox and topiramate. Effective medications for episodic migraine included topiramate, divalproex, timolol, propranolol, some beta blockers, angiotensin converting enzyme (ACE) inhibitors and the angiotensin II receptor antagonist candesartan. Topiramate, off label antiepileptics and antidepressants resulted in adverse effects that sometimes led to treatment discontinuation.\textsuperscript{101}

A similar review of 215 trials of preventive medications for episodic migraine examined 59 drugs from 14 drug classes. Topiramate, divalproex, timolol, propranolol; the off label beta blockers metoprolol, atenolol, nadolol and acebutolol; ACE inhibitors captopril and lisinopril; and angiotensin II receptor blocker candesartan reduced the monthly number of migraines. Adverse effects leading to treatment discontinuation were greater with topiramate, off label antiepileptics and antidepressants compared to placebo. Evidence was lacking about effects longer than three to six months, especially for quality of life.\textsuperscript{102}

One of the newest types of preventive medication available is calcitonin gene related peptide inhibitors. Examples of research about these medications are described in Box 2.
Box 2: Examples of research about calcitonin gene related peptide inhibitors (CGRP)

One of the newest pharmacological prevention approaches to prevent migraine is humanised antibodies acting on the calcitonin gene related peptide or on its receptor. Four monoclonal antibodies have been developed: one targeting the calcitonin gene related peptide receptor (erenumab) and three targeting the calcitonin gene related peptide (eptinezumab, fremanezumab and galcanezumab). A European guideline has summarised evidence of varying quality to recommend eptinezumab, erenumab, fremanezumab and galcanezumab in people with episodic migraine. There was higher quality evidence to recommend erenumab, fremanezumab and galcanezumab in people with chronic migraine.

32 studies of CGRP inhibitors in migraine and cluster headache suggested that eptinezumab, erenumab, fremanezumab and galcanezumab may prevent episodic and chronic migraine. Larger trials are underway to examine the efficacy and safety of this new drug class. Reviewers have suggested that it may be particularly important to assess the cardiovascular effects of long term CGRP blockade.

Another review of the efficacy and safety of CGRP medications found a reduction in monthly migraine days compared to placebo. There was no statistically significant difference in most adverse events, but CGRP inhibitors were associated with increased dizziness.

Focusing on erenumab, research suggests that this medication appears to be well tolerated. A review of five studies where erenumab was given as a subcutaneous injection found that a monthly dosage of 70mg or 140mg was associated with reduced days per month with migraine compared to placebo. There were no significant increases in adverse effects. The reviewers concluded that erenumab is an effective and well tolerated preventive treatment for adults with episodic and chronic migraine.

A trial in 104 centres in Belgium, the Czech Republic, Denmark, Finland, France, Germany, Italy, the Netherlands, Poland, Spain, Sweden, Switzerland, the UK and the USA tested subcutaneous fremanezumab for 12 weeks in adults with chronic or episodic migraine who had previously not responded to two to four classes of migraine prevention medications. Over a three month period, fremanezumab was associated with reduced average monthly migraine days. Adverse events were similar to placebo.

A review of six trials found that, compared to placebo, galcanezumab was associated with greater reduction in the number of days per month with migraine but also a greater number of adverse events (though minor). CGRP receptor antagonists have been associated with raised liver toxicity when used daily for as little a week. Therefore they may best be used intermittently. Further such medications are in clinical development.
Other medical interventions

Various other medical interventions have been researched to prevent migraine. These include stimulating or blocking nerves with electrical or magnetic pulses, manual therapies such as spinal manipulation and surgery. Themes in the research evidence are briefly summarised here.

Non invasive nerve stimulation

Non invasive nerve stimulation techniques use magnetic fields to stimulate nerve cells in the brain to improve symptoms. Brief magnetic pulses are used to induce electrical fields in the body that may help with pain relief. The most commonly researched of these therapies are non invasive vagus nerve stimulation, single transcranial magnetic stimulation, transcranial direct current stimulation and external trigeminal nerve stimulation.\textsuperscript{112,113,114}

A review of 19 studies found moderate quality evidence that transcranial magnetic stimulation may be associated with small reductions in migraine headache frequency, duration, intensity, functional impairment and depression. Eight studies examined transcranial direct current stimulation, but the evidence was too varied to draw conclusions.\textsuperscript{115} Other reviews have also concluded that transcutaneous electrical nerve stimulation resulted in a reduction in monthly headache days and use of painkillers.\textsuperscript{116}

A study in the UK compared the cost of botox versus a portable device for self administration of transcranial magnetic stimulation (TMS) in adults with chronic migraine. The TMS device delivered a brief preset magnetic pulse and was designed for use by people with migraine in their own home. Based on modelled data, 46% of people prescribed botox would continuously receive Botox over the course of a year and 54% of those prescribed TMS would still be on treatment at the end of year one. The total costs of botox treatment were estimated at £2,923 per year. TMS treatment would cost £1,466 in the first year (2016 prices). The researchers described how a risk share remuneration model of TMS in the NHS means that the NHS only pays for those people experiencing a reduction in migraine days. This means that TMS would cost less than conventional botox treatment.\textsuperscript{117}
Implanted stimulation devices

There has been some success with more invasive nerve simulation techniques, where devices are implanted into the body rather than being used externally. A review of 12 studies about occipital nerve stimulation (implants) for chronic migraine found an average reduction of three days per month of moderate to severe headache months. The average effect size was modest and may be confounded because it is difficult to blind participants and professionals to the treatment.\textsuperscript{118}

A review of ten studies of occipital nerve stimulation found some improvement in migraine disability, but the quality of evidence was low. The interventions varied widely between studies.\textsuperscript{119}

A UK study followed up people with chronic migraine for three years after occipital nerve stimulation implants. The study was small and uncontrolled, so it is difficult to make generalisations, but there was a reduction in the number of days per month of moderate to severe headaches, pain intensity and pain duration. There were few adverse events and no episodes of lead migration. The researchers concluded that occipital nerve stimulation may be a safe and effective treatment for people with chronic migraine.\textsuperscript{120}

Injections to block nerves

Another approach is injections into the nerves surrounding the neck and head to block pain receptors. Reviews have found that greater occipital nerve block can reduce pain intensity and the use of painkillers in people with migraine, but there are mixed findings about the impact on headache duration. This approach had few adverse effects,\textsuperscript{121} but the quality of available evidence is low.\textsuperscript{122}

A review of nine studies found that greater occipital nerve block for people with chronic migraine was associated with an average of four less headache days per month compared to a comparison group. There was also a decrease in headache severity. The reviewers concluded that greater occipital nerve blocking could be recommended, particularly in people who may require surgical intervention in future. Using a nerve block may help to assess whether people are good candidates for an operation on their nerves.\textsuperscript{123}
Surgery on nerves

Research has tested surgical decompression of one or more ‘trigger sites’ for migraine located at frontal, temporal, nasal and occipital head sites. A review of 14 studies of surgical procedures involving the extracranial nerves and / or arteries found that migraine headaches were eliminated in 38% of participants at six to 12 month follow up. The reviewers suggested that this may be an option for some people, but that more detailed research was needed.\textsuperscript{124}

A review of 23 studies found that peripheral nerve decompression surgery is effective in reducing migraine headache frequency and intensity. Not everyone experiences an improvement so researchers have suggested that more work is needed to understand how nerve compression works in people with migraine and why a subset of people do not respond to surgical treatment.\textsuperscript{125}

A review of procedures targeting the peripheral nerves included research about people with chronic headaches, migraines and occipital neuralgia. There were 26 studies of peripheral nerve surgery, radiofrequency therapy and peripheral nerve stimulators. The reviewers combined studies across the conditions and concluded that peripheral nerve surgery involving decompression of peripheral nerves was the best studied. Reported success rates for nerve decompression or excision were higher than those for peripheral nerve stimulation or for radiofrequency, although the study quality made it difficult to compare. Peripheral nerve stimulator implantation was associated with the most complications.\textsuperscript{126}

Physiotherapy and spinal manipulation

Physiotherapy may reduce the intensity, frequency and duration of migraine, but the quality of evidence is low.\textsuperscript{127}

A review of six studies examined spinal manipulation for two to six months as a preventive treatment for migraine pain and disability. In people living with episodic migraine, spinal manipulation was associated with a small reduction in the number of days with migraine and migraine pain intensity. The reviewers concluded that larger and more rigorous studies were needed to confirm these preliminary findings.\textsuperscript{128} Other reviews support the benefits of spinal manipulation or mobilisation for adults with migraine, but there is insufficient evidence for children.\textsuperscript{129}

A review of five studies suggested that osteopathic manipulative treatment could reduce the number of episodes of migraine per month as well as the use of pain killers. The studies were of poor quality.\textsuperscript{130}
Another review found that manual therapy was associated with improved health related quality of life in people living with migraine immediately after treatment and at longer term follow up, but it depended on the measure of quality of life used. The reviewers said there was only a low level of evidence available in this area.\textsuperscript{131}

Other reviews of spinal manipulation have suggested mixed findings, with some studies finding benefits and others demonstrating little effect of chiropractic spinal manipulation.\textsuperscript{132}

**Acupuncture**

There are mixed findings about acupuncture. A review of 22 trials found that adding acupuncture to medication for symptoms reduced the number of headaches in people with episodic migraine. The effect was small but the reviewers argued that acupuncture may be as effective as preventive drugs.\textsuperscript{133} Other reviews suggest similar benefits,\textsuperscript{134} including improvements to people’s quality of life.\textsuperscript{135}

A review of 14 trials found that in people with migraine without aura, acupuncture had a significant advantage over medication and placebo in reducing the number of migraines. It was better tolerated than medication, with fewer adverse events. However the quality of available evidence was mainly low.\textsuperscript{136}

Another review of 13 studies emphasised that research about acupuncture for migraine treatment is of poor quality, with conflicting results.\textsuperscript{137}

A review found that there might be both clinical benefits and cost savings associated with acupuncture for migraine, but only one cost effectiveness study was identified.\textsuperscript{138}

**Herbal medicine**

Some people living with migraine choose to use traditional or herbal remedies either in conjunction with or instead of conventional medicine.

A review of a Chinese medicine, Chuanxiong Chatiao san, included 37 studies. When Chuanxiong Chatiao san was added to conventional migraine prevention medicine there were reduced migraine episodes, headache duration and adverse events compared to when conventional medicine was used alone. The quality of the available studies was generally poor.\textsuperscript{139}
A review of 19 studies of herbal Chuanxiong (Ligusticum chuanxiong Hort. root) suggested that this could reduce the number, duration and pain severity of migraine. There were few adverse events.\textsuperscript{140}

Another review of traditional Chinese medicine treatments for migraine included 20 trials. The effectiveness varied depending on the specific herbal medicine.\textsuperscript{141}

A review of four trials found that the herbal remedy feverfew (Tanacetum parthenium L.) had beneficial effects for migraine compared with placebo in small studies, but a large high quality trial found no statistically significant difference between feverfew and placebo.\textsuperscript{142}

**Other initiatives**

A small number of other studies have examined other medical or interventional approaches for preventing migraine. For instance, caloric vestibular stimulation involves irrigating cold or warm water or air into the external ear canal. This may provide effective and tolerable therapy to prevent episodic migraine. A trial including adults from the UK and elsewhere found that three months of treatment with a caloric vestibular stimulation device reduced the number of days with migraine each month, acute medication use and pain intensity. There were no adverse effects on mood, cognition or balance.\textsuperscript{143}

People may have neurophysiological changes in their brains 24 to 48 hours before a migraine attack. A small study tested at home brain monitoring to identify pre attack changes. People self monitored their neural activity over the course of two weeks using a portable wireless EEG system and a mobile app. 24 hours before a migraine attack EEG changes were visible. The researchers concluded that being able to identify when a migraine was coming would allow early intervention.\textsuperscript{144}

Wet cupping is a traditional therapy in some countries. This has not been found to be effective for pain relief or prevention in migraine, but only one study was identified.\textsuperscript{145}
Other initiatives

We identified research about a small number of other interventions to support long term management of migraine. These focused on system level interventions to educate health professionals or ensure that care was accessible.

Nurses providing care
In the USA, a chronic care disease management model was tested for people with headache, including migraine. The aim was to be able to provide care to large numbers of people with headache, making best use of staff resources. A multidisciplinary team was coordinated by a neurologist. A nurse practitioner was the main provider of care and most care was delivered in primary care. Adults attended an educational session run by a neurologist and a nurse practitioner. They were then evaluated by the nurse practitioner who coordinated an individual treatment plan. Nine out of ten people said their headache symptoms improved and there was a reduction in primary care and emergency department visits. People had improved quality of life and this was maintained for six months after completing the programme.146

A study of introducing migraine nurses into primary care in Europe compared non randomised groups of people who received care from nurses trained in migraine management versus those receiving usual care. There was no difference between groups in the quality of care or outcomes. There was a trend towards increased direct practice costs from having migraine nurses in primary care, but this was a small non randomised study and the differences did not reach statistical significance so could have happened by chance.147

Updating health professionals
Another study in Europe found that training for GPs improved their diagnosis and management of migraine. The improvements remained two to three years later. Before education, about half the time GPs initiated migraine treatment once someone was diagnosed. This rose to 80% after training. There was a reduction in GP referrals to headache specialists. After three years some best practice approaches were beginning to decline so the researchers suggested that it may be worthwhile to refresh GPs about migraine every two to three years.148
Stratified care approaches
A UK study explored the cost effectiveness of a stratified care regimen whereby people with migraine were first stratified according to the severity of their condition and then prescribed different treatments according to severity. This was compared with a stepped care approach whereby the least intensive treatments are tried first and built up if they do not work. Based on data modelling, the estimated one year direct healthcare costs per person with migraine in primary care were £157 for stepped care and £152 for stratified care (2001 prices). The estimated treatment response rate was 40% for stepped care and 71% for stratified care. The estimated cost per successfully treated migraine attack was £23 for stepped care and £13 for stratified care. Stratified care was cost effective, especially where higher numbers of people had moderate or severe migraine. The researchers concluded that stratified migraine care in primary care can deliver improved clinical outcomes at no additional cost.149,150

Screening tools
A number of tools have been developed to support professionals to manage migraine in primary care. The Headache Under Response to Treatment (HURT) questionnaire was designed to be an easy to use tool to assess outcomes and provide guidance to professionals about a range of headache disorders. The tool was developed based on an evidence review and expert input. It was tested in the general population though mailed surveys in the USA and in headache specialist centres in Europe and primary care clinics in Saudi Arabia. The tool is an eight item self administered questionnaire which explores headache frequency, disability, medication use and effect, perceptions of headache control and people’s understanding of their diagnoses. The tool has been found to have good validity in different cultures and clinical settings.151 However whether it helps primary care professionals better manage migraine remains uncertain.

In the USA a screening tool has been developed to identify psychosocial risk in families of young people with medical conditions, including chronic migraine. The tool was found to be useful for identifying emotional and behavioural disturbances, parental distress and poor family functioning so support could be offered.152
Enablers and barriers

Enablers to care

The Migraine Trust was interested in whether there were some underpinning factors that may contribute to effective care, regardless of the specific treatment. Some of the most commonly identified enablers in empirical research were:

- involving people in coproducing their care
- supporting self management
- empathetic and well informed health professionals
- prompt diagnosis
- a pathway which provides holistic support in primary care with access to specialists where needed.

Examples to illustrate some of these points are provided here.

Involvement and preferences

An enabler to good care is considering the needs of individuals, involving them fully and tailoring care packages to address people’s preferences and needs. A study in Sweden found that people with migraine who actively managed their condition sought to amplify the good in life through increasing their energy and through accepting being affected by migraine. The researchers suggested that as well as preventive drugs, it is important to consider positive psychological strategies for coping and involve people actively in their care.153

A small UK study found that people with migraine said that they were actively involved in treating and preventing their headaches and in decision making about appropriate management.154 This study was not an intervention and did not test the ‘effectiveness’ of anything, it simply showed that people felt they were actively involved in their care.

Research has explored people’s preferences related to pharmacological treatment characteristics. A survey of more than 1000 people with migraine and their family members in the UK, Europe, USA and Canada found that 60% of people’s preferences about treatment choice was driven by formulation type and 40% by the speed of onset. As migraine disability increased, speed of onset became more important.155 Research in the UK supports that people prefer fast acting treatment during migraine attacks.156
In the USA researchers asked 300 people with migraine to choose between different characteristics of preventive migraine treatments to understand whether it was more important to be more effective or have fewer adverse events. Participants valued hypothetical medications with greater reductions in migraine attacks more highly than avoiding higher levels of adverse events. However avoiding some adverse events was more important than others. Avoiding a 10% weight gain was more important than avoiding thinking and memory problems. Participants preferred a once monthly injection or daily pill to twice monthly injection.\textsuperscript{157}

**Professionals with empathy**

Researchers in the USA explored factors that contribute to whether people with migraine seek treatment. They found people’s beliefs about the attitudes of healthcare professionals and whether they had a supportive social network had a greater influence than people’s demographic characteristics, beliefs about medications and migraine frequency and severity.\textsuperscript{158}

A large study in France examined what influenced adults to consult a doctor about migraine. 28% of those with migraine had never consulted a doctor about this, 31% were actively consulting and 41% had previously sought medical help but were no longer doing so. People were most likely to consult a professional if they did not have good social support or ways to express themselves. They were most likely to continue with medical care if they had good previous consultation experiences.\textsuperscript{159}

In the Netherlands researchers examined the qualities of lay trainers with migraine. Characteristics viewed positively by those taking part in training included the trainers’ warmth, expertise, organisational skills, clear explanations, active control of their own migraine and availability to provide guidance. Trainers who had the highest control of their own migraine were associated with more improvements in the self confidence and migraine symptoms of their trainees. Humour, fellowship and individualisation had no benefits for migraine control. Acting as a trainer helped people improve their own migraine control and quality of life.\textsuperscript{160}

In the UK a self management education programme has been tested for people with migraine. Key success factors included having a short intervention, detailed educator training and having a mix of educators with empathy and a welcoming approach.\textsuperscript{161}
Identification and tracking progress

Prompt and accurate diagnosis helps people receive appropriate care. Some of this is influenced by the attitude and education of health professionals. A range of tools are available to help make identifying migraine easier.

A review identified 11 tools to screen for migraine and six tools for both migraine and tension type headache. There was moderate certainty evidence that a tool known as ‘ID Migraine’ had a high degree of diagnostic accuracy.\(^\text{162}\)

Tools to help diagnosis people with migraine are important, but regular follow up is essential too. To assist with this, several tools have been developed to help track people’s outcomes over time. A review of multi item patient reported outcome measures (PROMs) for adults with chronic or episodic headache included 46 articles about 23 PROMs. Five tools focused on the health related impact of migraine and six assessed migraine specific treatment response or satisfaction. Evidence of measurement validity was strongest for two measures of impact, the Migraine Specific Quality of Life Questionnaire and the Headache Impact Test 6-item, and one tool about treatment response, the Patient Perception of Migraine Questionnaire.\(^\text{163}\)

Integrated and holistic approach

Focus groups with people with migraine found that people wanted a more holistic, collaborative, long term treatment approach. They thought medication should be a short term solution and wanted more information and access to approaches to support self care. People from less advantaged social and economic groups were more likely to rely on traditional / folk remedies, often describing these as more affordable and culturally accessible than medical options.\(^\text{164}\)

Research in Italy that tracked people living with migraine over time found that continuity of care had a positive impact on people’s health status and functioning.\(^\text{165}\)

In the UK researchers asked 20 people with headache, including migraine, for feedback about a service where GPs could make direct referrals for an MRI rather than referring to a specialist to decide whether an MRI was needed. People wanted rapid access to scan results that were clearly explained to them, whether this was via a GP or specialist. Some reported long waits to receive scan results, including from their GP. This suggests that changing access to scans may not in itself help people with migraine. Rather it is speed of access and explanations of results that helps people move on and focus on symptom management.\(^\text{166}\)
Barriers to care

The empirical research suggests that barriers to optimal migraine care include:167,168,169,170,171,172,173,174,175,176,177,178,179

Factors related to people with migraine
- people not recognising that they have migraine
- people with migraine not seeking care from a professional
- difficulty communicating pain and symptoms
- low adherence to preventive treatments, perhaps due to adverse events

Factors related to healthcare teams
- lack of knowledge about migraine amongst primary care professionals
- lack of knowledge about migraine amongst pharmacists
- lack of routine use of screening tools to identify people with migraine
- under diagnosis
- time taken to receive a diagnosis
- under treatment by health professionals
- lack of treatment optimisation
- lack of follow up
- lack of integrated working between primary care and hospital
- lack of access to specialist professionals, including headache nurses

Factors related to medication availability
- lack of effective pain relief medication available over the counter
- use of over the counter medications as a first line therapy even if other medications are prescribed
- lack of availability of medications early in an attack, when they may be most effective
- lack of preventive medication over the counter
- quantity limits on medications prescribed
- not being offered a regimen with both acute and preventive treatments

Factors related to medication efficacy and safety
- treating headaches with simple analgesics, which if ineffective, leads to dissatisfaction with treatment
- fears about the safety of migraine medications
Factors related to research and guidelines

- Lack of evidence base for best practice for holistic care
- Few guidelines setting out which people with episodic migraine would benefit from preventive therapy
- Insufficient understanding of whether treatments are most effective for episodic migraine, chronic migraine or both
- Traditionally conditions affecting more women than men being less researched or resourced

Examples of research about some of these points are provided here.

Diagnosis

Studies have repeatedly highlighted that many people with migraine do not receive a diagnosis or that it takes a great deal of time to be diagnosed. This is a barrier to optimal care.

It has been estimated that migraine may be undiagnosed and undertreated in about 50% of people living with migraine. Less than half of people living with migraine visit a doctor about this.\textsuperscript{180}

Headache centres in seven countries examined people’s awareness of migraine and their experience of diagnosis and treatment. Over 1,000 people living with migraine were interviewed. Only 28% were aware that their condition was migraine. Two thirds thought they had simple headache. There was also reported lack of awareness amongst clinicians they had consulted. The researchers concluded that it is important to raise awareness about migraine amongst both the public and professionals and this would reduce unnecessary investigations when seeking a diagnosis.\textsuperscript{181}

A study in 15 countries found that people with a stable pattern of episodic, disabling headache and a normal physical exam should be considered to have migraine in the absence of contradictory evidence. Headache diaries can be used to help confirm the diagnosis.\textsuperscript{182}

In the USA a study found that the top three barriers to consulting a doctor were people thinking that their migraine was a simple headache (50%), being satisfied with their current management approaches (45%) and the inconvenience of doctor appointments (41%). The top three reasons for lapsing from migraine care were not having as many headaches (40%), self identification of effective therapy (40%) and effective care found via a doctor (30%).\textsuperscript{183}
Knowledge and attitudes

Another frequently mentioned barrier to migraine care is the knowledge and attitudes of people with migraine and health professionals. Two decades ago, about 10,000 people with migraine in the UK were surveyed. Most people believed that they could not control their migraine and a significant proportion said that migraine controlled their day to day life. People said they did not consult GPs due to poor previous experience, an expected lack of empathy or an expected lack of effective treatment.¹⁸⁴

A smaller UK study had similar findings. Peoples beliefs about the extent to which they could control or manage their condition influenced how proactive they were about treatment and self care. A number of the participants did not feel well educated about self care and did not take steps to manage their condition.¹⁸⁵

Researchers in Canada explored factors related to access to medication for episodic migraine attacks. People with migraine, GPs, neurologists and other clinicians and pharmacists shared their views. The awareness of doctors, pharmacists and patients about appropriate medications was a barrier. So too was apathy in terms of people not seeking care and doctors’ lack of prioritisation of migraine. These issues may delay diagnosis and the provision of appropriate treatment. The researchers reported that if people engaged in self advocacy this enhanced their ability to seek timely and appropriate care.¹⁸⁶

A review of 27 studies examined what predicted outcomes in people with chronic headache, including migraine. Depression, anxiety, poor sleep and stress, medication overuse and poor self efficacy for managing headaches were associated with unfavourable outcomes from preventive treatment in chronic headache. There was inconclusive evidence about the impact of treatment expectations, age, age at onset, body mass index, employment, and headache features. The reviewers noted that the majority of predictors of poor outcomes were modifiable.¹⁸⁷
Integral role of primary care

Researchers in the USA examined primary care professionals’ knowledge about migraine diagnosis and management. Primary care doctors were aware of the prevalence of migraine but unclear about good management. Less than one third were familiar with national guidelines about preventive treatment and one third were aware that opioids can cause medication overuse headache. Non pharmacologic treatment was not usually recommended to people consulting them. The researchers noted that there was much scope for education for primary care doctors. The doctors favoured educational opportunities involving direct contact with headache specialists.¹⁸⁸

A survey of 200 people referred to specialist headache clinics in the UK suggested that there was room for development in the treatment of migraine and other headache disorders in primary care. Most people did not receive a firm diagnosis at their first attendance at primary care, or in subsequent attendances. The treatments provided in primary care were often ineffective. Upon referral to a specialist clinic many people thought that there was a serious underlying cause of their headaches and wanted further investigations. Many had unrealistic attitudes and medication overuse was widespread. Few people had been offered triptans in primary care. The researchers summarised that important deficiencies in primary care management included failure to provide a formal migraine diagnosis, inadequate understanding of the nature and mechanism of headaches and failure to follow a robust management strategy.¹⁸⁹

An audit of the records of almost 5000 people attending a UK specialist headache clinic over a three year period found that, prior to referral, most people had treated their migraines or other headaches with analgesics (simple pain relief). There was little use of preventive medication. The researchers suggested that education of GPs may improve the management of migraine in UK primary care.¹⁹⁰

These themes in published research mirror the feedback that The Migraine Trust collated from the UK migraine community in 2019. In a survey and discussion groups with more than 1,800 people, a key concern was that even if a GP could recognise and diagnose migraine, they may not have the knowledge to support long term management. People thought that GPs may not understand the ‘fundamentals’ of migraine, including the trial and error nature of migraine management, the balancing act between the positive effect of a particular medication and the adverse effects, the higher prescribing levels necessary to see impact and the dangers of medication overuse headache. As a consequence, people with migraine may be compelled to seek help from a specialist unnecessarily, instead of receiving support in primary care.
Treatment uptake

Another barrier to good care is that people may not be offered the range of effective treatment options available. A study in ten European countries, including the UK, found that too few people with migraine consult doctors and proportionately too many of those that do see specialists. Migraine specific medications were used inadequately, even among those who consult GPs and specialists. Fewer than one in five people with migraine had seen a GP about this. Fewer than one in ten were taking triptans or preventative medication. People with migraine who had consulted specialists were more likely to be receiving appropriate medications than those treated by GPs.¹⁹¹

In Germany, research with almost 2,000 people with migraine found that 50% had undergone unnecessary diagnostics prior to being referred to a specialised outpatient clinic and 34% had not been treated according to evidence based treatment guidelines. More than half had not been prescribed a preventive treatment, even though most qualified for a preventive treatment. The researchers concluded that many people with migraine do not receive optimal care, even though there are national and international guidelines about this.¹⁹²

A large study in the USA found that fewer than 5% of those with chronic migraine had avoided all three common barriers to successful care: consulting a healthcare professional about migraine, receiving an accurate diagnosis and being prescribed minimal but appropriate acute and preventive pharmacologic treatments.¹⁹³

The use of non pharmacological interventions such as cognitive behavioural therapy and relaxation techniques is low, even though there is some evidence of effectiveness. Researchers in the USA found that barriers to using non pharmacological treatment included people’s attitudes and beliefs, lack of motivation to change, poor awareness of triggers, poor self efficacy, low levels of acceptance, maladaptive coping styles and psychiatric comorbidities. They suggested that clinicians should help people make best use of available care.¹⁹⁴

Other researchers in the USA explored the reasons people did or did not begin behavioural therapy for migraine following a headache specialist’s recommendation. About half of people started behavioural therapy and half did not. People who had previously seen a psychologist for migraine were more likely to initiate behavioural migraine treatment. There was no difference based on gender, age, age at diagnosis, years with headaches, healthcare visits, migraine disability or whether people thought they were in control. Time constraints were the most common barrier cited for not initiating treatment.¹⁹⁵
Treatment adherence

Even if people are begin pharmaceutical or non pharmaceutical treatment, they may not continue with it. Poor adherence to preventive medications may affect treatment outcomes. A lack of adherence may in part be due to issues with treatment tolerability. When people take painkillers for migraine attacks, they may experience an escalation of migraine attacks or transformation to chronic daily background pain with exacerbations.  

A study in the USA found that about one quarter of those with episodic migraine and half of those with chronic migraine had discontinued or switched preventive medications. The most common reason given was perceived lack of efficacy and tolerability / safety (70%). The researchers suggested that there is an unmet need for efficacious therapies that reduce migraine frequency and severity and have better tolerability for patients.  

A review of 33 studies found that one quarter to half of people with migraine may stop taking oral preventive medication within four to six months. The most common reason provided was adverse effects. 

Another barrier to successful preventive treatment is that people may become used to a treatment and it is no longer effective. A review of research found that tolerance may occur in up to 8% of people receiving preventive medications for migraine. Some types of tolerance could be addressed by adapting drug administration, the order in which drugs are used and by using other medications alongside. 

A survey of more than 5,500 people in the UK, France, Germany, Italy and the USA found that more than half of those with migraine did not seek medical care. Less than one in five who did consult a doctor were prescribed triptans. More detailed exploration with 500 people found that migraine therapy was consistently effective in less than one third of participants and less than half were satisfied with their current treatment. Many people supplemented prescriptions with alternative management strategies such as herbal and homeopathic remedies, stress management, relaxation therapy, bed rest and avoidance of triggers. Three quarters of people said they would value a dissolve in the mouth pain relief tablet.
Summary

What we know

Thousands of studies have been published about treatment and care for people living with migraine. Despite this, much remains to be learnt about the most effective and safe treatments for people with different types of migraine and various clinical and demographic characteristics.

Tables 1 and 2 summarise research trends about the safety and effectiveness of various interventions described in this review.

There is reasonable evidence that certain medications can be useful during migraine attacks and for preventing future attacks. There is some evidence that initiatives such as devices to send pulses to the nerves, behavioural therapy, education and workplace programmes can help. Much is left to learn about other approaches such as specialist headache nurses in primary care, digital support or herbal medicine.

Most research does not compare treatments with one another or explore the effectiveness for people with different types of migraine or various demographic characteristics. Therefore it is not possible to set out the ‘best types’ of care.

The type of care that is most useful for an individual may be a matter of trial and error, and may change over time. What seems essential for good care is that people living with migraine feel supported and understood by health professionals, their family and school and work colleagues. A key barrier to coming forward to discuss care and to adhering to treatment is feeling that professionals do not have the knowledge, understanding or empathy that people with migraine need.

Barriers to effective care have been identified at an individual level and at a wider system level. Examples of individual level barriers include the knowledge and attitudes of people with migraine and health professionals, communication difficulties and lack of adherence to treatment. Broader barriers may include lack of time allocated to support self care, lack of prompt access to specialists and medications and lack of research about interventions other than medications. Addressing these and other barriers may help to improve migraine care in the UK.
### Table 1: Summary of evidence about different types of care

<table>
<thead>
<tr>
<th>Reasonable evidence of safety and effectiveness</th>
<th>Acute management</th>
<th>Prevention / long term management</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Antiemetic medications</td>
<td>• Antiepileptic drugs such as topiramate (but side effects)</td>
<td></td>
</tr>
<tr>
<td>• Corticosteroids (but not large effect)</td>
<td>• Botox</td>
<td></td>
</tr>
<tr>
<td>• Simple pain killers such as ibuprofen and aspirin</td>
<td>• CGRP receptor antagonists</td>
<td></td>
</tr>
<tr>
<td>• Triptans (but side effects)</td>
<td>• Education programmes</td>
<td></td>
</tr>
</tbody>
</table>

| May be effective but evidence is limited         | • Antiepileptic drugs such as topiramate (but side effects) |
| • Antipsychotic medications                     | • Botox         |
| • New CGRP receptor antagonists, not yet on the UK market | • CGRP receptor antagonists |
| • Cognitive behavioural therapy                 | • Education programmes |
| • Hyperbaric oxygen therapy                      | • Some beta blockers and ACE inhibitors |
| • Hypnotherapy and relaxation therapy           | • Acupuncture |
| • Non invasive nerve stimulation                 | • Nerve block injections |

| Evidence that approach is probably not effective| • Gabapentin (antiepileptic) |
| • Hormones                                      | • Selective serotonin reuptake inhibitors |
| • Lidocaine                                     | • Wet cupping |
| • Naproxen                                      | • Acupuncture |
| • Octreotide                                    | • Nerve block injections |

| Too little research available to draw conclusions | • Gabapentin (antiepileptic) |
| • Cannabis                                       | • Selective serotonin reuptake inhibitors |
| • Cryotherapy                                    | • Wet cupping |
| • Magnesium sulphate                             | • Acupuncture |
| • Propofol                                       | • Nerve block injections |

| • Avoiding foods that people are intolerant of | • Gabapentin (antiepileptic) |
| • Caloric vestibular stimulation                | • Selective serotonin reuptake inhibitors |
| • Dietary supplements                           | • Wet cupping |
| • Drinking 1.5 litres of water daily            | • Acupuncture |
| • Exercise                                       | • Nerve block injections |
| • Filtered eye glasses                          | • Psychological therapies |
| • Graduated exposure to triggers                 | • Smartphone apps |
| • Herbal remedies                                | • Surgery |
| • Hormones                                      | • Workplace based education |
| • Melatonin                                     | • Gabapentin (antiepileptic) |
| • Physiotherapy and spinal manipulation         | • Selective serotonin reuptake inhibitors |
| • Relaxation and mindfulness                    | • Wet cupping |
| • Sleep interventions                           | • Acupuncture |
| • Specialist headache nurses                    | • Nerve block injections |
Table 2: Overall trends in research about intervention impacts

<table>
<thead>
<tr>
<th>Treatment type</th>
<th>Impact on migraine frequency or intensity</th>
<th>Impact on quality of life</th>
<th>Cost effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute medications</td>
<td>Analgesics, CGRP and triptans reduce migraine pain severity and duration</td>
<td>Limited evidence available</td>
<td>Evidence for some medications, but limited comparisons</td>
</tr>
<tr>
<td>Acupuncture</td>
<td>Mixed evidence, but positive trends</td>
<td>Limited evidence but positive trends</td>
<td>Limited evidence but positive trends</td>
</tr>
<tr>
<td>Avoiding food and light triggers</td>
<td>Insufficient evidence to draw conclusions</td>
<td>No evidence identified</td>
<td>No evidence identified</td>
</tr>
<tr>
<td>Dietary supplements</td>
<td>Mixed evidence about various types</td>
<td>No evidence identified</td>
<td>No evidence identified</td>
</tr>
<tr>
<td>Drinking water</td>
<td>No impact</td>
<td>Improved quality of life, but limited evidence</td>
<td>No evidence identified</td>
</tr>
<tr>
<td>Education for patients and professionals</td>
<td>Mixed evidence of impact, though most show some benefit</td>
<td>Short term improved quality of life and self efficacy</td>
<td>No evidence identified</td>
</tr>
<tr>
<td>Exercise</td>
<td>Mixed evidence about various types of exercise, but positive trends</td>
<td>No evidence identified</td>
<td>No evidence identified</td>
</tr>
<tr>
<td>Herbal remedies</td>
<td>Mixed evidence, some positive trends but low quality evidence</td>
<td>No evidence identified</td>
<td>No evidence identified</td>
</tr>
<tr>
<td>Invasive nerve stimulation and surgery</td>
<td>Findings are mixed, but some positive trends</td>
<td>Some evidence of improved quality of life</td>
<td>No evidence identified</td>
</tr>
<tr>
<td>Nerve block injections</td>
<td>Positive trends but findings are mixed</td>
<td>Limited evidence available</td>
<td>No evidence identified</td>
</tr>
<tr>
<td>Non invasive nerve stimulation</td>
<td>Some positive trends for acute and preventive treatment but insufficient consistent evidence</td>
<td>Limited evidence</td>
<td>Limited evidence, but positive trends for some techniques</td>
</tr>
<tr>
<td>Nurse led care</td>
<td>Mixed evidence</td>
<td>Mixed evidence</td>
<td>Limited evidence</td>
</tr>
<tr>
<td>Physiotherapy and spinal manipulation</td>
<td>Mixed evidence, with some benefits noted</td>
<td>Positive short term trends</td>
<td>No evidence identified</td>
</tr>
<tr>
<td>Preventive medications</td>
<td>Botox, topiramate, beta blockers and some other drugs have been found to be effective</td>
<td>Improved quality of life from some medications</td>
<td>Botox is cost effective for people with chronic migraine</td>
</tr>
<tr>
<td>Psychological and behavioural interventions</td>
<td>Some evidence of impact for acute and long term management, but there are mixed findings</td>
<td>Some evidence of improved quality of life and self efficacy</td>
<td>No evidence identified</td>
</tr>
<tr>
<td>Workplace based support</td>
<td>Some evidence of benefit though the quality of evidence is low</td>
<td>Some evidence of benefit though quality of evidence is low</td>
<td>Limited evidence available, but positive trends</td>
</tr>
</tbody>
</table>
Knowledge gaps

The World Health Organization has declared migraine a major public health problem due to a lack of knowledge about its causes and effective treatment options.\textsuperscript{201}

In a number of areas, research is sparse (see Table 2). This includes research about effective self management strategies, alternatives or supplements to medication, the cost effectiveness of smartphones and digital technologies, facilitators and barriers to care, and factors that influence treatment adherence, amongst others.\textsuperscript{202}

Researchers and reviewers have repeatedly called for more research into migraine causes and care, particularly preventive approaches. Many studies do not explore whether treatments are equally effective for people with different types of migraine and people with various demographic and clinical characteristics. A major gap relates to whether care is equally effective for people from different ethnic backgrounds. There is some international research suggesting that access to care may be more difficult amongst people from black and minority ethnic groups, but little has been published about this in the UK.\textsuperscript{203}

In feedback provided to The Migraine Trust by more than 1,800 people affected by migraine, a lack of prompt and accurate diagnosis was a major issue. This mirrors published research findings about barriers to effective migraine care. In The Migraine Trust’s survey, more than half of participants experienced symptoms for more than a year before seeking help from their GP. Only around one third were diagnosed on their first visit and more than one quarter needed to see a health professional five or more times before they received a correct diagnosis. People from black and minority ethnic backgrounds were even less well served, with three quarters experiencing symptoms for more than a year before seeking help and 41% needing to see a health professional five or more times before they received a correct diagnosis. Further research may explore why accurate diagnosis is not possible quickly, why there may be ethnic differences and what could be done to alleviate this.

Other important gaps include a lack of research about public health or population based interventions to prevent the development of migraine, potential environmental changes, what could be done to develop supportive workplaces and the cost effectiveness of care.
More could also be done to explore risk factors that could be targeted for intervention. For instance, a review of 17 studies found that frequent use of acute pain relief medication and depression were both risk factors for increasing the number of migraine attacks each month. These are potentially modifiable risk factors.\textsuperscript{204}

Much of the research focuses on medications rather than strategies for identifying and educating people with migraine, their families and health professionals and looking at how they could do things differently. Given that key barriers to care include a lack of education amongst people with migraine, health professionals and employers, it may be important to explore effective strategies to raise awareness and increase empathy.

Some researchers suggest that not enough public research funding is devoted to migraine, and that there is a mismatch between the high prevalence and significant impact of migraine versus the small amount of research funding available.\textsuperscript{205}

There may be a need for high quality randomised controlled trials which use standardised protocols and standardised definitions of migraine to allow comparisons between studies and initiatives.

**Implications**

In 2019, more than 1,800 people told The Migraine Trust about their experience of living with migraine. There were examples of good care, but many people said that migraine care in the UK is falling short of acceptable standards and that they are not being well supported to manage their migraine in the long term. Less than one third of people said they were satisfied with their care and only 15\% thought that the NHS currently manages migraine well for children and adults.

There may be an appetite for change. In 2019 the NHS RightCare programme released a Headache and Migraine Toolkit to help NHS organisations prioritise better care. The Toolkit notes that improving care would not only be better for people with migraine and their families, it would also be positive for the health and care system. Simple improvements to migraine care could help to avoid almost 16,500 emergency hospital admissions, saving the NHS about £11.5m per year.\textsuperscript{206}
Other estimates suggest that migraine may cost the UK economy around £9.7 billion a year once lost work days are added to healthcare costs, so there is a significant financial incentive to help people with migraine manage the condition.\textsuperscript{207}

The research summarised in this review suggests that many care options have been tested. Some have been around for a long time and some are relatively new so evidence is just beginning to emerge. It is not possible to say that some types of care or management approaches are ‘best’ solely based on the research. Instead what appears important is to:

- have access to caring and empathetic health professionals
- be given a clear diagnosis promptly
- be supported to manage migraine in the long term and avoid triggers
- be supported to test different approaches that may work for an individual
- have access to medications for prevention and for treating migraine attacks promptly as soon as they occur

This individualised pathway approach is in line with NICE guidelines.\textsuperscript{208}

Based on the themes in published research, priority areas to improve migraine care in the UK may include:\textsuperscript{209}

- embedding ways to screen and identify people with migraine into routine primary care practice and in community and workplace venues
- raising awareness about migraine amongst people with migraine, employers and health professionals
- increasing the knowledge and confidence of GPs, general practice nurses and pharmacists to manage migraine
- improving access to medications, including preventive medications
- increasing the use of non pharmaceutical therapies
- actively supporting self management, with tools and information
- improving how people with migraine are followed up over time and how treatment outcomes are measured

The Migraine Trust will continue to work with the migraine community, the NHS and other stakeholders to consider practical ways to move forward with these and other priorities identified as important to people living with migraine. Box 3 provides The Migraine Trust’s initial reflections about the implications of this review.
This review is excellent reading for anyone wanting to learn how migraine is currently treated. It presents evidence about novel approaches to managing migraine in settings outside of traditional healthcare, such as the community and workplace.

We were very surprised by the lack of research into public health approaches to prevent migraine. Migraine is one of the most prevalent and debilitating non communicable diseases in the world and is recognised as the second highest cause of disability worldwide. As such, it is a major public health issue. We had hoped to find evidence that migraine was being tackled through tried and tested population level interventions, such as awareness raising campaigns or screening programmes, or through more innovative initiatives such as ‘migraine friendly’ town planning or urban design.

But after reading more than 2,500 studies published in the last twenty years, our reviewers found very little research into these kinds of interventions. This is especially surprising considering the fact that the prevention of other long term diseases, such as diabetes, is commonly researched. We think this begs the question as to why migraine appears to be viewed as inevitable, whereas other non communicable diseases are viewed as preventable.

We were also surprised by the lack of research into approaches to migraine care and treatment within the NHS. Most published research into migraine treatment and prevention pertains to common medications used during migraine attacks or to prevent migraine attacks. This is a very important part of the picture of migraine care, but doesn’t tell us very much about what ‘good’ migraine care and management looks like or how the NHS can better deliver ‘good’ care. The section in the review exploring barriers and enablers to optimal migraine care sheds some light on this issue, but it’s important to note that most of those research studies come from outside of the UK.

We were most intrigued by the examples in the review around workplace interventions to help employees with migraine. These interventions have included information leaflets, online education, screening tools and relaxation or exercise programmes. We think there is so much potential here for employers to learn about ‘what works’ when it comes to supporting their staff with migraine and to start taking proactive steps to do so. These studies have demonstrated that it can be straightforward and inexpensive to help employees with migraine get the support they need.

These are our first thoughts on what this review into migraine care is telling us. We’d now love to learn yours. To let us know what you think, email policy@migrainetrust.org
# Appendix 1

## Research about medications used during migraine attacks

<table>
<thead>
<tr>
<th>Drug type</th>
<th>Key themes in findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaesthetics</td>
<td>Lidocaine is a local anaesthetic that causes temporary numbness. Evidence does not support the use of intranasal lidocaine for migraine attacks. There is mixed evidence of effectiveness in acute pain reduction and no evidence of preventing headache recurrence. Another review of nine studies found that propofol was effective for migraine in adults visiting the emergency department. There were mixed results in studies with children. Safety has not been fully examined.</td>
</tr>
<tr>
<td>Analgesics</td>
<td>Analgesics (pain killers) are often used when people have a migraine attack. Many of these have been found to be safe and useful. For instance, paracetamol is widely available and low cost so may be a useful choice for people who cannot take non steroidal anti inflammatory drugs or aspirin. Two reviews found that paracetamol had benefits but was not as good as other analgesics. It provided pain relief in about half of adults, but complete pain relief only for a minority. Higher doses were more effective and soluble formulations provided more rapid relief. Adverse events were mild. A review of three trials and 10 reviews found that ibuprofen and paracetamol might be effective for treating migraine attacks in children. Thirteen trials found that aspirin 1000mg was effective for acute migraine headaches. Adding metoclopramide 10mg improved the relief of nausea and vomiting. Adverse events were mainly mild and transient.</td>
</tr>
<tr>
<td></td>
<td>Naproxen is a non steroidal anti inflammatory drug (NSAID). A review of six trials found that naproxen was more effective than placebo for relieving migraine pain but it was effective for less than 20% of people so the reviewers suggested that this was not clinically useful. Adverse events were mostly mild or moderate in severity and rarely led to withdrawal.</td>
</tr>
<tr>
<td></td>
<td>A review of eight trials found that parenteral ketorolac, another NSAID, is effective for the relief of acute migraine headache in the emergency department. It is associated with similar pain relief and is potentially less addictive than meperidine and more effective than sumatriptan. It may not be as effective as metoclopramide / phenothiazine.</td>
</tr>
<tr>
<td></td>
<td>A review of five trials found that oral diclofenac potassium 50mg provided relief from pain and associated symptoms, although few people experienced pain free responses. Adverse events were mostly mild and transient.</td>
</tr>
<tr>
<td>Drug type</td>
<td>Key themes in findings</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Antiemetics</td>
<td>Antiemetics aim to reduce nausea and vomiting. For instance, a review found that although there was not enough good evidence, there was a trend towards intravenous metoclopramide stopping migraine headache more promptly than placebo or active comparators. The reviewers concluded that it may be reasonable to use metoclopramide in emergency departments.</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Antipsychotic medications may have a calming effect that helps to reduce pain during a migraine attack. Olanzapine (atypical antipsychotic) has been found to reduce pain in people having a migraine attack. Prochlorperazine is an antipsychotic and antiemetic. A review of 11 studies found that prochlorperazine was effective for treating adults with acute migraine in the emergency department. Prochlorperazine had a similar safety profile as other treatments and reduced requests for rescue analgesia.</td>
</tr>
<tr>
<td>Calcitonin gene related peptide (CGRP) receptor antagonists</td>
<td>CGRP antagonists are a new type of medication. Drugs include telcagepant, olcegepant, BI 44370, rimegepant (BMS-927711), MK3207 and ubrogepant. A review of ten studies examined these six drugs for acute migraine treatment. Olcegepant, ubrogepant and BI 44370 were more effective in ensuring pain relief within two hours than placebo. BI 44370 was associated with an increased risk of adverse events compared to placebo. Out of the six medications, olcegepant was most effective and ubrogepant had the lowest risk of adverse events. The reviewers concluded that CGRP antagonists are promising for the acute treatment of migraine, especially among people who are unable to take triptans. Another review of CGRP antagonists for acute care included 16 trials. There was a reduction in migraine pain, but the effect seemed to gradually reduce between the first month and the third month of treatment. The reviewers concluded that anti CGRP treatment can reduce migraine pain in the short term, but the long term effect needs further investigation. The effects may be influenced by the type and dose of anti CGRP.</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Treatment with corticosteroids during an acute attack may be associated with recurrent headaches becoming milder. In a review of 25 studies and four systematic reviews spanning a 65 year period, three quarters of the studies found that corticosteroids had benefits. On average, corticosteroids reduced the risk of headache recurrence within 24 hours by 30%. Single dose intravenous dexamethasone 10mg was the most commonly used for managing resistant, severe or prolonged migraine attacks. Outcomes were most favourable when migraines were more severe, when pain relief was incomplete and when there was a history of headache recurrence.</td>
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<tr>
<td>Hormones</td>
<td>A small UK study assessed the effect of estradiol supplements (commonly used for hormone replacement therapy) on menstrual attacks of migraine. Although percutaneous estradiol was beneficial during acute treatment, this was offset by deferred oestrogen withdrawal which triggered migraine after the gel was stopped. Subcutaneous octreotide 100mg has not been found to be effective in the acute treatment of migraine.</td>
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<tr>
<td>Drug type</td>
<td>Key themes in findings</td>
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<td>Magnesium sulphate</td>
<td>A review of six trials of magnesium sulphate administered intravenously in the emergency department found mixed results. There were some benefits in pain control after one hour, reduced aura duration and reduced need for rescue analgesia compared to other medications.</td>
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<td>Triptans (serotonin receptor agonists)</td>
<td>Many studies have explored triptans, comparing them to other medications, to different types of triptans and different doses. Triptans have been found to reduce migraine pain in adults and children. Various types of triptans are available. For example, sumatriptan can be administered orally, subcutaneously, intranasally and rectally. The most common dosing and routes in Europe are oral 25mg, 50mg, 100mg; subcutaneous 4mg, 6mg; intranasal 5mg, 10mg, 20mg; and rectal 25mg. High quality research reviews found that subcutaneous administration was the most effective, with six out of ten people taking sumatriptan 6mg having pain reduced from moderate or severe to none within two hours (59%). The most commonly used doses of oral, rectal and intranasal sumatriptan also provided useful pain relief. Subcutaneous administration provided more rapid pain relief than the other routes, but also had higher rates of adverse events. Taking medication early, when pain was mild, was more effective than waiting until the pain was moderate or severe. The reviewers concluded that sumatriptan is an effective treatment for acute migraine attacks, but has more adverse events compared to placebo. In 16 trials, intranasal sumatriptan reduced migraine pain. Higher doses were associated with faster pain relief but also more adverse events, including taste disturbance. Another example is zolmitriptan 2.5mg and 5mg, which has been found to be effective for pain relief for some people, but had increased adverse events compared to placebo. A review of 141 trials of 15 oral treatments found that triptans were associated with an increased risk of adverse events compared to placebo. A cost effectiveness analysis of oral triptans for migraine used data from the UK, France, Italy and Spain. Triptans included almotriptan, brand name and generic sumatriptan and zolmitriptan. The average cost effectiveness ratio showed wide variations across different countries. Generic sumatriptan was the most cost effective of the medications studied. The researchers warned that it may not be appropriate to transfer conclusions about cost effectiveness between countries, even close neighbours. A study modelling what would happen if a specific triptan was available over the counter in the UK, France, Spain, Italy, Germany and Poland found that savings would be about €75 million in direct costs (2013 prices). The authors concluded that this would be a useful policy approach.</td>
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## Appendix 2

**Research about medications used to prevent migraine**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Key themes in research findings</th>
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<tr>
<td>Analgesics</td>
<td>In eight studies about the impact of aspirin on preventing migraine the dose varied from 50mg to 650mg per day. The optimal dose was unclear but studies reported a reduction in the number of migraines at a dose of at least 325mg per day.(^{238})</td>
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<tr>
<td>Antiepileptic drugs</td>
<td>A review of antiepileptic medications taken regularly by adults with episodic migraine found that topiramate, sodium valproate and divalproex reduced migraine attacks. Topiramate 100mg and 200mg was more effective than 50mg, but was associated with more adverse events. There was insufficient evidence to support the use of gabapentin.(^{239})</td>
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<td></td>
<td>A review of 10 trials found that valproate (valproic acid or sodium valproate or a combination of the two) reduced the number of migraine attacks in adults with episodic migraine. It was reasonably well tolerated.(^{240})</td>
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<tr>
<td></td>
<td>A review of 17 trials found that topiramate 100mg per day reduced the number of migraine attacks in adults with episodic migraine. It was reasonably well tolerated.(^{241})</td>
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<td>A cost effectiveness study in the UK found that the incremental cost of topiramate versus no preventive treatment was about £10 per migraine averted and £5,700 per quality adjusted life year gained (2005 prices). Savings from reduced work loss were about £36 per month. The researchers suggested that topiramate would be cost saving compared with no preventive treatment once societal costs were considered.(^{242})</td>
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<td></td>
<td>A review of six trials found that gabapentin was not effective for reducing the number of migraine attacks in adults with episodic migraine. Adverse events were common. The reviewers concluded that gabapentin should not be used in routine clinical practice.(^{243})</td>
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<td></td>
<td>A review of 10 trials of antiepileptic drugs other than gabapentin, pregabalin, topiramate and valproate found that most drugs were no better than placebo in preventing episodic migraine. Acetazolamide, carisbamate, clonazepam, lamotrigine, oxcarbazepine and vigabatrin were not more effective than placebo in reducing the number of migraines. In one trial each, carbamazepine and levetiracetam were better than placebo in reducing the number of migraines.(^{244})</td>
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<td></td>
<td>Eleven studies of levetiracetam suggested this is well tolerated and may help to prevent episodic migraine. The evidence for chronic migraine remains unclear.(^{245})</td>
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<tr>
<td>Beta blockers</td>
<td>A review of 108 studies found that beta blockers can prevent migraine, in particular propranolol reduced episodic and chronic migraine headaches.(^{246})</td>
</tr>
</tbody>
</table>
**Treatment**  | **Key themes in research findings**  
---|---  
Botox (botulin toxin type A)  | Botox is recommended by the National Institute for Health and Care Excellence (NICE) for chronic migraine. A review of 28 trials assessed the effects of botox injections into the head and neck in adults with chronic or episodic migraine. The reviewers concluded that in chronic migraine, botox may reduce the number of migraine days per month by an average of two days compared with placebo. The evidence was uncertain for adults with episodic migraine. The longest treatment duration was three rounds of injections with three months between treatments so it was not possible to analyse long term effects. The risk of adverse events was double that of placebo, but this risk was lower compared with other migraine prevention treatments.

A review of 17 trials found a positive trend towards botox injections reducing the number of headaches in people with episodic and chronic migraine. Botox was also associated with improved quality of life at three months. There were some adverse events but these were few and mild.

Other reviews have found that botox is safe and effective for adults with chronic migraine, although there are some adverse events. In some studies about one quarter of people reported one or more treatment related adverse events, the most frequent of which was neck pain. High proportions of people receiving botox treatment were satisfied with it.

In the UK and Europe long term botox use was studied in 633 adults with chronic migraine. People received botox every 12 weeks and were followed up for two years after beginning treatment. The number of headache days per month reduced from an average of 21 to 7. Quality of life and health functioning were improved. 18% of participants reported an adverse event, mostly mild to moderate.

An audit with 200 people in the UK sought to examine the use of botox following NICE guidelines. After two treatments, two thirds of participants had at least a 30% reduction in headache days. Those who continued treatment up to three years reported that the beneficial effect continued. Many participants were able to be reclassified with episodic rather than chronic migraine around six months.

UK cost effectiveness analyses show that botox is cost effective for adults with chronic migraine. Botox was associated with an increase in costs of £1,367 (2013 prices) and an increase in quality adjusted life years (QALY) of 0.1 compared to placebo. This provided an incremental cost effectiveness ratio of £15,028. Botox reduced headache days by an estimated 38 days per year at a cost of £18 per headache day avoided. A more recent cost effective effectiveness analysis (2019) found that botox resulted in total discounted incremental costs of £1,204 and an incremental discounted QALY gain of 0.07 compared with placebo in patients with chronic migraine who previously failed three or more preventive treatments. This equates to an incremental cost effectiveness ratio of £16,306 per QALY gained. Administration by a specialist nurse rather than a neurology consultant reduced this to £13,832 per QALY gained.
<table>
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<th>Treatment</th>
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<td>Calcium channel blockers</td>
<td>A review of 25 studies found that flunarizine 10mg per day reduced the number of headaches by an average of 0.4 attacks per four weeks compared with placebo. It was effective in adults as well as children. The effectiveness was similar to propranolol. It was well tolerated. The most frequent adverse effects were sedation and weight gain. 256</td>
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<tr>
<td>Calcitonin gene related peptide inhibitors</td>
<td>See Box 2</td>
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<tr>
<td>Magnesium</td>
<td>Five trials found that high doses of magnesium dicitrate (600mg) appear to be safe and effective for reducing the number of migraines. 257</td>
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<tr>
<td>Melatonin</td>
<td>Melatonin may affect the circadian rhythm, influencing people’s rest cycles. A review of seven studies found conflicting evidence about whether melatonin prevents migraine, but there were positive trends. Immediate release melatonin 3mg was found to be effective in some studies. Melatonin receptor agonist (agomelatine) 25mg and prolonged release melatonin 4mg were found to be effective in lower quality studies. At least three months of treatment may be needed. Melatonin was generally safe, but there were some adverse effects such as liver injuries and reproductive system dysfunctions. The reviewers emphasised that the research about both safety and effectiveness is limited. 258</td>
</tr>
<tr>
<td>Hormones</td>
<td>A review of four trials found that melatonin reduced the number of days with migraine pain and painkiller consumption compared with placebo, but the quality of evidence was low. The reviewers said that the evidence is not sufficient to support the use of melatonin in clinical practice for people with migraine. 259</td>
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<tr>
<td>Selective serotonin reuptake</td>
<td>A review of 11 studies found no evidence that five selective serotonin reuptake inhibitors and one serotonin norepinephrine reuptake inhibitor reduced migraine frequency, intensity or duration over two to three months of treatment. There was insufficient evidence about longer term follow up. 262</td>
</tr>
<tr>
<td>Tonabersat</td>
<td>A review of two trials found that there was insufficient evidence about tonabersat for migraine prevention. Tonabersat was well tolerated. 263</td>
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</table>
References


42 Short AL. Enhancing migraine self-efficacy and reducing disability through a self-management program. J Am Assoc Nurse Pract. (Published online ahead of print November 2019).


Láinez MJ. The effect of migraine prophylaxis on migraine-related resource use and productivity. CNS Drugs. 2009;23(9):727-38.


167 Bigal M, Krymchantowski AV, Lipton RB. Barriers to satisfactory migraine outcomes. What have we learned, where do we stand? Headache. 2009;49(7):1028-41.


https://www.migrainetrust.org/blog/improving-public-funding-for-migraine-research/

NHS RightCare. RightCare: Headache & Migraine Toolkit optimising a headache and migraine system, 2019.


Hollier-Hann G, Curry A, Onishchenko K, Akehurst R, Ahmed F, Davies B, Keyzor I. Updated cost-effectiveness analysis of onabotulinumtoxinA for the prevention of headache in adults with chronic migraine who have previously received three or more preventive treatments in the UK. J Med Econ. (Published online ahead of print November 2019).


