CLARINESS

Migraine clinical trials: Leveraging patient insights to improve recruitment

Digital patient recruitment

Migraine

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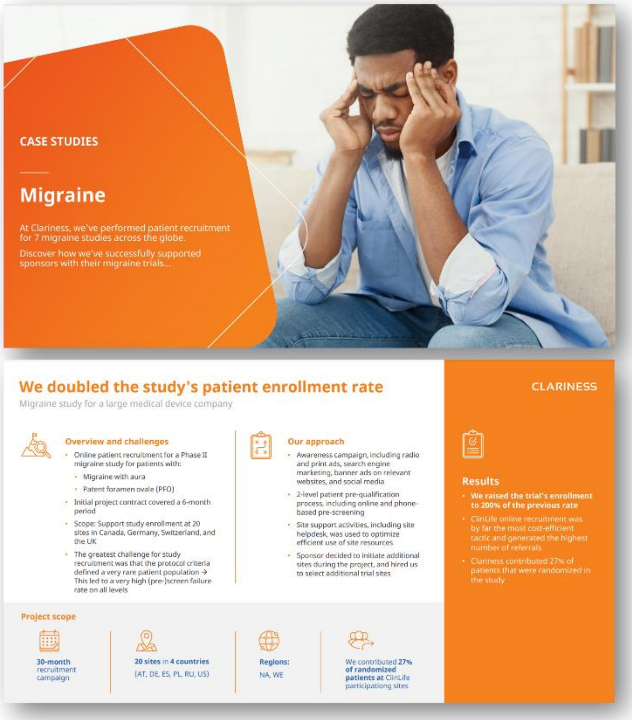

CASE STUDIES

Migraine

At Clariness, we've performed patient recruitment for 7 migraine studies across the globe.

Discover how we've successfully supported sponsors with their migraine trials...

We doubled the study's patient enrollment rate

Migraine study for a large medical device company

Overview and challenges

- Online patient recruitment for a Phase II migraine study for patients with:
  - Migraine with aura
  - Patent foramen ovale (PFO)
- Initial project contract covered a 6-month period
- Scope: Support study enrollment at 20 sites in Canada, Germany, Switzerland, and the UK
- The greatest challenge for study recruitment was that the protocol criteria defined a very rare patient population → This led to a very high (pre-)screen failure rate on all levels

Our approach

- Awareness campaign, including radio and print ads, search engine marketing, banner ads on relevant websites, and social media
- 2-level patient pre-qualification process, including online and phone-based pre-screening
- Site support activities, including site helpdesk, was used to optimize efficient use of site resources
- Sponsor decided to initiate additional sites during the project, and hired us to select additional trial sites

Project scope

30-month recruitment campaign

20 sites in **4 countries** (AT, DE, ES, PL, RU, US)

Regions: NA, WE

We contributed **27% of randomized patients at** ClinLife participationg sites

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Results

- **We raised the trial's enrollment to 200% of the previous rate**
- ClinLife online recruitment was by far the most cost-efficient tactic and generated the highest number of referrals
- Clariness contributed 27% of patients that were randomized in the study

Interested in how we can support your migraine survey, patient recruitment or patient education materials?

DOWNLOAD OUR CASE STUDY

Summary: Understanding the patient perspective in migraine clinical trials

Migraine is a common condition that causes a variety of symtoms but generally a pulsing headache on one side of the head. The condition affects between 10 and 18% of people worldwide, or some 1.3 billion people, with estimated 39 million people in the United States and 41 million in Europe according to recent estimates published in Frontiers in Neurology and by the World Health Organization.

An ongoing challenge in migraine research is that it is often not taken seriously by both the public and sufferers themselves, who often see the condition as "just a headache", as the US Migraine Foundation states in a recent report. This is problematic, as the condition most commonly occurs between the ages of 25 and 50, severely impacts productivity and quality of life and thereby the economy. The Global Burden of Disease Report 2016 puts it as the second leading cause of healthy life lost to disability (YLD). More so, migraine has a long list of associated comorbidities including stroke, vascular brain lesions, coronary heart disease, hypertension and psychiatric diseases (depression, panic disorder, and suicide), restless legs syndrome.

While this highlights the necessity of clinical trials for improved treatments and therapies, a challenge is that a large proportion migraine sufferers remain undiagnosed and therefore unable to be reached by most outreach methods. Only an estimated 7.7% of people with chronic migraine (CM) is diagnosed, with some 75% estimated to be undiagnosed according to Marcus et al, in a recent publication in *Neurology*. Indeed, as prominent migraine researcher Parisa Gazerani, associate professor in the Faculty of Medicine, Aalborg University, Denmark, notes:

> *"The biggest challenges in Migraine clinical trials remains the timely recruitment of patients into our studies."*

Challenges in patient recruitment for migraine clinical trials

In early August 2022, there were 210 clinical trials for migraine disorders in, or shortly before, the recruitment phase. One of the challenges for migraine clinical trials patient recruitment compared to other common health conditions as atopic dermatitis, diabetes type 2 and for example psychiatry disorders, is that there is very little scientific literature on successful enrollment strategies. For clinical trial organizers, this means that the benefits, but also the necessity, of partnering with a third-party provider with proven experience in patient recruitment of the local and global patient population are particularly important.

Top 3 challenges for patient recruitment in migraine trials

1. **Inability to recruit the required number of migraine patients within the recruitment phase of the study:** Migraine trials comparing two types of medication are often delayed due to inadequate recruitment. First, recruitment often relies too much on physician referrals and traditional "offline" marketing channels, and second, due to the high number of undiagnosed patients. Digital outreach methods need to be based on qualitative understanding and data that enable data-driven methods.
2. **Unbalanced gender enrollment clinical trials:** while migraine is at least three times as common in women as it is in men, studies and the International Headache Society Clinical Trials have highlighted that in clinical trials there are often fewer male participants and too many female because of gender selection bias. For example, migraine clinical trials often rely on referrals from GP practices, and women have a higher consultation rate for migraine than men, leading to unequal referral.
3. **Small patient group repeatedly take part in studies:** A problem for the scientific generalizability of the study results of migraine clinical trials is that a small group of participants try to participate in a large number of studies. For this reason,

researchers suggest that "investigators establish a database of the number of migraine studies of any kind in which each particular patient has participated in the last 2 years."

The importance of the Patient Perspective

What all these challenges to migraine patient recruitment have in common is a lack of understanding of the local and global patient population by organizers of clinical trials. This understanding consists of a number of elements:

1. **The demographics of local migraine patient populations related to the study protocol:** protocols for migraine should be optimized based on the potential study populations nearby accessible sites.

While it is generally known that migraine is more common in women (up to three times more common), recent studies show that this indication may occur with different frequency in different ethnic groups. For example, the prevalence is significantly higher in Caucasians (20.4%) than in Africans (16.2%) or Asians (9.2%), while a similar pattern is observed in men (8.6%, 7.2% and 4.2%).

As a recent survey concludes:

> *"Migraine has racial and ethnic variation in pain presentation, as well as communication about pain symptoms. It is also documented that migraine prevalence varies by country, with European countries reporting the highest rates and African countries the lowest, suggesting possible biologically driven racial as well as cultural differences."*
>
> - Alice Pressman et al (2016)

2. **Channel optimalization:** It is important to know which channels are most effective in recruiting different migraine patient groups (based on age, gender, ethnicity and socioeconomic status) and which types of advertising work best for specific digital patient communities.

3. **Screener optimalization:** Pre-screeners are an effective tool to improve the quality of referrals, but some questions are more often misunderstood or lead to a preliminary termination of the screener. Therefore, continuous optimization is needed.

4. **Reasons for participating or not participating:** reasons to participate or decide against participation often come down to a variety of perceived misconceptions, fears and benefits, understanding these helps boost recruitment and retention.

Surveys highlight that for migraine patients the biggest factors for participation are perceived benefits of the medication, the type of medication and altruistic reasons. Compared to other indications, altruistic reasons more often mentioned in migraine surveys, which researchers explain due to the fact that thus far, a lot of unknown about the causes of migraine.

> *“Results suggest that patients are interested in understanding their migraines and securing relevant information in addition to obtaining pain relief. Patients desired collaborative relationships with their physicians and a team approach to treatment.”*
>
> - Constance K. Cottrell et al 2007 (Perceptions and Needs of Patients With Migraine)

Improving the patient understanding

There are a number of ways that sponsors can improve their understanding of migraine patient populations for their planned clinical trial. As we've recently highlighted in our Whitepaper "Enhancing Clinical Trials", one way is partnering with a third-party provider with a proven record of experience in understanding the patient population. This is especially beneficial for indications such as migraine or headache trials, as there is little academic literature about the motivation and willingness to participate for this patient population.

At Clariness, we believe that a thorough understanding of the patient population is essential for any local or global patient recruitment campaign. We have three ways:

1. **Data-driven insights:** based on research literature and our own data from previous recruitment and survey campaigns for migraine, we have a thorough understanding of a variety of local patient populations and know which channels and methods of communication are most effective in reaching these.
2. **Interviews:** qualitative interviews can offer a more detailed understanding of the reasoning of patients and especially when conducted in focus groups, can bring patient-centric solutions to participation and retention challenges, as Cottrell et al note.
3. **Surveys:** digital surveys are a great opportunity to reach migraine patients from various ages, backgrounds and regions. At Clariness, we have conducted several patient surveys for migraine, as well as supported sponsors with their own surveys.

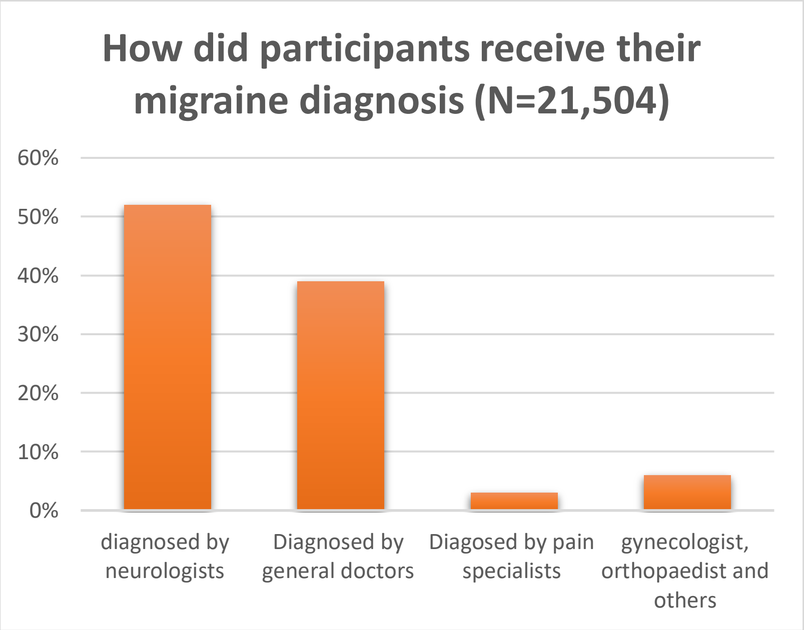
Patient Insights through surveys

To illustrate the great opportunity that large-scale digital surveys offer to gain a representative understanding of local patient populations, including migraine, we will look at a migraine survey that we recently supported. The results of this survey, called EPISCOPE, **the largest survey of migraine patients in Germany to date**, were recently published in Nature. You can read the article here.

> *"The EPISCOPE survey was rolled out by Clariness GmbH [..] and patients were informed about data storage, processing, and publication, and their informed consent was obtained. The survey software is hosted on the fully secured server environment of Clariness GmbH in Germany [..] and the questions and response options were developed together by Clariness GmbH and the authors."*

- Marie Groth, Zaza Katsarava, "Results of the German migraine Patient Survey on medical care and Prophylactic treatment Experience (EPISCOPE)", in: *Nature Scientific Reports* 12 (March 2022).

A total of **21,504 patients with migraine** of various degrees of severity throughout Germany participated in the digital survey using Clariness' **ClinLife patient-centric clinical trials database.**

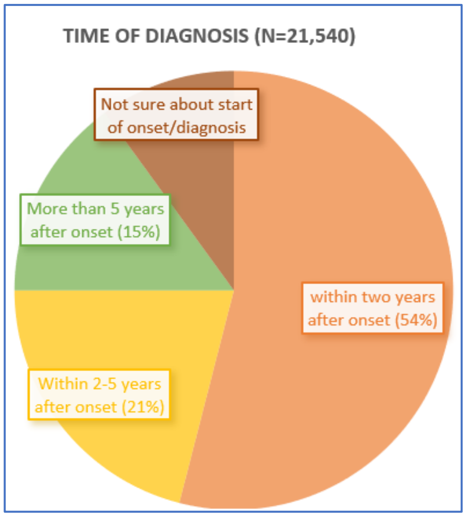


Patients were approached primarily via social media advertising on Facebook and Instagram as well as by search engine advertising. More so, the patient database of ClinLife® was included in various ways through newsletters.

> *"The advertisements were designed to appeal to people's interest towards migraine or their willingness to help improve awareness of migraine disease, and thus resulted in an interest-guided study population."*

- Marie Groth, Zaza Katsarava, "Results of the German migraine Patient Survey on medical Care and prOPhylactic treatment Experience (EPISCOPE)", in: *Nature Scientific Reports* 12 (March 2022).

The authors draw several conclusions from the survey results, the following 3 being the most important for sponsors and sites organizing clinical trials for migraine.



1. **Lack of patient education:** migraine patients generally have a lack of awareness of the disease and of potential treatment options, this results in minimal pro-active searching for diagnosis or new treatment options. As a result, most migraine patients need to be educated or informed before they will consider participating in a clinical trial. More so, it means that traditional forms of study recruitment, for example, through doctor offices and advertisement posters are insufficient.
2. **Fear of stigmatization is an additional barrier to participation:** many migraine patients do not see their disease as a health problem, but as "just a headache". This is also reinforced by the fact that the social environment is not informed about migraine. As the authors note, stigmatized patients are less likely to seek treatment or choose to participate in clinical trials.
3. **Differences between migraine patients:** as the authors note, earlier studies with migraine patients with a Turkish-background highlighted that “social disparities influence access to medical care and poor awareness” is one of the key factors why some groups “do not seek medical care.” The survey highlights that younger migraine patients have less awareness of the their condition, let alone of treatment options or the importance of clinical research.

As the authors conclude, it is striking that even in a country such as Germany with a well developed and easily accessible healthcare system, there is a lack of patient awareness and understanding of their condition and treatments. Indeed, clinical trial recruitment campaigns therefore always need to take a strong focus on patient education and patient-centric outreach methods.

CONTACT CLARINESS' PATIENT INSIGHTS

Digital patient recruitment for migraine studies

Digital patient recruitment is ideal for migraine clinical trials, as it enables a targeted and data-driven approach based on clear metrics such as prevalence statistics. While traditional marketing only allows for general targeting, e.g. through posters in the media or flyers in doctors' offices. Digital patient recruitment, if done right, can also find patients who do not yet have a diagnosis or are not interested in migraine therapies.

1. Women are disproportionately affected by migraine, almost in a 3 to 1 ratio.
2. People between the ages of 18 and 44 are significantly more likely to suffer from migraines; only 5.1% of migraine or severe headache diagnoses affect sufferers over 75 years of age.
3. There are large differences in prevelance between ethnic groups. In the USA, for example, Native Americans have by far the highest prevalence of migraine (19.2%), while sufferers of Asian descent have the lowest (11.3%).
4. There is a higher prevalence within families (up to 60% of patients with migraine have a family member who also suffers from migraine), suggesting that genetics plays a major role in migraine.
5. Prevalence is higher among people from lower socioeconomic backgrounds or living below the poverty line.

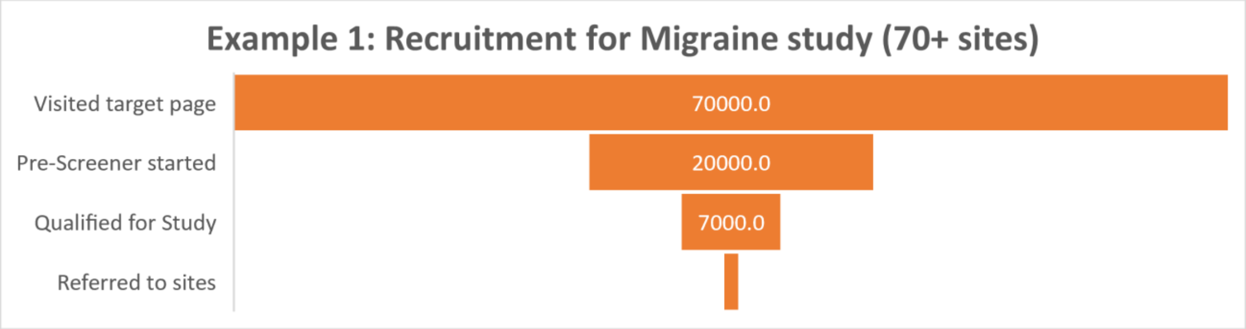
Digital patient recruitment can be conducted via two options:

1. Data-driven, "direct" outreach to patients, their families, caregivers and friends with advertisements for specific migraine studies.
2. “Indirect" outreach via a platform that allows proactive patients to find studies through online searches, indication-based marketing, collaboration with patient organizations and subscription-based databases.

Clariness’ solution to migraine patient recruitment

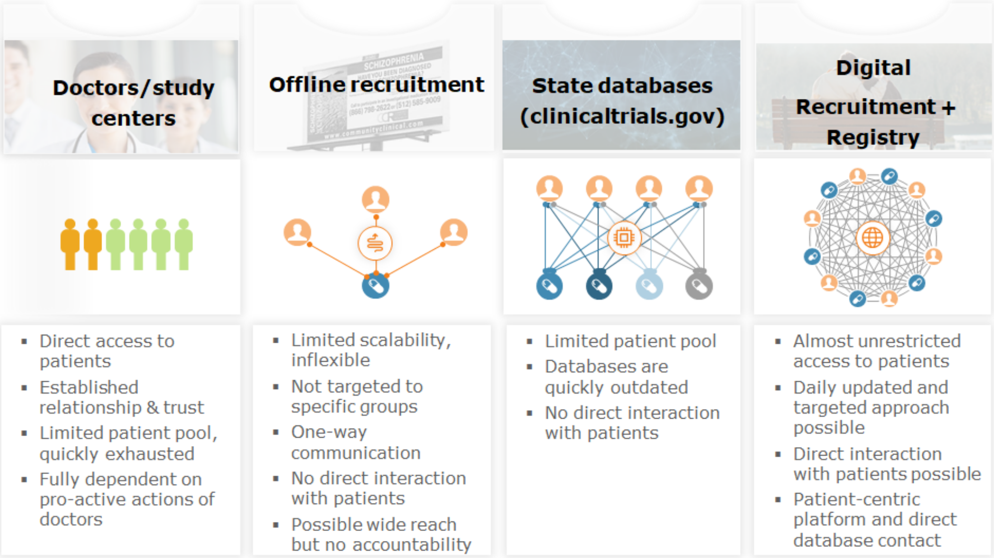
While there are an increasing number of third-party providers offering patient recruitment services, most of them do not specialize in individual indications, i.e. they lack the experience and data to run cost-effective campaigns that recruit within the required time. At Clariness, we have a proven track record of understanding of the local and global migraine patient populations.

Based on the study protocol we identify challenges up front and adjust our digital patient recruitment strategies over 40 possible channels, including our own ClinLife® database with over 50,000 subscribers.



In a recent campaign for a largescale international migraine clinical trial with over 70 involved sites, we focused on reaching as many potential patients as possible due to the high number of undiagnosed patients. Our data-driven pre-screener was able to successfully filter patients most likely to qualify for the study, leading to a reduced workload of the sites.

Clariness' combined digital recruitment + Registry approach compared to other forms of patient recruitment:

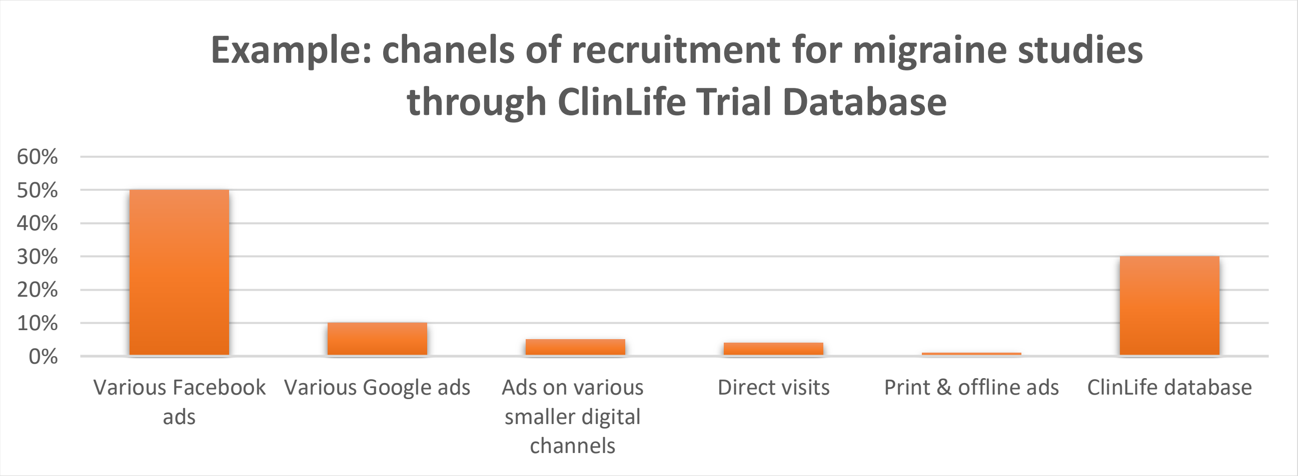


Doctors/study centers	Offline recruitment	State databases (clinicaltrials.gov)	Digital Recruitment + Registry
▪ Direct access to patients ▪ Established relationship & trust ▪ Limited patient pool, quickly exhausted ▪ Fully dependent on pro-active actions of doctors	▪ Limited scalability, inflexible ▪ Not targeted to specific groups ▪ One-way communication ▪ No direct interaction with patients ▪ Possible wide reach but no accountability	▪ Limited patient pool ▪ Databases are quickly outdated ▪ No direct interaction with patients	▪ Almost unrestricted access to patients ▪ Daily updated and targeted approach possible ▪ Direct interaction with patients possible ▪ Patient-centric platform and direct database contact

ClinLife®: a patient-centric trial database

At Clariness, we have expanded our focus over the past year to include indication-based recruitment services through our ClinLife® clinical trial database. Study organizers who have a smaller budget or need to start recruitment quickly can add their studies to our ClinLife® database and benefit from indication-based marketing. This enables a quick start to recruitment as no EC approval is required.

ClinLife® Registry enables a steady stream of referrals through a variety of channels, as Example 2 shows. However, it can be complemented by the Active Recruitment Service, which performs constantly adjusted, data-driven recruitment across more than 40 channels.



This is how ClinLife Registry works:

1. ClinLife Registry displays all of your clinical trials on ClinLife® and creates a dedicated trial page and pre-screener.
2. Interested persons search the Internet for information or studies on their indication or click on personalized ads promoting the specific indication.
3. The data of potentially interested persons who have decided to participate in a study will be securely transferred to the study center in compliance with all GDPR, European as well as national, data protection laws.

ClinLife® was developed in direct collaboration with patients and lists studies of different sponsors, CRO's, SMOs and single sites. The platform enables patients to learn more about clinical trials, test their eligibility and apply to participate in them.

What sites say:

"We struggled to get the number of participants we wanted and spent a lot of time and effort recruiting participants. Since we published our study on ClinLife® we don't have to do anything and suddenly we have a list of interested people!"

- Dr Laura Blauth, FHWS (Germany)

What patients say:

"I usually never click on ads, but this ad about a clinical trial really appealed to me, so I applied right away. The research center was only 2 km away, so the personal approach was optimal."

2021 Patient's Voice Participant

Read more about Patient's Voice:

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