CLARINESS

Patient recruitment for cardiovascular disease clinical trials

Understanding, informing, recruiting and retaining cardiovascular patients

Contents

Summary

Heart disease is one of the leading causes of death worldwide. Although the overall incidence worldwide is roughly 1% of the population, there are big differences between parts of the world, individual countries and population groups. With an average of over 20% of the elderly population being affected, the number of patients with heart diseases in Western nations is estimated to rise especially hard (up to 200 to 250% according to some studies) due demographic aging.

Organizers of clinical trials for heart diseases for long have struggled finding the required number of patients to participate in their trials. Where a lot of attention in the literature focusses on the recruitment challenges of cardiac clinical trials in the acute setting, other heart studies also struggle in the recruitment phase.

There are different reasons for the fact that patient recruitment for cardiovascular disease studies often falls short, causes studies to delay or worse, be permanently postponed. On the one hand, the fact that many clinical trial organizers still rely on old methods of patient recruitment of wrongly implemented digital methods, means that many patients who potentially could participate are simply not reached. On the other hand, studies have increasingly highlighted barriers for specific groups as women, elderly people and minority populations as well as a general lack of willingness under heart patients to participate in trials.

About Clariness

Clariness has over 17 years of experience in digital recruitment for cardiovascular disease. Based on deep knowledge of patient populations and data-driven methods, we identify study-eligible subjects and qualify them through pre-screener questionnaires. The quality of our pre-screener is demonstrated by the fact that in our most recent cardiovascular disease study, 50% of our referrals were successfully randomized.

Contact us now for more information

Challenges in patient recruitment for cardiovascular disease studies

Whereas there are some general facts about the prevalence of heart diseases significantly affecting elderly people as well as women more than men, at the same time it is important to recognize that nearly 20 percent of those who die of heart disease are under the age of 65.

More so, it is crucial for any patient recruitment campaign to take into account that cardiovascular disease covers a wide range of conditions from abnormal heart rhythms, angina, coronary artery disease, peripheral arterial disease, stroke and heart failure. This means that for each study, a specific outreach campaign is required based on a thorough understanding of the, in the case of international studies, various local patient populations.

As Scott D. Solomon et al show in a recent review, for cardiovascular trials in general, both recruitment and retention remain big challenges. This is one of the reasons that heart disease, that as many scholars note, has become completely dependent on large-scale randomized controlled trials as any other indication, have failed to make significant progress in developing new medications and therapies over the past decades.

With some types of cardiovascular disease studies requiring patients who are in relative stable conditions or acute state of treatment, others simply require hundreds if not thousands of patients.

For this reason it is crucial for organizers of cardiovascular disease trials to opt for a patient recruitment provider that builds its campaign around a qualitative understanding of the specific type of disease, its patient populations, concerns and needs.

Learn more about our experience here

Peripheral artery disease patient recruitment challenges

As McDermott and others note (2016) there are several challenges specific to **peripheral artery disease studies** that limit recruitment and above that, screening success. In their study they screened over 372 patients that were initially referred from primary care practices, yet only 23 (6%) of these patients were ultimately randomized.

Despite that, organizers of clinical trials often assume that primary care professionals have a better understanding of the patient and therefore provide a so-called "higher quality of referrals", they managed to find only 10% of their total required participants via this route.

Challenges:

- **Lack of or inadequate pre-screener** causes a high number of referrals to be ultimately unsuitable for randomization.
- **Lack of patient-friendly** information causes misconceptions and many initially referred patients ultimately still decided against participation.

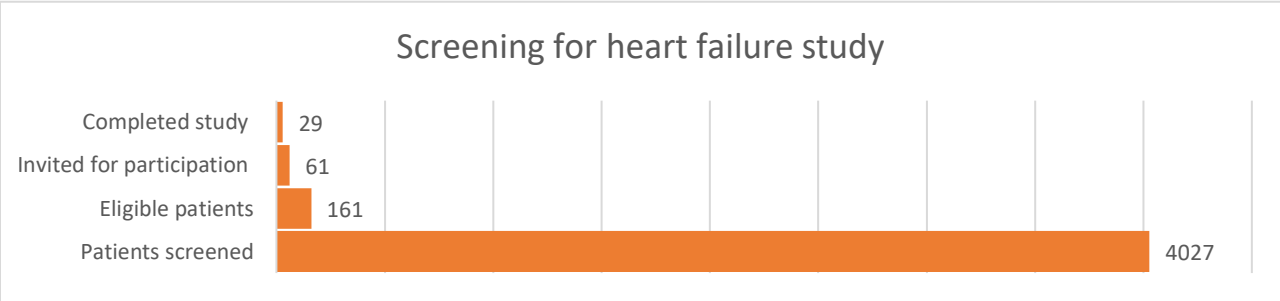
Heart failure/ heart attack patient recruitment challenges

As Harrinson et al note in 2018, in general "compared with other populations of healthy persons or persons with less serious medical conditions, heart failure (HF) patients may be challenging to enroll in research studies".

There are a number of specific challenges that Harrinson (2018) and others as Bei-Hung Chang et al (2007) have noted for heart failure patient recruitment:

1. **Frequent hospitalizations:** make it difficult for patients with heart failure to visit the study center.
2. **High symptom burden:** as for example severe fatigue stops patients from participating in a study as they fear that the travel but also necessary participation actions will be very burdensome.
3. **Specific inclusion criteria**: criteria, as for example the heart failure type or stage are a reason that many patients who want to participate are still eventually excluded at the first screening visit.

As Susan J Pressler and Harrinson both conclude, this means that "as the pool of eligible participants becomes smaller", recruiting should "involve screening a large number of people" (Pressler et al. 2008). This is clearly demonstrated by Pressler's own example:



Patient understanding and patient recruitment

Whereas the above shows it is crucial to take into account the challenges for specific cardiovascular disease, in the end most studies show that patient recruitment for most cardiovascular disease depend on reaching a large amount of potential participants.

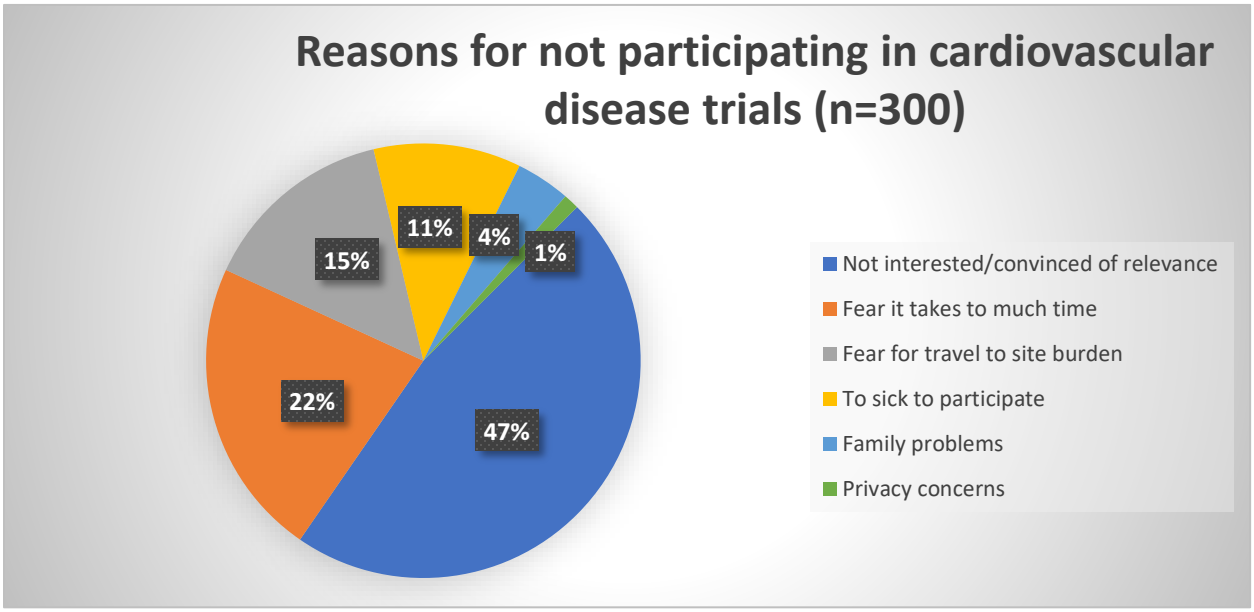
At the same time, merely reaching a large amount of patients through various channels is not enough. After all, as shown by Harrison et al (2018), even patients who are referred by doctor clinics, in the end often decide against participation when they are not properly informed.

"Future efforts to increase the efficiency of recruitment should focus on improving convenience for participants in this acute setting and ***improving basic understanding of clinical trials****"*

- Mimi Sen Biswas et al (2017).

As Harrison argues, with "lack of interest" being "overwhelmingly cited as the top reason for refusal to participate, employing strategies to stimulate interest in studies is essential for recruiting heart failure patients". Furthermore, it is important to recognize as Bernice C Yates argues, that ''no interest'' may also simply mean

being "reluctant to participate due to uncertainty about what participation will entail".



Harrison et al study (2018).[1]

Strategies to encourage participation in heart disease studies

- **Surveys and questionnaires:** by understanding a study populations "reasons for ambivalence" and addressing these concerns in the trial outreach materials, interest could be improved and thereby recruitment Beckie et al. (2009), Kim and Menon (2009).
- **Individualized 'orientation sessions' and phone screeners** to introduce the study procedure to patients. At Clariness, we notice that we regularly receive questions from patients about their concerns via our ClinLife® platform since we have added a phone number. Furthermore, we employ phone screeners to be able to address concerns immediately.
- **Patient friendly study material and information:** as Yates (2009) show, presenting patient friendly explanations of cardiovascular study's objectives can significantly boost participation rates. In her study, 54% of patients who

[1] Refusal reasons from 300 patients (66% men, mean age 65 33) included: not interested (n = 163), too busy (n = 64), travel burden (n = 50), too sick (n = 38), family problems (n = 14), too much commitment (n = 13) and privacy concerns (n = 4).

received patient friendly information said they would participate, compared to only 22% in a group of patients who didn't receive information.

Recruiting elderly people in cardiovascular clinical trials

The number of internet users over age 65 is growing rapidly in the past years.[2] In 2020, Denmark recorded the highest share (94%) of people aged 65-74 used the internet in the last 3 months, followed by Luxembourg and Sweden (both 91%), the Netherlands (90%). Germany is a little bit behind at 78%.

Experts have for this long argued that to increase the proportion of older participants, it is crucial to use digital recruitment channels. At the same time, studies highlight that digital patient recruitment is often not specified for elderly people. Examples of necessary adaptions are:

- **Patient-friendly study materials:** adapting study information into larger font size and understandable wording. Studies highlight elderly patients have a low health literacy (Berkman et al. 2011), meaning they often don't understand complex descriptions.
- **Patient-friendly screener measures:** allowing older patients to use telephone-based screening or screeners with basic questions to improve likeliness patients can participate.
- **Decentralized trials adaption:** allowing telephone visits or home visits instead of travelling to the study site. A recent study by Sally Eames *et al* (2013) with stroke patients and their caregivers show that many participants still preferred initial face-to-face education sessions and afterwards preferred to receive follow-up support by telephone.

[2] According to the Pew Research Center, 59% of Americans over age 65 reported using the Internet in 2014, compared to just 35% in 2008

Recruiting women in cardiovascular disease trials

A large-scale review of 740 completed cardiovascular studies between 2010 and 2017 that was published last year found that women are still significantly underrepresented in heart disease clinical trials, making up only about 38% of participants. Despite the fact that women are being affected more often as men and having more severe consequences of cardiovascular diseases and with clinical trials for most other indications are able to reach a more balanced recruitment in terms of men and women. The review understandably received widespread media coverage and in an interview with the Guardian, the author, Dr Jeske van Diemen, of Amsterdam University Medical Centre in the Netherlands, explained that a big reason for the underrepresentation of women was inadequate or failed patient recruitment.

"Enrolment of a representative proportion of women in heart failure studies has proven elusive and may require significant effort from researchers, who ***should proactively approach a greater proportion of women and patients over age 65****"*

- Jordan M Harrison et al (2018)

She notes that while some of the motivators for participating in clinical trials were the same between both men and women (possibility of receiving better care, wanting to help advance science), women more often mentioned specific barriers. Examples of women specific barriers for heart disease trials are:

- **Higher fear for negative effects:** women more often had fears of negative side-effects, thus more need to address specific concerns.
- **Various time constraints reasons:** women more often cited the need to care for children or, in the case of elderly patients, their grandchildren as a reason for not participating.
- **Transport to site problems:** women more often cited not having a driving license as a reason for not participating.
- **More diverse research teams** and clinical trial leadership that understands women and promote the feeling of being represented. This also is an important factor for improving retention.
- **Including female participants in trial design** to improve accessibility.

- Ensuring that the **inclusion criteria** are not based on male-centric presentations could also assist in increased inclusion of women.

Minority population recruitment for cardiovascular diseases

Although many minority populations are disproportionately affected by cardiovascular disease, they remain underrepresented in clinical trials (Prasanna 2021). Although some studies have suggested that there are no real "differences in refusal rates by age, gender or ethnicity" (Mimi Sen Biswas 2007).

In 2021, a working group of the American Society for Preventive Cardiology (ASPC) published a review paper with suggestions on how to improve the patient recruitment of minority populations.

Our recent whitepaper (2022) on improving diversity in clinical trials looks at what measures organizers of clinical trials can take to improve diversity in their studies.

Download the Diversity Whitepaper **here.**

Digital patient recruitment for cardiovascular disease studies

In 2018, people in Western countries spent around 3 hours of their day actively online, for example in Germany alone 31.6 million people are regularly active on Facebook and other social media platforms.[3] Scholars have shown that these

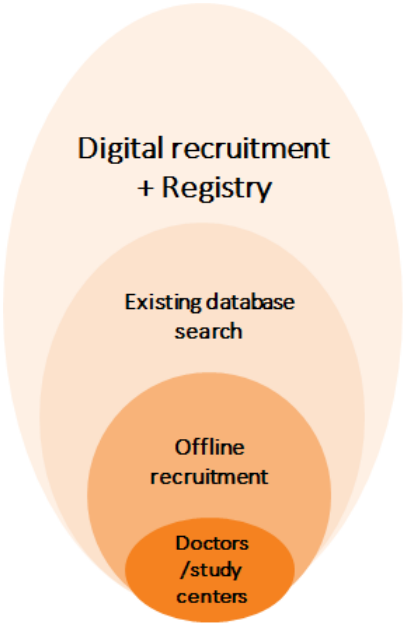
[3] (Statista, 2021).

numbers are even higher for people with health problems.[4] Accordingly, online medical searches are increasing both before and after doctor visits. In fact, Google (Dr. Google, as some researchers have called it) has become the primary way patients search for answers to their medical questions and has undeniably assumed a major role alongside medical professionals.[5]

Digital patient recruitment can be conducted via two options.

First, data-driven, "direct" outreach to cardiovascular disease patients, their families, caregivers and friends with advertisements for specific cardiovascular disease studies.

Second, "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.



The necessity of digital patient recruitment for cardiovascular disease studies is reflected in the analysis made by most academic experts.

"Successful recruitment in studies involving patients with heart failure ***often requires screening of a large group of patients****."*

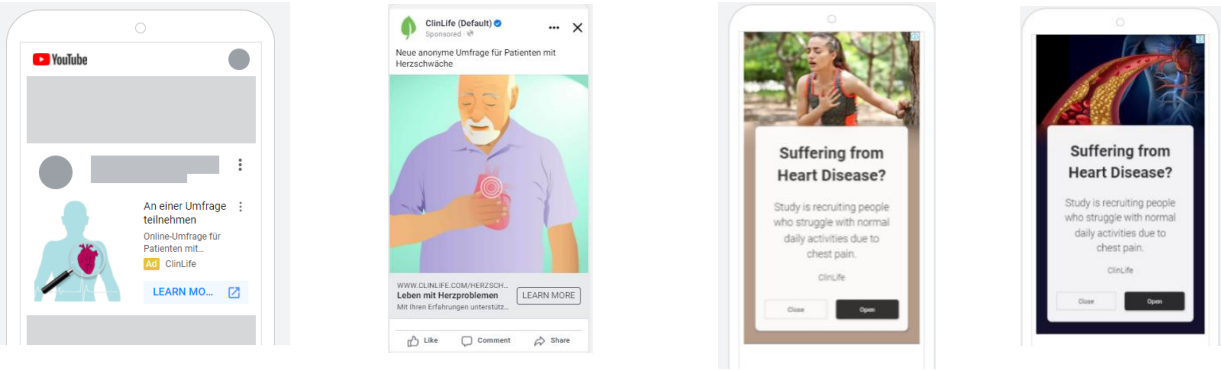
- Susan J Pressler et al (2008).

[4] Van der Eijk, Martijn; Faber, Marjan J; Aarts, Johanna WM; Kremer, Jan AM; Munneke, Marten; Bloem, Bastiaan R (2013-06-25). "Using Online Health Communities to Deliver Patient-Centered Care to People With Chronic Conditions". Journal of Medical Internet Research. 15 (6) 115.
[5] Van Riel, Noor et al. 'The effect of Dr Google on doctor-patient encounters in primary care: a quantitative, observational, cross-sectional study', in: BJGP open vol. 1,2 17 May. (2017) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6169945/

Advantages of digital patient recruitment for cardiovascular disease

1. Customizing the patient profile based on study criteria: depending on the type of cardiovascular disease and location of the site, we create a **detailed patient profile**. When necessary, we also define the need to reach potential caregivers and other family members or contacts.

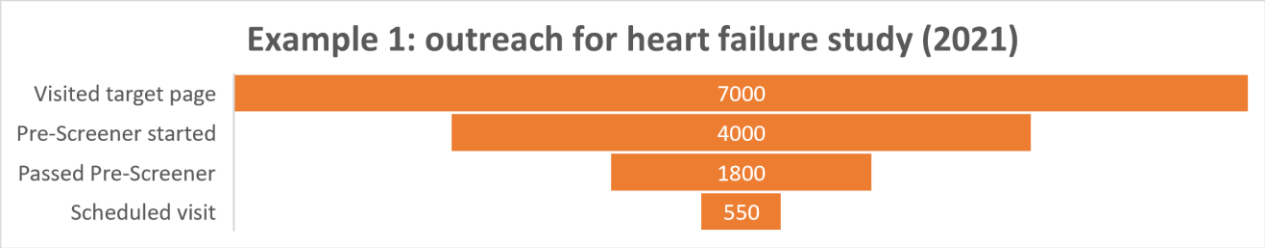
Through analysis of social media responses and questions, large-scale surveys and qualitative interviews, our **Patient's Insights team** forms an overview of the needs and wishes of the local patient group.



Examples of cardiovascular disease studies and survey ads: It is crucial to create ads that are easily understandable and representative.

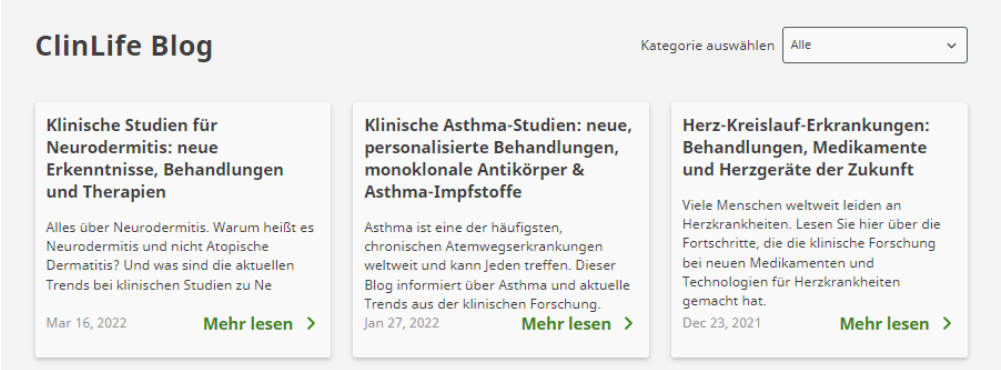
2. Individualized targeting: patients likely to qualify receive an advertisement depending on the **location** and **enrollment capacity** of the site. We use a variety of channels to target patients, based on **categories as age, gender, risk factors** that we know from past experiences and annual surveys to be of interest to cardiovascular disease patients. Other examples are online forums, social media groups and keywords that are (often very indirectly) related to heart disease.

3. Behavioral targeting: data-driven algorithms identify people with similar online behavior to those who have already registered for the study or people who visited the study site but did not register. This allows for the specific targeting of only people who are likely to pass the pre-screener.



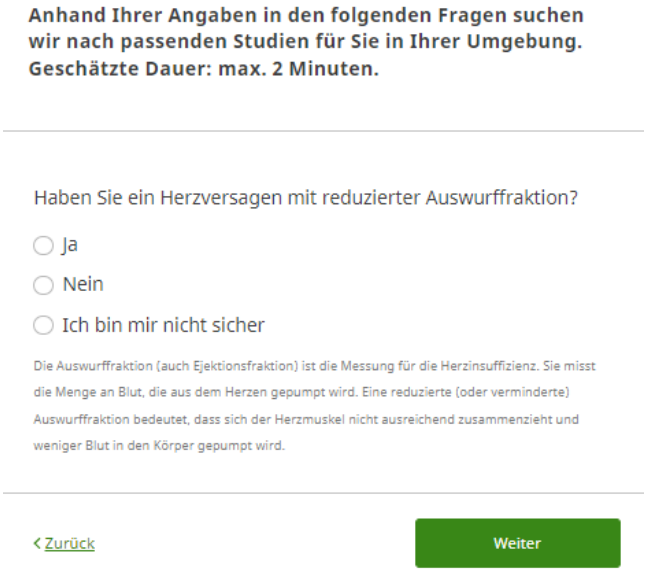
As Example 1 shows, these data-driven education campaigns increase the likelihood that patients will qualify for prescreening and can be scheduled for testing at the site.

4. Lay-friendly information and study materials: we create study-specific patient-friendly information, e.g. on the importance of clinical trials for this specific patient community and larger society, as well as on the study process procedure and misconceptions on placebo usage, which leads to higher participation and lower drop-out rates.

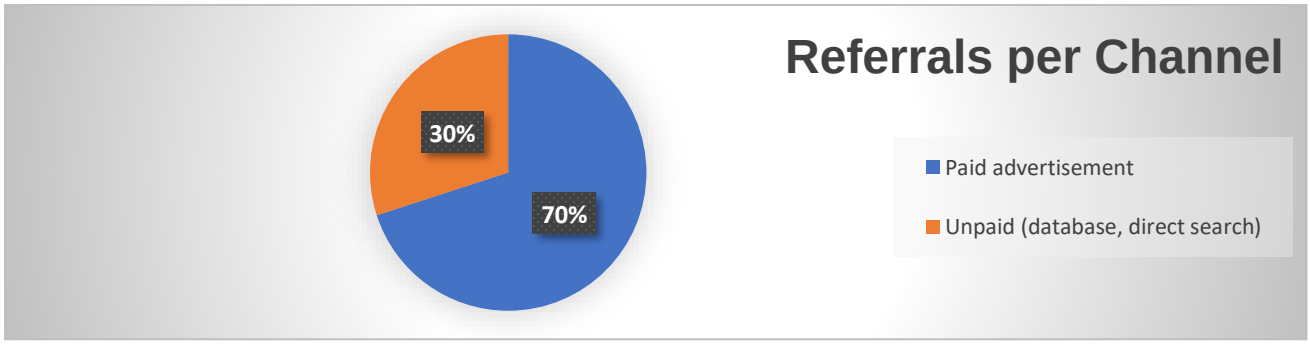


With our ClinLife® blog initiative we answer common questions patients have as well as provide a general overview of clinical research. This creates understanding and builds trust, thereby boosting pre-screener completion rates.

5. Study specific or indication specific pre-screener: depending on the type of recruitment campaign, either a study specific or indication specific pre-screener with easily understandable medical questions.



In looking at the graphs (below) it becomes clear that while this data-driven digital patient recruitment approach of using a wide variety of social media ads is responsible for the majority of the landing page visits, ultimately our database and direct visitors still represent 30% of the ultimate referrals. From experience we know that direct visitors and database subscribers are more likely to qualify the pre-screener and be randomized.



ClinLife: a neutral, patient-centric platform

After clicking on an advertisement, potentially interested persons are directed to our patient platform, ClinLife©. 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 for studies 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 centre was only 2 km away, so the personal approach was optimal."

- **2021 Patient's Voice Participant** Read more about Patient's Voice

Request a demo for a patient recruitment campaign for your Cardiovascular diseases study here.