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Opinion

What we wish we had known before starting a headache clinical registry: insights from the Italo-Brazilian partnership

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Headache registries have emerged as a logical solution for bridging the gap between *what we know* and *what we do*, empowering disease awareness, enhancing knowledge and facilitating personalized management. The role of headache registries in expanding our understanding of patients' journeys, sociodemographic characteristics, endophenotypes, treatments and healthcare resource utilization is well documented around the world. This perspective article will explore some practical ideas to develop a headache clinical registry from the ground up, through the original contributions of Italian and Brazilian registries.

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Introduction

Headache registries have emerged as a logical solution for bridging the gap between *what we know* and *what we do*, empowering disease awareness, enhancing knowledge and facilitating personalized management. The role of headache registries in expanding our understanding of patients' journeys, sociodemographic characteristics, endophenotypes, treatments and healthcare resource utilization is well documented around the world (1–5).

This perspective article will explore some practical ideas to develop a headache clinical registry from the ground up, through the original contributions of Italian and Brazilian registries.

Step 1:
Set the main purpose of the registry: think carefully about the reasons, but be aware that the most interesting findings can be unexpected

The planning for a registry is often not a linear process and the purpose becomes clearer as it is discussed with different stakeholders. Registry data can be valuable for patients and their families, healthcare providers, healthcare systems, regulatory agencies, pharmaceutical companies, employers and policymakers (6). In defining the purpose of a headache registry, researchers should consider *what* is important and to *whom*? They should explore the connection with different stakeholders and think about how the registry could be useful for them. Patient advocates are keystone stakeholders in this process, given that they can highlight the most important goal of clinical research: to bridge the gap in unmet patient needs (6).

The well-known goals of clinical registries include investigation of the natural course of diseases, prognostic features, treatment patterns, safety profiles in a wide variety of special populations and disparities in the delivery and outcomes of care (7). Perhaps the greatest opportunity for those involved in a clinical registry is to contribute to the development of science and the generation of new hypotheses for clinical trials. Registries bring researchers closer to the fundamental ability to discover new phenomena and develop hypotheses based on their observational and analytical skills.

Step 2:
Think about the implications of the data you are collecting for the registry: what are the most useful and the riskiest information you will collect?

Registries provide opportunities to investigate populations excluded from clinical trials and to answer questions that have intrigued healthcare professionals for years: What is the best strategy for treating pregnant and breastfeeding women? What about children and the elderly? How should patients with severe psychiatric and medical comorbidities be managed? What are the outcomes when treating patients with polypharmacy? What can be expected from long-term treatment with different strategies? What are the specificities of headache care in developing countries?

In seeking answers not usually provided by randomized clinical trials, researchers need to ask themselves about the ethical implications of the data. If data about adverse events from multiple treatments are collected, how can comprehensive recording of these events be ensured? What precautions should be taken when reporting adverse events to regulatory agencies and pharmaceutical companies? If suicidal ideation is investigated, what is the patient support system when the answer is affirmative? With data comes responsibility.

Step 3:
Learn from the experience of other researchers: whatever you think, it is probably not new

The importance of connecting with researchers in the same field and also with other experts in epidemiology, statistics and public policies cannot be overstated. These connections can be transformative and become opportunities for unexpected working partnerships. The challenges faced by others can be minimized or exacerbated depending on the setting in which the registry is developed. Knowing the work carried out by other researchers also enhances the chance of bringing new and complementary ideas to the field.

Step 4:
Set up a team committed to the idea: it is a marathon, not a 100-meter sprint

Several different kinds of knowledge, expertise and skills are needed for planning and implementing a registry, such as project management, epidemiology, biostatistics expertise, data collection and database management, and there needs to be a team responsible for legal issues and patient privacy. It is crucial to team up with a group of committed scientists, especially in low and middle-income countries, where resources are scarce. Working on developing a registry is always a long-term commitment and resilience is the key word in the process.

Step 5:
Access the feasibility of the registry: think about the process of research in your daily routine

Registries should engage participants for the long term. It is better to continue enrolling a small number of patients on a steady basis than to enroll a large sample and lose follow-up. Explore the steps for implementing the research protocol in the outpatient routine, in order to balance the amount of data collected and the potential disruption to routine care. A pilot study to analyze multiple parameters of the protocol is very useful within this scenario. Flexible protocols involving a core questionnaire seeking mandatory data and optional questionnaires for complementary data are a useful strategy for multicenter designs, considering that different centers use different strategies for care and treatment.

Step 6:
Take advantage of technology: choose carefully how to collect, store, review and keep the data safe

Concerns regarding data quality and transparency of registries have driven the development of digitalization strategies such as electronic headache diaries, for example. Like other research assets, access to technology is an expensive resource and should be carefully evaluated. The choice of software depends on the available resources, who will input the data, the amount of data collected and the storage strategies. It is also crucial to develop a protocol to control the quality of data and levels of access to patient-sensitive data. Ethical and legal issues must be kept central when choosing all the technological strategies involved in the registry.

Step 7:
Never stop thinking about improving the process: clinical registries are living entities

Keep in mind that the scope and focus of a registry may be adapted over time to reach broader or different populations, assimilate additional data, expand to different geographical regions, or address new research questions. Registry planners should also recognize the importance of periodic critical evaluations of the registry by key stakeholders to ensure that the objectives are being met. This is particularly important for patient registries that collect data over many years.

Being involved in developing and improving a clinical registry is a transformative experience. Sharing knowledge that only experience provides can be a powerful tool for optimizing patient care and developing science.

Conclusion

In conclusion, establishing a headache registry is a multifaceted endeavor that demands careful planning, a clear purpose, ethical consideration of data, collaborative efforts, and a commitment to continuous improvement. By learning from existing models, leveraging technology, and fostering dedicated teams, researchers can build robust registries that not only deepen our understanding of headache disorders but also directly contribute to improved patient care and the advancement of scientific knowledge. These "living entities" are invaluable tools for bridging the gap between research and real-world practice, ultimately leading to more personalized and effective management strategies for individuals living with headaches worldwide.

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