

# A collaborative EHDEN Neuroscience Research Program on Cluster Headache across a standardized health data network

## Abstract

Here, we report on an ongoing neuroscience research program that leverages real world data to better understand patient populations and disease trajectories in Cluster Headache. The research program is a collaborative effort, involving EHDEN (the European Health Data & Evidence Network – a public-private partnership under the EU Innovative Medicines Initiative<sup>4</sup>) and Lundbeck A/S (a pharmaceutical company specializing in brain diseases). In the research program, we bring together biological and clinical experts on headache disorders with experts in epidemiology, data science, and statistics to design and execute studies across a federated network of European databases, utilizing the OMOP Common Data Model. We will present how we have structured the program, share learnings about how to run such a federated research program (operational challenges and effective practices), and share preliminary scientific findings related to Cluster Headache.

## Introduction to Cluster Headache

Cluster headache (CH) is a primary headache disorder characterized by episodes of severe, strictly unilateral pain, that lasts 15–180 minutes and occurs from once every other day to eight times a day [1]. CH affects 0.1% of the population and although considered to be male-predominant, a time-related decline in the male-to-female ratio has been observed in several countries [2]. Only roughly half of patients respond to acute treatments and a diverse array of preventive treatments (often borrowed from other conditions) are employed, many with limited supporting evidence.

Acute treatments recommended by the European Federation of Neurological Societies (EFNS) include high-flow oxygen, sumatriptan or zolmitriptan, lidocaine, and octreotide, while the EFNS recommends for prophylaxis verapamil, steroids, methysergide, lithium, topiramate, ergotamine tartrate, valproic acid, melatonin, and baclofen.

## The EHDEN Neuroscience Research Program

The EHDEN Foundation Research Programmes aim to foster non-competitive research collaborations with Data Partners, Academia, and Industry across various therapeutic areas. The first programme focuses on neuroscience, from migraines and cluster headache to neurodegenerative diseases.

Research Programmes enable the use of EHDEN's unique European open science network [3]. This is expected to facilitate the creation of high-quality, timely real-world evidence for improved disease comprehension and intervention evaluation. With brain disorders being a leading cause of disability and death, particularly in low-income countries, there's an urgent call for comprehensive research.

Future initiatives within the NRP include expansion of Research Use Cases to more indications to better understand diseases in real world patients, and eventually measure and improve patient outcomes.

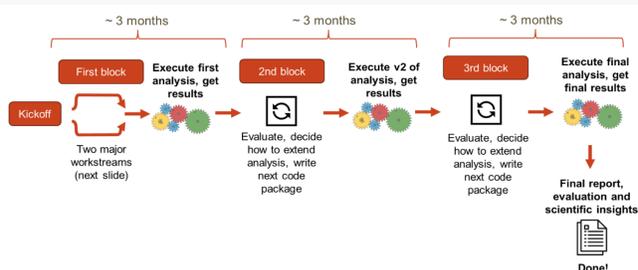
## Preliminary Cluster Headache demographics



Prevalence and treatment patterns across age and genders. Here is an example showing annual age-and-gender specific prevalence of CH, and Verapamil treatment in cluster headache patients per 100,000 commercially insured US patients in 2021. (Source: IQVIA Pharmetrics® Plus)

Notably, in a commercially insured US population the gender ratio of CH diagnosis is close to 1:1, while most studies of other populations find higher male-to-female ratio [4]. Verapamil treatment for CH, shows an expected male-to-female ratio, though.

## Focused and adaptive innovation in the EHDEN NRP



To facilitate a great collaboration, it is important to ensure a close feedback loop with recurrent milestones, so all parties are on board with the progress of the project and analyses are adapted to the data at hand.

The initial pilot is split up into three major blocks, an initial data partner feasibility block, a protocol finalization block, and a final analysis block. We are currently onboarding data partners, and while that is ongoing, we are testing phenotypes and protocols exploratively on US claims data.

## Research Questions

The pilot project's aim is to gain better understanding of Cluster Headache patients in a real-world clinical setting:

- What are the characteristics of the Cluster Headache patient population (sex, age, social determinants, geography)?
- Cluster Headache often follows a relapse-remitting pattern. How long are the different phases of the disease and what is the variation in the population?
- What are the disease and treatment patterns among patients with Cluster Headache?
- What comorbidities are common in the Cluster Headache patient population, and do they affect prognosis?
- Are there geographical differences in treatment?
- What are indicators of treatment failure?
- What off-label treatments are used and how do they affect the patient's prognosis?
- Many patients notice a seasonality in their symptoms. Can this be seen in Real-World data?

## References

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