Identifying clusters of patients with similar chronic pain, in terms of characteristics, intensity and temporality and studying the associations between these clusters and chronic conditions reported by patients

Background

Chronic pain is defined as “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage” that persists or recurs for more than 3 months (1). In the literature, studies have estimated that from 28% to 48% of Europeans experience chronic pain of moderate intensity (2). Chronic pain has many consequences including sleep, cognitive processes and brain function, mental health, cardiovascular health and overall quality of life (3).

Chronic pain is usually categorized through its underlying cause. For example, the International Association for the Study of Pain (IASP) identified seven subgroups of pain (chronic primary pain, chronic cancer-related pain, Chronic postsurgical and post-traumatic pain, chronic neuropathic pain, chronic secondary headache or orofacial pain, chronic secondary visceral pain, chronic secondary musculoskeletal pain) (1). Chronic pain can also be categorized through its mechanism. Classifications distinguish nociceptive, neuropathic, and nociplastic pain (4). However, studies tend to prove that 50% of patients with chronic pain experience a “mixed pain phenotype”(5).

To date, no studies have aimed at identifying homogeneous patient groups (i.e., clusters) in terms of pain intensity, characteristics and temporality and evaluate how these groups are associated with underlying causes.

Objectives

Objective 1: Identify clusters of patients with similar chronic pain (characteristic, intensity, frequency, etc.) among a population of patients reporting chronic conditions and chronic pain.

Objective 2: Evaluate the association between the identified clusters and the conditions self-reported by participants.

Methods

The study was co-constructed with patient associations. In particular, the objectives were decided during a discussion with the scientific committee involving Association AMI, Association AFPric, Asso'SOPK, Sed'in FRANCE and Spondyloaction.

Data sources

This study will be nested in the ComPaRe cohort (Communauté de Patients Pour la Recherche, www.compare.aphp.fr). ComPaRe is promoted by the Assistance Publique – Hôpitaux de Paris (AP-HP) and Université Paris Cité, and is a nationwide e-cohort of 60000 adults (≥18 years) with chronic conditions in France. Participants answer online questionnaires that collect patient-reported outcome measures (PROMS) and patient-reported experience measures (PREMS). Recruitment in ComPaRe entails direct outreach to potential participants by widespread advertising in general and social media and partner patient associations. All participants provide electronic consent before participating in the e-cohort.

ComPaRe also functions as a platform enabling any public research team to use the data already collected to answer research questions on chronic conditions or multimorbidity. A sub-cohort dedicated to study chronic pain was initiated in April 2025 in co-construction with 31 patient associations.

Population

This study includes adult patients (over 18 years old) and reporting chronic pain (defined as experiencing pain for at least 3 months).

Recruitment

As part of this study, we will conduct several recruitment actions to increase the number and diversity of participants in the ComPaRe chronic pain cohort.

- We hypothesize that initial respondents to the cohort were those with higher pain. People with fewer chronic pain may have felt less legitimate and concerned by this study. We will therefore write an e-mail intended for this specific population to encourage them to participate. The writing of this e-mail and all the following content will follow evidence-based rules found in literature.

- We will adapt existing communication materials from ComPaRe with a focus on chronic pain and with a patient perspective. We will disseminate these materials:
    - On social media
    - Via collaborating patients' associations
    - In collaborating doctors' offices
- During the study, we will organize seminars to directly interact with patients that could be interested in the study.

All materials generated for this study will be discussed and tested with patients for clarity and appeal.

Data collected

Our study will use data collected in the initial assessment of the sub-cohort dedicated to study chronic pain in ComPaRe. In short, all participants from ComPaRe received an invitation mail. Those who reported to have pain lasting for over 3 months were offered to participate and then provided electronic consent if they wished so.

The initial assessment of the sub-cohort dedicated to study chronic pain in ComPaRe involves the following measurements:

- McGill Pain Questionnaire (6). This measure aims at describing the typology and words representing pain. Participant select the word in each subclass that best corresponds to their pain, and each chosen descriptor carries a numerical value reflecting its relative intensity. These values are used to calculate the Pain Rating Index score (PRI score).
- Brief Pain Inventory (BPI) (7,8). This measure captures pain intensity, functional disability, social and family impact, and the level of psychological distress related to pain. It contains 3 parts: pain intensity (four numeric scale items), pain relief (two items) and pain interference (7 scales items). These values are used to calculate one pain severity score (mean of the pain intensity items, from 0 to 10) and one pain interference score (mean of the pain interference items, from 0 to 10). A higher score indicates greater severity and more interferences.
- Pain disability Index (PDI) (9). This measure captures the perceived impact of pain on daily life: family/domestic responsibilities, leisure activities, occupation, social activities, and independence. For each domain, respondents rate the impact of pain on an 11-point scale (0 = no disability, 10 = total disability). The total PDI score is the sum of the five domain scores, ranging from 0 (no disability) to 50 (complete disability). Higher scores indicate a greater degree of interference of pain with daily functioning.

- Neuropathic pain Diagnostic questionnaire (DN4) (10). This tool is used to identify neuropathic pain. It is composed of 10 items with binary responses (Yes/No). The total score is calculated as the number of "YES", ranging from 0 to 10. A score of 4 or higher is generally considered indicative of neuropathic pain.
- Additional questions on:
    - Rhythm of pain: participants were asked whether the pain occurred daily over the past 6 months, whether it was constant or intermittent, the time of day when it was most severe, and whether it was related to specific activities.
    - Neuropathic and nociplastic pain: participants were asked if they had ever experienced neuropathic or nociplastic pain and if they had in the past 6 months.

We will use other data collected in ComPaRe:

- Age at the time of the initial assessment of the chronic pain cohort.
- Gender at cohort entry.
- Biological sex at cohort entry.
- Weight.
- Height.
- Professional situation (Employed, Unemployed, Recipient of RSA (French minimum income benefit), student, Retired, pre-retired, Homemaker, Disabled / on long-term sick leave, Other) at cohort entry.
- Level of education through the highest diploma (Lower education, Middle school or equivalent, High school or equivalent, associate's degree, Undergraduate or graduate degree) at cohort entry.
- Marital status (Married, in relationship, divorced, widowed or single) at cohort entry.
- Chronic conditions using ICPC-2 list.
- List of medication.
- EPICES questionnaire, capturing precarity, at the closest moment to the initial assessment of the chronic pain cohort. Scores range from 0 to 100, with higher scores indicating greater precarity. A score above 30 is considered critical (11).
- Health-related quality of life using EQ-5D-5L at the closest moment to the initial assessment of the chronic pain cohort (12).
- Physical activity, assessed using IPAQ at cohort entry. We will use the continuous score (MET-minutes/week) and the categorial score: low, moderate or high (13)
- Depression level with PHQ-9 at cohort entry. The score goes from 0 to 27 and is stratified into 5 categories : minimal depression (0-4), mild depression (5-9), moderate depression (10-14), moderately severe depression (15-19) and severe

depression (20-27) (14).

- Anxiety level with GAD-7 at cohort entry. The score goes from 0 to 21 and is stratified into 4 categories: minimal anxiety (0-4), mild anxiety (5-9), moderate anxiety (10-14) and severe anxiety (15-20) (15).

Statistical analyses

Analyses will be limited to patients with complete data regarding the initial assessment of the sub-cohort dedicated to study chronic pain in ComPaRe.

First, we will describe participants characteristics through number (proportion) for categorical variables and mean (standard deviation) for continuous variables.

Second, we will identify clusters of patients with similar chronic pain, in terms of characteristics (as captured by the McGill Questionnaire and the Neuropathic pain Diagnostic questionnaire and anatomy as captured by the BPI), intensity (as captured by the BPI questionnaire, excluding questions on impact) and temporality (as captured by the unvalidated questions). We will describe the number of participants in each cluster as well as participants' characteristics, conditions and impact of chronic pain in each cluster.

Third, we will study whether some conditions are associated with specific clusters through multivariable logistic regressions. Covariates included in the models will be age, sex, physical activity, psychological state, and education economic conditions (2,16,17) . Associations will involve $p<0.05$.

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