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# A pain research strategy for Europe: A European survey and position paper of the European Pain Federation EFIC

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## Abstract

**Background:** Pain is the leading cause of disability and reduced quality of life worldwide. Despite the increasing burden for patients and healthcare systems, pain research remains underfunded and under focused. Having stakeholders identify and prioritize areas that need urgent attention in the field will help focus funding topics, reduce 'research waste', improve the effectiveness of pain research and therapy and promote the uptake of research evidence. In this study, the European Pain Federation (EFIC) developed a Pain Research Strategy for Europe.

**Methods:** The study used multiple methods, including literature searches, multidisciplinary expert debate, a survey and a final consensus meeting. The cross-sectional survey was conducted among 628 European pain researchers, clinicians, educators and industry professionals to obtain the rating and hierarchy of pain research priorities.

The final consensus meeting involved a multidisciplinary expert panel including people with lived experience from 23 countries. The survey results guided discussions where top priorities were agreed.

**Results:** Content analysis identified nine survey themes, of which five emerged as top priorities: (i) understand the pathophysiology of pain; (ii) understand and

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For affiliations refer to page 22.

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address comorbidities; (iii) critically assess current therapies; (iv) develop new treatments; and (v) explore the biopsychosocial impacts of pain. Physical, psychological and social approaches were prioritized at the same level as pharmacological treatments. The top priorities were endorsed by a multidisciplinary expert panel. The panel emphasized the importance of also clearly communicating the concepts of prediction, prevention self-management and personalized pain management in the final strategy.

**Conclusions:** The content of the final top research priorities' list reflects a holistic approach to pain management. The equal importance given to physical, psychological and social aspects alongside pharmacological treatments highlights the importance of a comprehensive biopsychosocial-orientated research strategy. The expert panel's endorsement of five top priorities, coupled with an emphasis on communicating the concepts of prediction, prevention, self-management and personalized pain management, provides a clear direction for future basic, translational and clinical research.

**Significance:** EFIC has developed a Pain Research Strategy for Europe that identifies pain research areas deserving the most focus and financial support. Implementation and wide dissemination of this Strategy is vital to increase the conduct of urgent pain projects, pain research funding and the implementation of research findings into practice, to ultimately decrease the personal, societal and financial burden of pain.

## 1 | INTRODUCTION

Pain is one of the most prevalent medical conditions in Europe and worldwide, the most common reason people seek healthcare and the leading cause of disability and reduced quality of life (Cohen et al., 2021; Vos et al., 2020). Chronic pain is defined as pain that persists or recurs for more than 3 months. It can be classified as chronic primary or secondary pain (Treede et al., 2019). Pain-related conditions such as headache (e.g. migraine) and musculoskeletal disorders (e.g. low back pain, pain due to hip and knee osteoarthritis and neck pain) are two of the largest contributors to years lived with disability according to the Global Burden of Diseases, Injuries and Risk Factors Study, which includes a comprehensive assessment of incidence, prevalence and disability for 354 causes in 195 countries and territories (Vos et al., 2020). It was recently shown that most countries fail to prioritize health issues according to the burden they cause, meaning that insufficient resources are directed to improve health outcomes for people with those health conditions (Oliveira et al., 2023). Although the disability burden due to pain is increasing and threatens the sustainability of European healthcare systems, pain research remains significantly underfunded compared to other health areas (Berger & Baria, 2022; Cohen et al., 2021). Underinvestment in

important health research is considered a key contributor to knowledge gaps and poor access to care (Asher & De Silva, 2017). The implementation of the EFIC Research Strategy is an opportunity for funding agencies to take the lead and offer funding to research topics that primarily bring value for society/patients.

Recently, the European Commission conducted a scoping review to identify research needs of high burden under researched medical conditions in the EU. Several pain conditions in need of attention and innovation were identified (European Commission, Research D-Gf, Innovation, et al., 2023). The development of a research priority setting for pain is a crucial step in addressing these gaps.

The setting of research priorities involves stakeholders in identifying, prioritizing and reaching consensus on areas, topics or questions that research needs to address (Grill, 2021; Tong et al., 2019; Viergever et al., 2010). It promotes the uptake and implementation of research evidence (Tong et al., 2019), secures optimal return on investment (Boaz et al., 2018), reduces 'research waste' (Chalmers et al., 2014), fosters the relevance and legitimacy of research overall (Tong et al., 2019) and is likely to lead to significant improvements in research efficiency and ultimately in therapy (Álvarez-Bornstein & Bordons, 2021).

The publication of research roadmaps by other professional organizations has successfully mobilized researchers to align their projects with identified priorities, ultimately advancing implementation. For example, following the publication of the European League Against Rheumatism's (EULAR) Research Roadmap researchers developed projects like the BIODAM cohort study and IMI-PRECISE, which focused on stratified medicine and personalized treatments for rheumatic diseases. Similarly, the TREAT-EARLIER trial directly aligned with the roadmap's focus on early diagnosis and prevention in rheumatoid arthritis. Collaborative initiatives like ERA-NET NEURON call have also facilitated interdisciplinary research across Europe, translating strategy into action. These examples demonstrate that the publication of research strategies not only sets priorities but also drives implementation by aligning research efforts and promoting coordinated action across sectors. We believe that our research strategy will similarly catalyse progress in pain research by mobilizing researchers and funders around clear priorities, laying the foundation for further implementation initiatives.

This study aimed to develop a Pain Research Strategy for Europe. The European Pain Federation (EFIC) guided the collaborative development of a set of research priorities. The Pain Research Strategy for Europe will help advocate for increased support and funding, but also crucially to communicate a clear set of priorities to all research stakeholders. This concerted effort seeks to raise the profile of pain research in Europe and facilitate the translation of high-quality pain research into European policy and practice.

## 2 | METHODS

### 2.1 | Strategy working group

The development of the Pain Research Strategy for Europe was an initiative of the EFIC Research Committee. It began in June 2021, with 14 individuals forming an EFIC Strategy Working Group (EFIC-SWG), whose members were selected based on their clinical and research expertise (basic, translational and clinical) within medicine, neuroscience, physiotherapy, psychology and nursing. They all had at least 10 years of clinical/academic work in the field of pain and a steady track record of international publications covering various aspects of the biopsychosocial model of pain. The EFIC-SWG played a crucial role in the development of the Research Strategy methodology. They advised on literature search strategies, suggested research priorities based on their expertise, reviewed potential priorities for inclusion in the cross-sectional survey and participated in

meetings to reach consensus on the research priorities in the final version of the Research Strategy.

### 2.2 | ERA-NET Neuron working group

In July 2023, the EFIC SWG received funding from ERA-NET NEURON (The Networking of European Funding for Neuroscience Research) to establish a European networking group about the future of pain research (Pain Research Strategy for Europe: PRiSE). This initiative was aimed at advancing the development and implementation of the EFIC Research Strategy. The ERA-NET Working Group (ERA-NET WG) included all 14 members of the EFIC-SWG and expanded to include 12 new members who brought additional perspectives and clinical and research expertise from European countries not initially represented. With a total of 26 individuals from 23 European countries, the ERA-NET WG met for face-to-face and online meetings over a 12-month period.

The primary objective of this funded project was to reach a consensus on the priorities to be included in the final version of the Pain Research Strategy for Europe and, critically, to maximize its future implementation by identifying enablers and barriers across diverse European contexts.

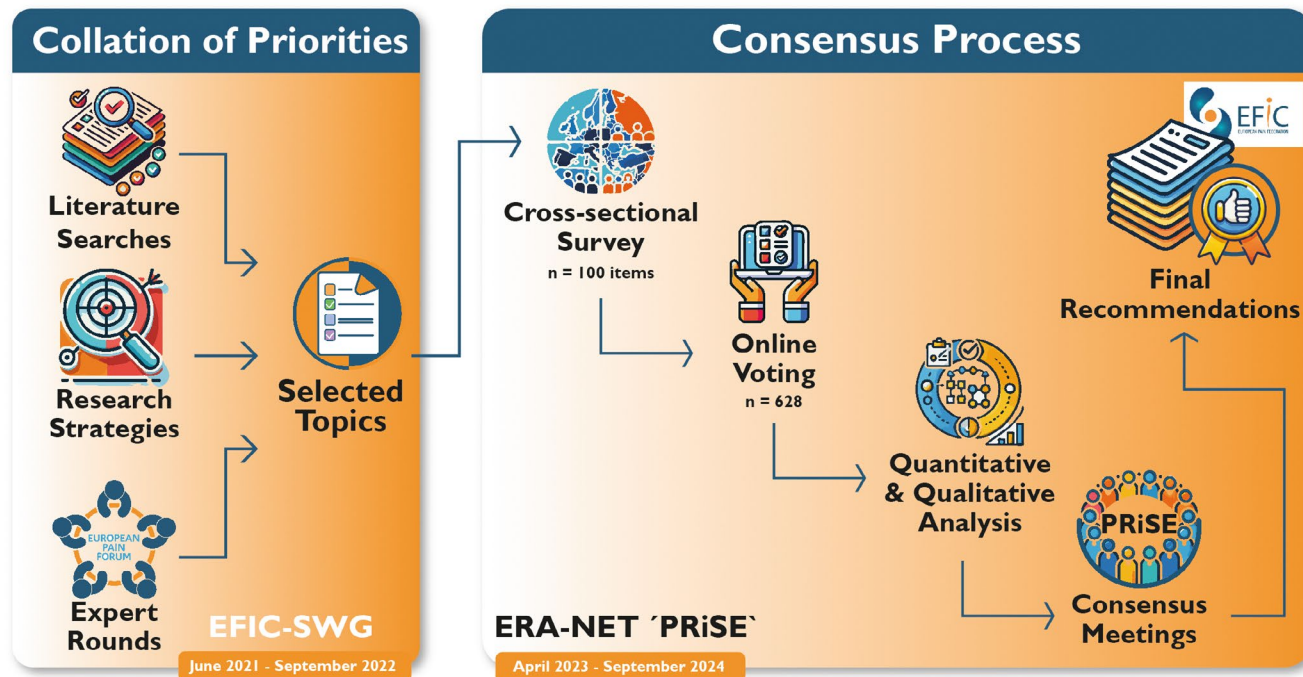
The current paper focuses on the development of the Pain Research Strategy for Europe.

### 2.3 | Study design

The development of the Pain Research Strategy for Europe employed an iterative multifaceted approach, using multiple methods to ensure comprehensive insights and perspectives: expert consultations, literature reviews to identify potentially relevant priorities, a cross-sectional survey of European researchers, clinicians and industry professionals and consensus meetings consisting of the initial EFIC SWG and the ERA-NET WG (Figure 1). Online meetings of the EFIC SWG were held at various stages throughout the project to provide feedback on the methodology and provide updates on the project.

#### 2.3.1 | Expert consultations

In addition to the two Working Groups, several European organizations with expertise in the pain domain were consulted. The European Pain Forum (which includes EFIC and 12 other medical, scientific and patient organizations) identified key priorities that the EFIC-SWG had not yet



**FIGURE 1** Summary of methodology.

addressed. Of note, Pain Alliance Europe is a member of the European Pain Forum. This Pan-European umbrella organization represents over 400,000 people living with chronic pain from 40 national associations in 17 European countries.

Additionally, the EFIC Executive Board and key opinion leaders of the EFIC community (authors of previous position papers, EFIC Committee members) also commented on a draft priority list and proposed other priorities that they deemed important. All recommendations emerging from these consultations were reviewed by the EFIC SWG and considered for inclusion in a cross-sectional survey.

### 2.3.2 | Literature searches

Several literature searches (including peer-reviewed literature, existing Pain Research Strategies, EFIC and International Association for the Study of Pain (IASP) Position and Opinion papers and Cochrane priority lists) were performed to identify pain research priorities or research gaps previously put forward by clinicians, people living with pain and researchers (see details below). Priorities that emerged from these searches were considered for inclusion in the cross-sectional. Our aim was to communicate a set of relevant priorities across the entire field of pain; broad and general research priorities were considered more relevant than highly refined research questions.

### 2.3.3 | Peer-reviewed literature search

We conducted a scoping review of previous priority setting projects for pain conditions and reported it according to the recommendations of the PRISMA extension for scoping reviews [PRISMA-ScR] (Tricco et al., 2018). It was not prospectively registered, as PROSPERO does not accept scoping reviews registrations. Our aim was to synthesize the priorities that have been identified previously.

We included articles that reported on research prioritization for any type of pain condition. Articles were included if they directly identified research priorities or research gaps from stakeholders, including clinicians, researchers and patients. There was no limitation in study design, age of participants or setting. We excluded studies that reported only on clinical guidelines or clinical priorities.

We searched PubMed and EMBASE from inception to 4 July 2022 (and updated again on 24 April 2023), unrestricted by language, using rows of keywords related to pain and research priorities. The search was structured in two blocks, joined by an 'AND' operator, one including terms related to pain conditions (80 search terms), the other including terms related to research and priority agendas (6 Mesh terms). The structure of the search was as follows: ("research agenda" [Title/Abstract] OR "funding priorities" [Title/Abstract] OR "priority setting"[Title/Abstract] OR "agenda setting" [Title/Abstract] OR "research priorities" [Title/Abstract] OR



priorities [Title/Abstract]) AND (pain OR “acute pain” OR “chronic pain” OR “chronic non-cancer pain” OR “musculoskeletal pain” OR fibromyalgia OR “widespread pain” OR...) up to 80 pain-related and condition-related items. The full search terms are provided in Supplementary File 1—Data S1. We also searched the reference lists of included articles to identify additional relevant studies.

The title and abstracts of identified articles were independently screened by two authors (GP and MOK), who also obtained and independently screened the full texts of potentially eligible articles. We did not appraise the methodological quality of the included studies. The following data were extracted into a Microsoft Word document by one author (MOK) from eligible articles: pain condition(s), research priorities identified, country, priority setting methodology and participants (clinicians, researchers, people living with pain, policy-makers, industry representatives, etc.). The results were presented descriptively.

### 2.3.4 | Review of publicly available pain research strategies

We performed a review of a convenience sample of four international pain research strategies that were known to the EFIC Executive Office for producing recent comprehensive recommendations. Key criteria in their selection were international dissemination, comprehensiveness, different countries represented European-wide, inclusion of one US-based and recent accessible publications. These were the UK Versus Arthritis Roadmap (Versus Arthritis, 2018), the US National Institutes for Health (NIH) Pain Research Strategy (National Institutes of Health, 2022), the EULAR RheumaMap (European League Against Rheumatism (EULAR), 2019) and the German Pain Society Research Strategy (Deutsche Schmerzgesellschaft, 2017). The strategies were read and data were extracted by two authors (GP and MOK).

### 2.3.5 | Review of James Lind Alliance patient, carer and clinician pain priorities

The James Lind Alliance (JLA) is a prominent non-profit initiative that brings patients, caregivers and healthcare professionals together in Priority Setting Partnerships, to identify and prioritize the unanswered questions about health conditions that they agree are most important. One author (MOK) reviewed the website's Priority Setting Partnerships for pain priorities and extracted the relevant ones.

### 2.3.6 | Review of Cochrane priority lists

We reviewed [Cochrane Priority Setting Methods Group](#) and the [Cochrane Pain, Palliative and Supportive Care](#) for their priority lists for reviews on pain. One author (MOK) reviewed these websites for priority review questions related to pain and extracted relevant ones.

### 2.3.7 | Review of EFIC and IASP position and opinion papers

We reviewed published EFIC and IASP Position and Opinion Papers (Bennett et al., 2019; Goebel et al., 2019; Haroutounian et al., 2021; Häuser et al., 2018, 2021; Krčevski Škvarč et al., 2021; Mouraux et al., 2021; Truini et al., 2023). One author (MOK) reviewed the eight papers and extracted the research priorities suggested.

Input from these were analysed and combined with the results of literature searches and the priorities proposed by the EFIC-SWG, to develop the final items of the survey. The EFIC-SWG assessed the commonalities and overlaps of the suggested priorities received, and devised meta-priorities, whereby similar proposals from different sources could be collapsed into one single survey item. Some of the proposals received were not incorporated into the survey because the topic was considered too selective to be of general interest (e.g. research on a specific outcome measure for Parkinson's disease) or the suggestion arrived after the survey had been finalized. The result of this analysis was a compact series of 100 core items which were disseminated as a web-based Survey to be rated and hierarchized by individual respondents.

## 2.4 | Cross-sectional European survey

To obtain data from experienced clinicians and researchers responding individually (i.e. not representing an organization), a cross-sectional online (web and email) survey was conducted via SurveyMonkey software between 18 October 2022 and 15 January 2023. The survey did not require log-in details or a password ('open survey'). A participant information sheet detailing expected duration to complete the survey, the voluntary nature of the study, data storage techniques, the investigators and the purpose of the survey formed the introduction to the survey after which informed consent was obtained from all participants using a tick the box function. No personal information was provided to the research team from SurveyMonkey. We pilot tested our survey with five EFIC team members prior to recruitment so that we could perform data checks, correct typographical errors in the survey and participant

information forms and evaluate survey usability and technical functionality. The survey was reported according to the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) (Eysenbach, 2004). Ethical approval was obtained from University Hospital Clermont-Ferrand, France (IRB number 2022-CF034).

**Advertising and Recruitment:** The survey was only advertised online only and participants were recruited for survey participation through several Internet avenues.

(i) EFIC's online communication channels (quarterly newsletter, social media and LinkedIn).

(ii) [EFIC's Pain Scientist Network](#) (an online internal listing of pain scientists, organized by their fields of research expertise and activity, comprising ~900 members).

(iii) [Expertscape](#). Emails were sent to European based pain experts featuring in the 'top 10' under any lists on Expertscape including the word 'pain' (e.g. pain, cancer pain, procedural pain, pain insensitivity, back pain and facial pain).

(iv) [European Pain Forum](#). Members were encouraged to share the survey with their networks.

(v) Word of Mouth and Snowballing. E-mail correspondence, social media channels by members of the EFIC SWG, who shared information about the survey with their networks. Participants could also suggest other clinicians and researchers to contact.

**Participants and Procedure:** Participants included researchers, clinicians, educators, or industry representatives with an interest in pain based in Europe. Items in the survey were selected based on the literature searches, review of publicly available strategies and expert consultation as described above. The survey was in English only and included 131 items. The survey included 100 specified research priorities to be rated. The other 31 items were related to consent, demographic details (professional title, gender, number of years post PhD, professional role, discipline/field of practice, country of residence and core research domains), as well as suggestions of new items not included in the survey.

Participants were asked to rate the relative importance of each potential priority on a six-point scale ranging from 'Extremely Important' to 'Not at all important', plus the additional items 'I do not have an Opinion' and 'I don't know'. Participants were also asked to rank groups of similar priorities in order of importance (e.g. ones focusing on pathophysiology, diagnosis and measurement and clinical treatment). They were encouraged to answer items related to their expertise in basic, translational and clinical research. For example, a basic scientist researcher could, but was not expected to rate perceived importance of a clinical priority outside their expertise. Participants were

also given the opportunity to suggest additional priorities that were not covered in the survey (Supplementary File 7—Data S1). The full survey can be accessed in Supplementary File 2—Data S1.

**Analysis:** Quantitative and qualitative analyses were performed.

**Qualitative (content analysis):** To organize our research strategy effectively, we grouped the 100 survey items with research priorities into broad categories. We used content analysis to help identify important themes or concepts in qualitative data—in this case, the words used in each survey question. This approach (Weber, 1990) involved several steps.

1. *Development of coding categories:* Two researchers (MOK and NS) independently analysed a subset of survey items (30) to create an initial framework of codes. A 'code' is a label that represents an important aspect of the survey items and helps organize and classify the whole set. The researchers compared their frameworks, discussed them and combined them into one framework for the next step, grouping in one category survey items that focused on conceptually related items.

2. *Testing the reliability of the framework:* After developing the framework, two researchers (MOK and NS) independently applied it to a different subset of survey items (20% randomly selected). Kappa statistics ( $k$ ) and 95% confidence interval (CI) and exact agreement (%) were calculated to assess the level of agreement between the two researchers to code responses to each item.  $k$  values were interpreted as follows:  $<0.00$  = 'poor',  $0.00$ – $0.20$  = 'slight',  $0.21$ – $0.40$  = 'fair',  $0.41$ – $0.60$  = 'moderate',  $0.61$ – $0.80$  = 'substantial' and  $\geq 0.81$  = 'almost perfect' (Landis & Koch, 1977). Analyses investigating level of agreement were performed using Stata (V.16.1) and 5000 bootstrap replications were used to calculate 95% CI. Reliability of the coding framework was deemed acceptable if the level of agreement from coding a random sample of responses was  $k \geq 0.8$ .

3. *Applying the coding framework:* Once we achieved acceptable agreement, we applied the framework to all 100 survey items rating the importance of specific priorities. To analyse suggestions put forward by participants (free-text data), the two same authors (MOK and NS) independently reviewed suggestions. Uninformative suggestions (e.g. 'more pain research needed') were excluded. Where a suggestion was deemed to be a duplicate of an existing survey item, it was excluded. Where appropriate, suggestions were incorporated into the themes of the coding framework. Where a suggestion did not seem to fit within one of the coding framework themes, a new theme/category was created.

**Quantitative analysis:** Descriptive statistics (counts and percentages) were used to summarize the characteristics of the participants and analyse the importance rating for the

proposed list of research priorities in the survey. The stratification of the survey responses through graphic presentation and thresholding was performed using polar histograms (by BP and GP). Each survey item was classed according to the percentage of responses it received (from 'extremely important' to 'not at all important' and 'No opinion').

The items were then classed in descending order or priority according to the Total importance (i.e. the sum of percentages for the ratings 'extremely important' and 'important'). Items ranking in the first quartile (Q1) of the distribution of positive ratings were considered as first-line ('top') priorities. A mixed-model ANOVA was performed to analyse the distribution of response ratings across the 100 items, using one within-factor 'type of response' (Four levels: 'extremely important'; 'important'; 'not-so important' and 'not at all important') and one between-factor 'quartile' (Four levels Q1–Q4). This analysis specifically investigated the interaction between the quartile and the distribution of responses, from 'extremely important' to 'not at all important'.

Factorial analysis of variance was used to compare the number of people responding to the survey items across the four quartiles.

Linear Pearson product–moment regression analysis between the order of presentation of each item and the number of respondents to them was conducted to examine the possible effect of participant fatigue on responses to items presented at different stages of the survey, distinguishing between those appearing earlier and later in the sequence.

Three-by-two comparisons between the responses for each item and sex and profession (clinical practitioner, researcher and clinical practitioner and researcher) were performed using chi-squared or Fisher's exact tests according to categorical nature of items.

## 2.5 | Final consensus meeting

The consensus process was held during a 1-day hybrid meeting (5 April 2024, Brussels) with  $n = 27$  participants from the EFIC and ERA-NET WGs. The meeting discussed the results of the survey and used a 'World Café' format (<https://theworldcafe.com/>), to include these results within the context of the experience of the committee members. The participants could address other priorities and explore the reasons for the disparities in the priority ratings. The overarching goal was to discuss and recommend research priorities based on the survey findings, ultimately presenting a final proposal supported by EFIC. Before the meeting, all members of the working group received a document containing pertinent information on the progress of the development of the research strategy. The meeting schedule included presentations on the research strategy's status, including methods used, results of literature reviews and survey findings.

Subsequently, participants engaged in discussions organized into four breakout groups, one of which was held virtually. Facilitation of post-presentation discussions was provided by one member (LGL), while breakout groups were facilitated by four members (BMF, MOK, LGL and EPZ). Each breakout group was tasked with addressing two questions.

1. Of the themes and specific items that received the best rankings (first quartile) by respondents to the survey, which of them appear as of greatest value and most impact in the near term? Do you think that something important is lacking in the list of top priorities or that there is some significant bias? How would you remediate this?
2. Of the themes and specific items that received the worst rankings (last quartile) by respondents to the survey, what are in your opinion the reasons why they were considered relatively unimportant compared to others? Do you think significant efforts should be made to promote them, despite their lower rank? Do you think there is some significant bias?

The opinions and insights collected from all breakout groups in response to each of the three questions were then presented to the entire group by the facilitators of the breakout groups (BMF, MOK, LGL and EPZ) to facilitate a wider discussion and exchange of ideas.

## 3 | RESULTS

### 3.1 | Literature review and analysis of existing research agendas

#### 3.1.1 | 1A. Peer-reviewed literature search

We retrieved 5268 records from electronic databases. After excluding 1443 duplicates, we screened 3825 potentially relevant studies by title and abstract. Of these, 112 studies had their full text evaluated for eligibility and 87 were finally included in the review (Figure 1). The list of excluded articles is provided in Supplementary File 3—Data S1. This resulted in 872 priorities suggested in the peer-reviewed literature, the full list of which is provided in Supplementary File 4—Data S1.

#### 3.1.2 | Review of publicly available pain research strategies proposals

A total of 253 priorities were proposed by the four pain research strategies we reviewed, many of which overlapped with those retrieved from peer-reviewed literature: Versus



Arthritis Roadmap (Versus arthritis, 2018) proposed 14 priorities of research, all on musculoskeletal pain; EULAR RheumaMap (European League Against Rheumatism (EULAR), 2019) suggested 99 research priorities in different types of arthropathies, back and neck pain, carpal tunnel syndrome and fibromyalgia; US NIH Pain Research Strategy (National Institutes of Health, 2022) proposed 50 priorities on pharmacological and non-pharmacological treatments, screening and prevention tools, registries and datasets, precision medicine and acute-to-chronic pain transition; the German Pain Society Research Strategy (Deutsche Schmerzgesellschaft, 2017) produced 90 very comprehensive proposals covering virtually all aspects of acute and chronic pain.

### 3.1.3 | Review of James Lind Alliance patient, carer and clinician pain priorities

Searches on the James Lind Alliance website revealed 308 priorities within 47 priority-setting partnerships.

### 3.1.4 | Review of Cochrane priority lists

We found one single priority list (Cochrane Musculoskeletal) with 14 priorities relating to treatments for osteoarthritis and rheumatoid arthritis.

### 3.1.5 | Review of EFIC and IASP position and opinion papers

Sixty-eight suggested priorities emerged from analysis of eight papers, comprising guidelines on neuropathic pain, complex regional pain syndrome (CRPS) and cancer pain, use of opioids and cannabis-based medicines, societal issues and translational research. See Supplementary File 5—Data S1 for all priorities.

## 3.2 | Expert consultations

2A. Consultation with European Pain Forum yielded 40 priorities, summarized in Supplementary File 6—Data S1. These included evaluating the quality of patient-reported outcome measures (PROMs) and patient-reported evaluation methods (PREMs) and a series of recommendations on pain in neurological conditions, multimodal interventions, substance use/addiction, patient safety, multicentre clinical data and pain registries. People living with pain represented in Pain Alliance Europe suggested the inclusion of people living with pain in the development of

PROMs and PREMs, establishing a gold standard for self-management programmes and the evaluation of the benefits and harms of psychedelic-assisted therapies for pain.

2B. The EFIC Executive Board and key opinion leaders from the EFIC community suggested 10 priorities, including pain in several neurological diseases and cancer and the development of neuromodulation and digital medicine.

The results of literature searches (1A–E) were analysed and combined with the input from the Expert Consultations (2A–B) and the priorities proposed by the Committee Working Group, to develop the 100 final research priority items of the survey.

## 3.3 | Cross-sectional survey

### 3.3.1 | Sample

According to Google analytics statistics, the EFIC website page containing the link to the survey was accessed by 1053 unique visitors between October 2022 and January 2023. A total of 628 individuals completed the consent form and responded to the survey. Although this represents 59.6% of those accessing the page, not all survey participants responded to all items. The average number of responses per item was  $331 \pm 29$ , that is, approximately half of the participants per item and there was a significant negative correlation between the order number of the items and the number of responses received ( $r = -0.86$ ;  $p < 0.001$ ). Key participant demographics are summarized in Table 1.

### 3.3.2 | Content analysis of survey items

Content analysis produced a coding framework of nine categories/themes. The level of agreement between the two researchers coding a random sample of responses was substantial to ‘almost perfect’ in the nine themes ( $k = 0.81–0.97$ ).

#### *Theme 1: Better understand pathophysiology of pain*

This included questions on understanding the biological processes and mechanisms underlying the onset, progression and manifestations of pain and pain-related disability and discovering potential targets and biomarkers for therapeutic interventions.

#### *Theme 2: Better assessment and diagnostic/prognostic tools*

This included questions on development and validation of outcome measures, diagnostic tools, prognostic and

**TABLE 1** Key demographics of survey participants.

	N (%)
Professional title	
Dr	299 (47.6)
Prof. Dr.	94 (15.0)
Prof	29 (4.6)
Mr	41 (6.5)
Miss	17 (2.7)
Ms	16 (2.5)
Mrs	25 (4.0)
None	13 (2.1)
Skipped question	94 (15.0)
Gender	
Man	275 (43.8)
Woman	259 (41.2)
Skipped question	94 (15)
Professional role	
Clinical practitioner	399 (63.5)
Academic/Researcher	243 (38.7)
Educator	154 (24.5)
Student	40 (6.4)
Industry professional	9 (1.4)
Skipped question	94 (15.0)
Field of practice/Discipline	
Anaesthesiology	192 (30.6)
Pain specialization/accreditation	184 (29.3)
Physiotherapy	71 (11.3)
Neuroscience	64 (10.2)
Psychology	47 (7.5)
Physical and rehabilitation medicine	41 (6.5)
Neurology	40 (6.4)
Pharmacology	39 (6.2)
Nursing	29 (4.6)
General practice	19 (3.0)
Skipped question	94 (15)
See Supplementary File 8—Data S1 for remainder of fields/ disciplines	
Core Research Domains	
Physical assessment and diagnosis	215 (34.2)
Pain mechanisms	190 (30.3)
Prevention of pain	146 (23.2)
Clinical pain neurobiology/physiology/anatomy	143 (22.8)
Pharmacological management	114 (18.2)
Outcome measurement	111 (17.7)
Interventional management	104 (16.6)
Health professional training and curriculum development	94 (15.0)

**TABLE 1** (Continued)

	N (%)
Physical management	82 (13.1)
Psychological assessment and diagnosis	74 (11.8)
Clinical pathophysiology	71 (11.3)
Psychological management	70 (11.1)
Communication and public education	69 (11.0)
Health services implementation and delivery	69 (11.0)
Preclinical pain neurobiology/physiology/ anatomy	64 (10.2)
Epidemiology	60 (9.6)
Mechanisms of action of treatments/ pharmacodynamics/pharmacokinetics	57 (9.1)
Definition and classification	50 (8.0)
Telehealth	48 (7.7)
Big data	43 (6.9)
Cost-effectiveness of care	38 (6.1)
Social management	33 (5.3)
Health literacy	28 (4.5)
Health economics	26 (4.1)
Societal impact of pain	24 (3.9)
Ethics and cultural sensitivity	23 (3.7)
Preclinical pathophysiology	22 (3.5)
Machine learning/Artificial intelligence	21 (3.3)
Genomics	14 (2.2)
Policy	11 (1.8)
Legal and regulatory matters	6 (1.0)
Skipped question	94 (15)

predictive tools, including better patient-reported outcome measures for various conditions, biomarker testing, multidimensional pain and disability profiling and risk stratification (e.g. poor outcome and transition to chronic pain/disability).

### Theme 3: New treatments

This includes different types of treatment including pharmacological, interventional (e.g. neuromodulation) and person-centred behavioural treatments (e.g. exercise and psychological therapies). This included questions on discovering and testing novel treatments, repurposing treatment for new uses and preventative care (e.g. secondary prevention for conditions that have a high risk of recurrence).

### Theme 4: Explore benefits, harms, costs and acceptability of tests and treatments

This included questions that addressed tests and treatments, including digital methods, based on their cost,

effectiveness, mode of administration, impact on quality of life and benefit / harm ratio, as well as strategies to increase patients' adherence to tests or treatments.

#### Theme 5: Explore mechanisms of various treatments

This included questions on mechanisms (e.g. biological, psychological and social processes) through which therapeutic interventions exert their effects on pain, disability and quality of life.

#### Theme 6: Incorporate the patient voice into research

This included questions about involving people with a lived experience of pain in co-design of research questions and studies.

#### Theme 7: Assess the biopsychosocial societal impact of pain

This included questions on understanding the consequences of pain on individuals, communities and societies, prevalence, incidence and distribution of pain within populations, healthcare utilization, costs, quality of life, functioning, impairments and impact on work and productivity.

#### Theme 8: Better understand and address comorbidities in pain

This included questions about obesity, sleep and mood disorders, substance use disorders as well as their epidemiology and prevalence, impact on pain outcomes, mechanisms of impact and treatment.

#### Theme 9: Improve the translation and implementation of best evidence

This included questions on closing the gaps between basic, pre-clinical and clinical scientific research findings and their application in real-world settings to improve healthcare outcomes, public and patient knowledge and inform policy and practice.

### 3.3.3 | Quantitative analyses

Figures 2 and 3 illustrate priorities colour-coded according to the ratings received and shown as a polar diagram following their actual presentation order (Figure 3) or classified according to the ranking attributed by respondents (Figure 4). The survey items were classified as first line (top) priorities if they belonged to the first quartile of the ranking, which comprised questions for which the sum of the 'important' plus 'extremely important' ratings reached 86–96% of the total (Figure 4). As shown in Table 2, the first quartile highlighted priorities related to the understanding of the pathophysiology of chronic pain conditions (Theme 1; eight items in first quartile), the assessment

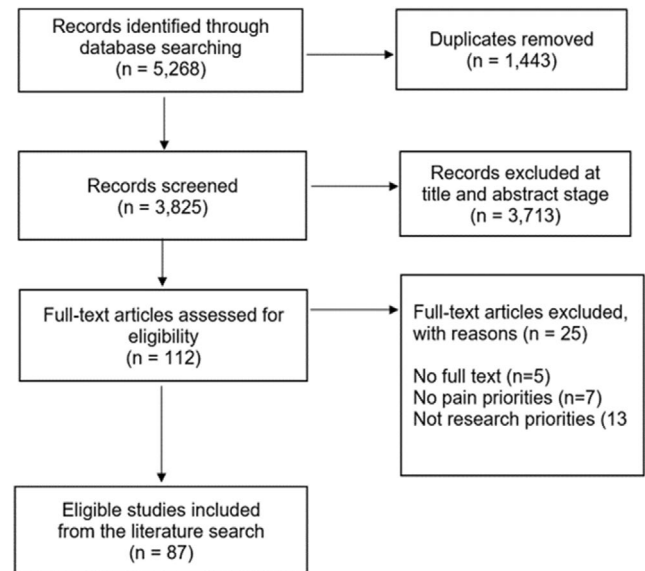
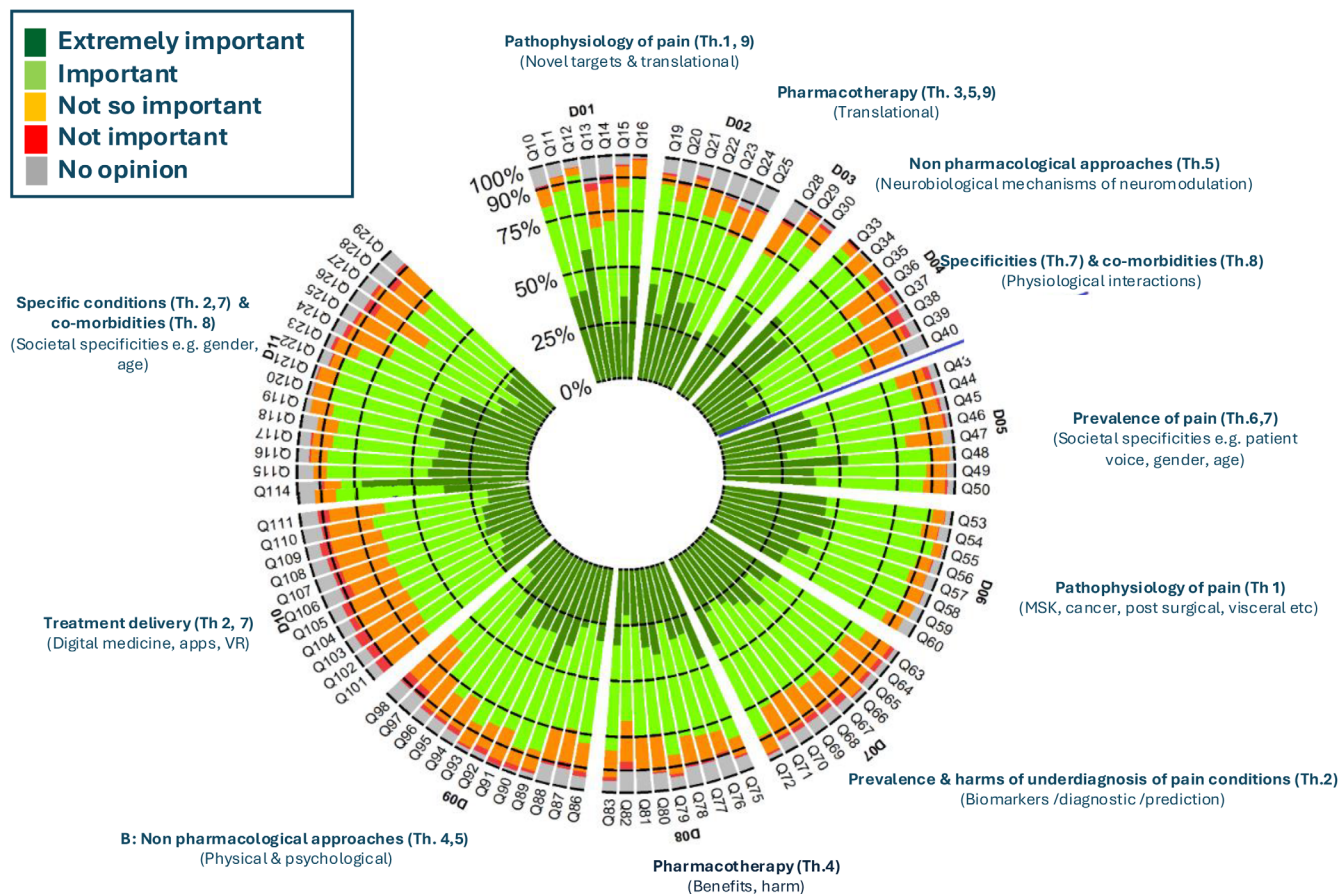


FIGURE 2 PRISMA scoping review flowchart.

and management of comorbidities (Theme 8; seven items in Q1), the need to critically assess current therapies and develop new treatments (e.g. pharmacological and behavioural approaches) (Themes 3–5, five items in Q1), the development of better diagnostic and prognostic tools (Theme 2; three items) and the further assessment of the biopsychosocial impacts of pain (Theme 7, three items).

Classification of items by order of priority showed a gentle descending slope in the proportion of 'important' and 'extremely important' responses (Figure 4, green bars) from the first to the third quartile of the distribution, the slope becoming steeper for the final quartile (lowest 25%). A mixed-model ANOVA (see Methods) showed significant effects of the main factors 'quartile' ( $F(3,96)=2.97$ ;  $p=0.03$ ) and 'type of response' ( $F(4,96)=2363$ ;  $p<0.001$ ) and a significant interaction between the two ( $F(12,384)=70.1$ ;  $p<0.001$ ). As shown in Figure 5, the interaction effect was explained by a steep decrease of the number of 'highly important' ratings from the first to the fourth quartile, which was almost exactly mirrored by a parallel increase in the number of 'not-so important' responses, whereas the proportion of questions rated 'important' remained identical across the four quartiles of the distribution. This implies that all the priorities included in the survey were considered as similarly 'important' by respondents, the difference in ranking being the result of a trade-off between the 'extremely important' and 'not-so important' responses (Table 3).

There was a significant drop in the number of respondents with the progression of the survey, with a strong negative correlation between the order number of the question and the number of participants responding to it. Such a drop, possibly related to progressively increased



**FIGURE 3** Polar graph of survey items in order of presentation. Responses are presented clockwise in the same order as they appeared in the questionnaire (Q1–Q10 represents demographics). Blocks of questions in different theme domains (D01–D11) are separated by a blank radius. Colours indicate rating levels, ranked as indicated in the upper left inset. Labels around the circle indicate the main topics in the questions, with the main theme(s) they map on between brackets. Themes were extracted by content analysis of the questions and several themes could be applied to one single block of questions. Th: theme, MSK: musculoskeletal, VR: virtual reality.

fatigue, concerned to a similar extent and was similarly significant, for items ranked in all four quartiles (Figure 6). Consequently, despite any other differences, on average there was roughly the same number of people responding to the survey in all quartiles ( $F(3,96)=2.6; p>0.05$ ) and fatigue could reasonably be ruled out as a main factor of the differences between quartiles.

Priorities ranked lowest in the survey (i.e. with the highest proportion of ‘not-so-important’ or ‘not important’ ratings) concerned questions related to some societal aspects (effect of gender, race and ethnicity; marginalized populations; patient’s involvement) (eight items), as well as digital medicine and new technologies (ten items) such as virtual reality. This lowest quartile was the only showing significant differences in ratings according to the sex of participants, as women respondents rated items related to improving the inclusion of older populations and animals, as well as female animals in preclinical trials, social support, marginalized groups, patient involvement and the physiological effects of sex difference on pain modulation significantly

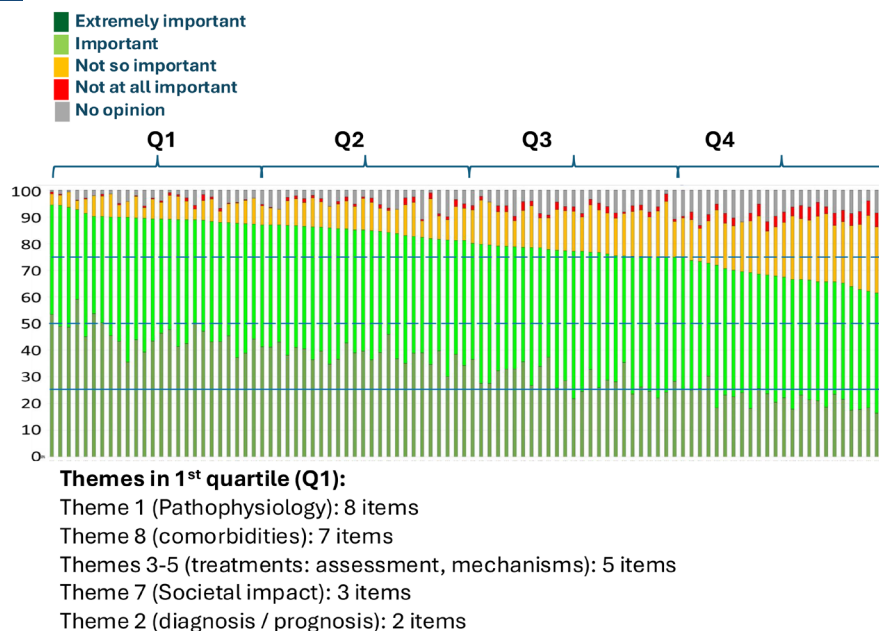
better than men respondents. Results according to sex and profession (researcher vs. clinical practitioner) are presented in Figure 7 and Tables 4 and 5.

A direct contrast between the nine themes emerging from content analysis was difficult since the number of items in each of them varied widely—some themes contained  $n = 30$  survey questions or more, while others only 2 or 3. Nevertheless, there were marked differences in the presence of certain themes in the first and last ranking quartiles: As illustrated in Figure 8, Themes 1, 3 and 8, respectively on pathophysiology, new treatments and comorbidities, loaded exclusively or predominantly in the first quartile, whereas Themes 4 and 9 (benefits/harms and translational aspects) predominated in the last quartile.

### 3.4 | Consensus meeting

The 26-member expert panel (EFIC SWG and ERA-NET SWG) of the consensus meeting highlighted the great





**FIGURE 4** Survey items classed in order of priority. The 100 priority research items of the Survey were ranked according to the Total importance, defined as the sum of responses ‘important’ and ‘extremely important’ they received. Colour codes of the bars indicated on top left of the figure. The abscissae represent the 100 Survey items, ordered by decreasing importance in the respondents’ rating. The themes included in the first quartile of the ranking are listed in the lower part of the figure. Note that the decrease of ‘extremely important’ items in the last quartile (Q4) is compensated by an increase in ‘not-so important’ (orange) ratings.

stability and lack of significant differences in the proportion of items classified as ‘important’ across the whole set of questions (Figure 5). Based on the results, the panel supported the overall relevance of all the priorities included in the survey and the validity of the multistage selection process.

The output of the ‘world café’ final panel discussion highlighted priorities of major importance which were not considered or insufficiently considered by the survey results and themes. These were as follows.

**Prediction:** It was emphasized that being able to predict individuals who are at risk of poor outcome; for example, transitioning from acute to chronic pain and predicting individual response to various treatments needs to be clearly communicated in the final strategy.

**Prevention:** It was highlighted that there is a dearth of research on prevention (both primary and secondary prevention of pain and disability) compared to research on interventions. Many panel members said efforts to prevent chronic pain and related disability need to be a clear message from the strategy.

**Self-management:** While several themes referred to treatments (e.g. behavioural approaches such as exercise and psychological therapies), many panel members highlighted the importance of explicitly including the word self-management given the importance of this treatment model in the management of chronic pain.

**Personalized pain management:** There is increasing evidence that personalized pain management is required to fit individual aspects of each patient with chronic pain. Given that pain is always a personal experience that is influenced to varying degrees by biological, psychological and social factors that differ from person to person, the panel felt the word ‘personalized’ or ‘individualized’ management should be communicated throughout the strategy, to overcome the limitations of one size fits all approaches.

## 4 | DISCUSSION

This first European Pain Research Strategy demonstrated high consensus on several research topics that need more focus. No research topic was ranked low in the survey, indicating that all priorities were relevant. Top-ranked priorities included better understanding pain pathophysiology, understanding and treating comorbidities, exploring benefits/harms/costs of current therapies, developing new treatments and understanding biopsychosocial impacts of pain. A final consensus meeting agreed on the identified priorities and recommended that the strategy communicate the importance of research into prediction (e.g. risk of poor outcome and response to different treatment), prevention of chronic pain, self-management and personalized pain management.

**TABLE 2** Research priorities rated as most important (questions ranked in the first quartile).

Item number	Theme number	% Extremely important	% Important	Research priority
Q33	8	53.4	41.1	Understand physiological interactions between pain disorders and comorbidities (mood, sleep, obesity...)
Q55	1	49.0	45.4	Understand pathophysiology of neuropathic pain (children and adults)
Q35	8–3	48.6	45.0	Develop novel treatments for pain comorbid with mood, sleep, obesity disorders
Q12	3–5	59.0	33.7	Discover and validate novel targets for safe and effective treatment of pain
Q53	1	45.1	46.3	Understand pathophysiology of acute/chronic primary and secondary musculoskeletal pain
Q48	4–7	53.7	36.5	Estimate the prevalence of unnecessary treatment (surgical and medical including opioids)
Q16	7–9	50.2	40.0	Integrate psychosocial factors into translational research
Q34	8–1	45.4	44.6	Identify mechanisms by which pain, mood, sleep, obesity and other comorbidities co-exist
Q122	8–7	43.4	46.6	Include individuals with comorbidities in pain research studies
Q59	1	35.5	54.3	Understand pathophysiology of acute/chronic primary headache and orofacial pain
Q120	8–1	44.0	45.6	Identify mechanisms by which pain, mood, sleep, obesity and other comorbidities interact
Q114	2–3	39.3	50.2	Understanding, assessment and management of pain in neurological conditions
Q58	1	43.5	45.8	Pathophysiology of fibromyalgia and chronic widespread pain
Q56	1	46.4	42.8	Understand pathophysiology of acute and chronic postsurgical and posttraumatic pain
Q29	5–3	47.7	41.5	Mechanisms whereby exercise and psychological therapies modulate pain
Q121	8–4	41.3	47.7	Effect of interventions targeting mood, sleep and obesity on pain intensity (comorbidities)
Q45	7–8	42.5	46.5	Relationship between chronic pain, other health conditions (e.g. cardiovascular) and life expectancy
Q21	4	50.1	38.9	Efficacy and safety of novel candidate analgesics and co-analgesics
Q90	3–7	47.1	41.7	Strategies to increase adherence to exercise and healthy lifestyle behaviour
Q72	2	43.1	45.2	Develop and/or validate models that may help to predict the risk of pain chronification
Q19	1–2	43.1	44.8	Neurobiology of signalling systems and brain circuitry in relation to pathological pain processing
Q54	1	45.4	42.4	Understand the pathophysiology of acute and chronic cancer pain
Q57	1	37.2	50.5	Understand the pathophysiology of complex regional pain syndrome
Q49	7	38.8	48.7	Estimate the prevalence of appropriate care (advice, appropriate medicine and exercise) across Europe
Q119	8–7	44.2	43.2	Assess impact of mood disorders, sleep problems, obesity and other comorbidities on pain

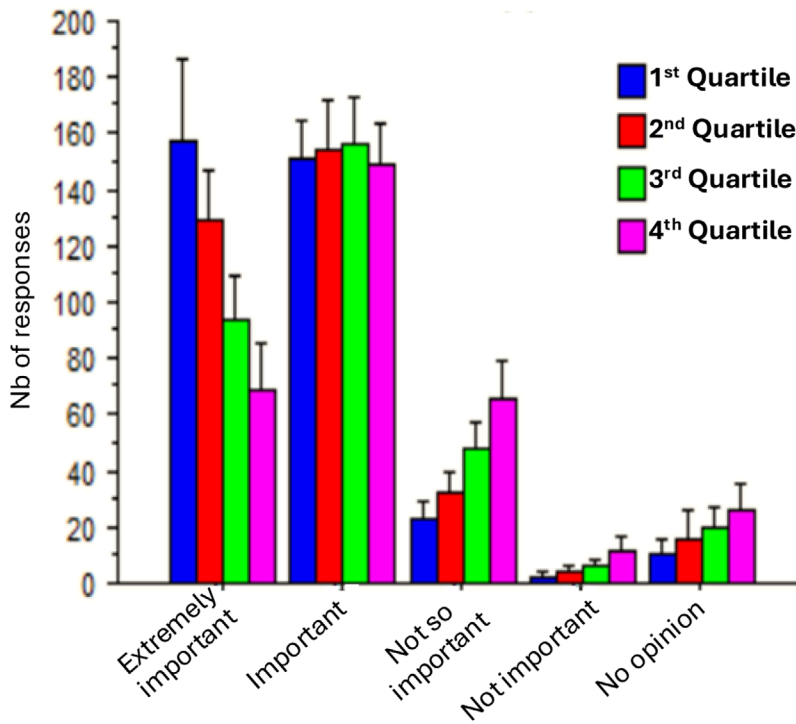
*Note:* Theme 1: Better understand pathophysiology of pain. Theme 2: Better assessment and diagnostic/prognostic tools. Theme 3: New treatments. Theme 4: Explore benefits, harms, costs and acceptability of tests and treatments. Theme 5: Explore mechanisms of various treatments. Theme 6: Incorporate the patient voice into research. Theme 7: Assess the biopsychosocial impacts of pain. Theme 8: Better understand and address comorbidities in pain. Theme 9: Improve the translation and implementation of best evidence.

#### 4.1 | Top-ranked research priorities

Seventy-five per cent of the priorities proposed in the survey were judged ‘important’ or ‘extremely important’ by ~95% of respondents and the lowest ranked items were considered

important in over 60% of responses (Figure 3). This supports the items included in the survey and the validity of the multi-stage priority selection process conducted before the survey. While the majority of items were considered relevant, variance in their ratings allowed to individualize those

	df	Sum of sq.	Mean sq.	F-value	p-value	Power
Quartile	3	1555.510	518.503	2.977	0.035	.686
Subject (Group)	96	16721.04	174.178			
Ratings	4	1610945.66	402736.41	2363.17	<.0001	1.000
Ratings * Quartile	12	143460.34	11955.02	70.15	<.0001	1.000



**FIGURE 5** Interaction effects ANOVA. On the number of responses according to rating (from extremely important to not important or no opinion) and quartile. Note that the progressive decrease of ‘extremely important’ items was compensated by a parallel increase in ‘not-so important’ ratings, whereas the number of priorities rates as ‘important’ remained stable across quartiles.

emerging as ‘absolute priorities’, which ranked in the first quartile of the distribution. These priorities reflected urgent needs: understanding pain pathophysiology; investigating and addressing pain comorbidities; critically evaluating current therapies, developing new treatments; and exploring biopsychosocial impacts of pain (Table 2).

These priorities align with those identified in other pain research. A better understanding of biological mechanisms was emphasized for spinal pain (Dionne et al., 2022), spinal cord injury-related pain (Hitzig et al., 2017) and neurological research (Boon et al., 2024). Prediction and prevention strategies were highlighted by other agendas (Boon et al., 2024; Gilbert et al., 2022) as was the need for better outcome measurements (Hitzig et al., 2017; Maxwell et al., 2015; Merlin et al., 2023). As expected, the need for effective treatments is often cited by others (Boon et al., 2024; Gilbert et al., 2022) including, as in our case, the identification of low-value options (Dionne et al., 2022).

The top-ranked priorities were prioritized equally by clinicians and researchers, and by men and women

respondents. Unlike previous agendas, our themes addressed broad categories rather than being specific to a condition. Thus, pathophysiology-related priorities with a similar level of importance included neuropathic, musculoskeletal, post-surgical, orofacial and cancer pains, as well as fibromyalgia and CRPS. Similar inclusiveness applied to comorbidities and treatment-related priorities: the comorbidities highlighted were diverse and included both the somatic and mental health spheres, while treatment priorities comprised pharmacological and behavioural approaches (e.g. exercise and psychologically based treatments)—and crucially addressed the issue of unnecessary treatments.

It is noteworthy that pathophysiology survey items were given as much weight as those related to treatment and may reflect participants’ conviction that the search for new therapies is not possible without a parallel improvement in knowledge of disease mechanisms. Inclusion of pathophysiology top research priorities is relatively new: a PubMed search for strategies and agendas on pain, anaesthesiology and neurology from

**TABLE 3** Top ranked priorities under the main themes.

Order	Priority	Extremely important	Important	Total importance
<b>Theme 1: Better understand pathophysiology of pain</b>				
1	Pathophysiology of neuropathic pain (Q55)	49.0%	45.4%	94.4%
2	Pathophysiology of acute and chronic primary and secondary musculoskeletal pain (Q53)	45.1%	46.3%	91.4%
3	Integrate psychosocial factors into translational research (Q16)	50.2%	40.0%	90.2%
<b>Theme 2: Better assessment, measurement and diagnostic tools</b>				
1	Develop and/or validate models that may help to predict the risk of pain chronification and recurrence and expected times to improvement (Q72)	43.1%	45.2%	88.3%
2	Better pain assessment tools for older/geriatric patients (Q116)	41.2%	45.8%	87.0%
3	Better assessment tools for infants and children across various pain conditions (Q115)	43.0%	44.0%	87.0%
<b>Theme 3: New treatments</b>				
1	Discover and validate novel targets for safe and effective treatment (Q12)	59.0%	33.7%	92.7%
2	Explore analgesic potential of receptors and targets outside the central nervous system, to overcome potential harms of central acting drugs. (Q23)	39.0%	43.3%	82.3%
3	Understand the 'dose' of exercise needed to optimize pain outcomes across different pain types (Q91)	34.6%	47.3%	81.9%
<b>Theme 4: Explore benefits, harms, costs and acceptability of tests and treatments</b>				
1	Estimate the prevalence of unnecessary treatment (e.g. ineffective surgeries and problematic opioid use) for various pain conditions across Europe (Q48)	53.4%	36.3%	89.7%
2	Better assessment of efficacy and safety of novel candidate analgesics and co-analgesics (Q21)	50.1%	38.9%	89.0%
3	Explore strategies of increasing long-term adherence to exercise and healthy lifestyle behaviours among patients with chronic pain (Q90)	47.1%	41.7%	88.8%
<b>Theme 5: Explore mechanisms of various treatments</b>				
1	Explore the neurobiological mechanisms of action by which exercise and psychological therapies modulate pain. (Q29)	47.7%	41.5%	89.2%
2	Assess the mechanisms by which exercise exerts its effect on pain and disability (Q89)	38.1%	48.7%	86.8%
3	Examine the mechanisms by which psychological approaches exert their effect on pain and disability (Q93)	36.4%	49.8%	86.2%
<b>Theme 6: Incorporate the patient voice into research</b>				
1	Prioritize meaningful public patient and involvement in pain research through the involvement of diverse populations in the codesign of research questions and analysis (Q128)	22.5%	47.6%	70.1%
<b>Theme 7: Assess the societal impact of pain</b>				
1	Estimate the personal and societal burden of pain in Europe. This research could include quality of life, mental health, social participation, healthcare costs, sickness absences and early retirement. (Q44)	40.5%	46.0%	86.5%

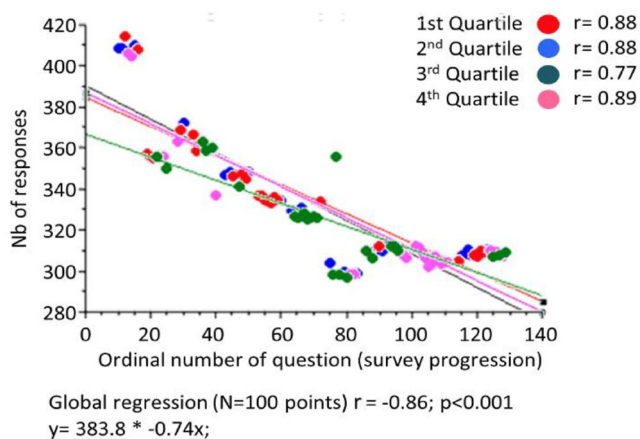
(Continues)



TABLE 3 (Continued)

Order	Priority	Extremely important	Important	Total importance
2	Estimate the prevalence of acute, chronic and disabling pain in Europe. This relates to both cancer and non-cancer pain. (Q43)	38.4%	42.8%	81.2%
<b>Theme 8: Better understand and address comorbidities in pain</b>				
1	Understand physiological interactions and reciprocal relationships between various pain disorders and mood disorders, sleep problems, obesity and other comorbidities (Q33)	<b>53.4%</b>	<b>41.1%</b>	<b>94.5%</b>
2	Develop novel treatment strategies for the treatment of pain comorbid with conditions including mood disorders, sleep problems and obesity (Q35)	<b>48.6%</b>	<b>45.0%</b>	<b>93.6%</b>
3	Identify underlying mechanisms by which pain, mood, sleep, obesity and other comorbidities co-exist and provide biomarkers (Q120)	45.4%	44.6%	90.0%
<b>Theme 9: Improve the translation and implementation of best evidence</b>				
1	Better understand clinician and patient beliefs about the underlying causes of pain and the benefits and harms of various treatments (Q46)	41.0%	45.7%	86.7%
2	Estimate the availability of multimodal pain treatment across Europe (Q50)	39.7%	46.6%	86.3%
3	Explore factors that hinder translation of basic science results to clinical settings (Q15)	36.6%	49.0%	85.6%

Note: Bolded sub-themes are the same in polar analysis. 'Total importance' is the sum of percentages of responders with 'Extremely important' and 'Important' responses.



**FIGURE 6** Survey responses versus ordinal position of questions. Regression analysis of the number of responses received per survey item, as a function of the position of the item in the survey. There was a progressing decline in the number of respondents to items with the progression of the survey, with a significant negative correlation between the ordinal number of the question and the number of participants responding to it. Such effect was likely related to progressively increased fatigue. It concerned to a similar extent and significance items ranked in all four quartiles.

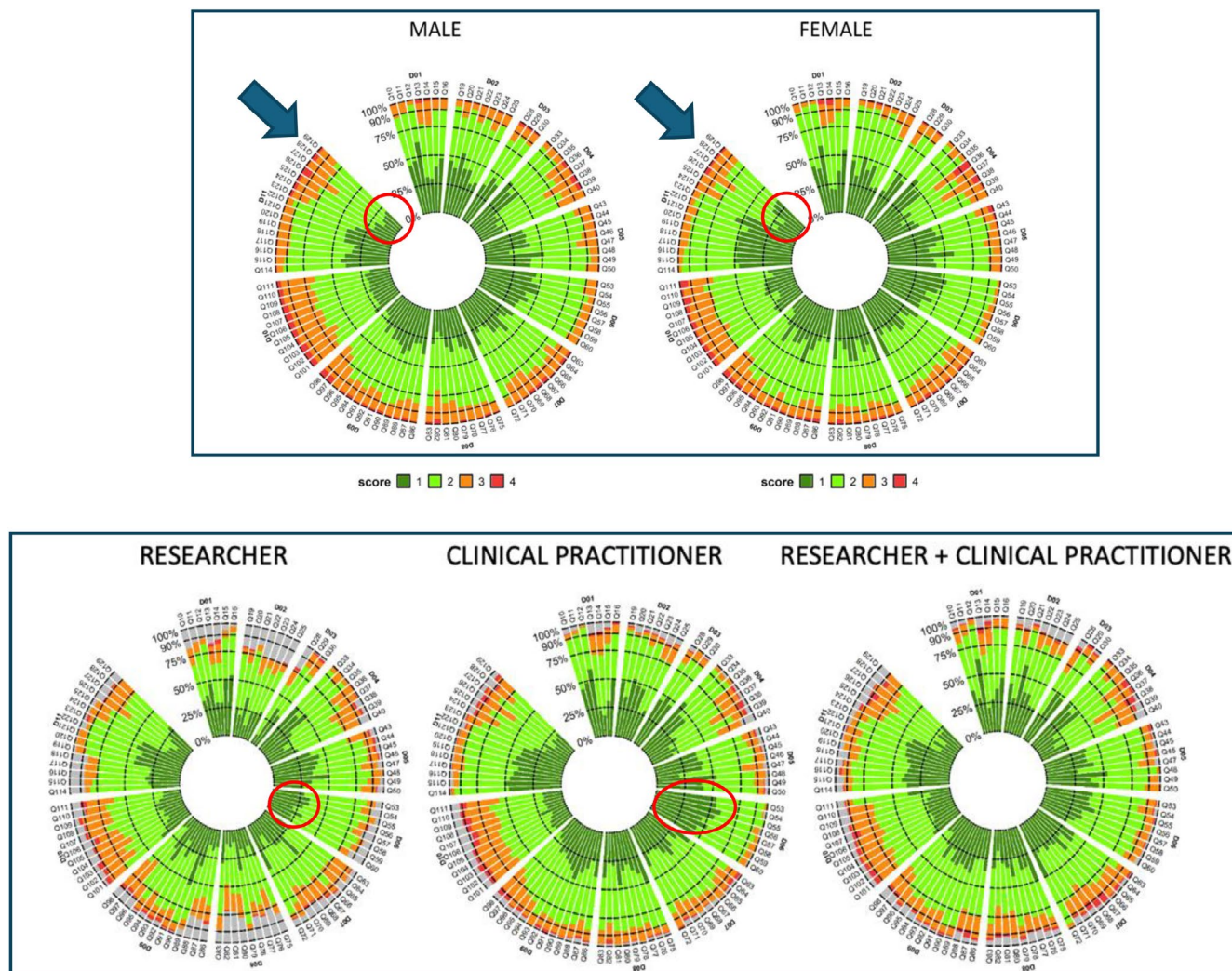
the 2021 to 2024 period returned 168 articles, of which only three identified pain pathophysiology as a priority, respectively, in cervical dystonia (Gilbert et al., 2022),

osteomyelitis (Mohanna et al., 2023) and fibromyalgia (Goebel et al., 2022). In contrast, the present survey placed the investigation of disease mechanisms as a core priority, at the same level as treatments. Not only is this approach scientifically sound, but it should strengthen translational research in future pain research programmes (Mouraux et al., 2021).

Also of relevance is that behavioural treatments (e.g. person-centred exercise and psychological approaches) were prioritized at the same level as pharmacological therapies, despite possible geographical differences (Koop et al., 2023). This implies that the biopsychosocial model is now 'anchored' in the mentality of the pain community. Although the biopsychosocial perspective on pain has been in existence since the 1980s (Nicholas, 2022), our approach allowed us to verify its relevance through input from clinical and research community.

## 4.2 | Descending ranks of priority

Although the proportion of 'important' ratings remained strictly stable across all survey items, response distribution showed a progressive decrease in the number of 'extremely important' ratings, almost entirely compensated by a parallel increase in 'not so important' scores (Figures 3 and 4). The most parsimonious explanation



**FIGURE 7** Distribution of individual survey responses according to gender and profession. *Upper panel:* Polar representation showing similar distribution of responses from men and women participants across all questions, except those related to social support (127), marginalized groups (129), patient involvement (128) and gender differences, where women gave a significantly greater proportion of positive responses (arrows and red circles). *Lower panel:* Similar distributions were also obtained for clinicians and researchers, except for items related to the pathophysiology of neuropathic, musculoskeletal, cancer and postsurgical pain (Questions 53–56) which were noted higher by clinicians (arrows and red circles).

seems to be a homogenous shift in scores, with a proportion of respondents downgrading some notes from ‘extremely important’ to ‘important’ and a similar proportion passing from there to ‘not-so important’, hence keeping the ‘important’ priorities steady overall. Less likely, some participants may have drastically changed their minds and downgrade items by more than one level, while others kept the total number of ‘important’ responses steady.

The descending slope of the distribution of positive responses was smooth for the first three quartiles and became more pronounced for the fourth one (Figure 4). Themes related to assessment, diagnosis and prognosis (Theme 2), mechanisms of treatments (Theme 5) and forward-back translation (Theme 9) appeared

consistently in the second and third quartiles of the distribution, while items referring to digital medicine and assessment of complex populations were mostly concentrated in the last quartile. As questions on these relatively ‘low ranked’ priorities tended to appear late in these, participant fatigue cannot be ruled out. Participant fatigue as the survey progressed is supported by the linear decrease in the number of respondents as the survey advanced. However, such a decrease affected items in all quartiles and the number of responses provided did not change significantly across quartiles and could not explain the differences. As many items in the bottom quartile referred to special populations (e.g. older adults) and specific aspects of pain assessment, their lower rank may reflect a predisposition of respondents to privilege

**TABLE 4** Relationships between top ranked priorities and sex and professional role of survey participants.

	Male	Female	<i>p</i>	Researcher	Clinical practitioner	Researcher + clinical practitioner	<i>p</i> *
<i>First-line priorities</i>							
Q12 Discover and validate novel targets for safe and effective treatment of pain							
Not at all important <i>n</i> %	1, 0.5	0, 0.00	0.787	0, 0.00	0, 0.00	1, 0.9	0.284
Not so important <i>n</i> %	8, 3.7	6, 3.3		4, 5.3	4, 2.1	5, 4.5	
Important <i>n</i> %	72, 33.2	68, 37.2		31, 40.8	70, 37.4	34, 30.4	
Extremely important <i>n</i> %	136, 62.7	109, 59.6		41, 54.0	113, 60.4	72, 64.3	
Q16 Integrate psychosocial factors into translational research							
Not at all important <i>n</i> %	1, 0.5	2, 1.0	0.398	0, 0.00	3, 1.6	0, 0.0	0.701
Not so important <i>n</i> %	19, 8.8	13, 6.6		5, 5.6	14, 7.5	11, 9.8	
Important <i>n</i> %	93, 43.3	74, 37.6		35, 39.3	75, 40.3	48, 42.9	
Extremely important <i>n</i> %	102, 47.4	108, 54.8		49, 55.1	94, 50.5	53, 47.3	
Q33 Understand physiological interactions and reciprocal relationships between various pain disorders and mood disorders, sleep problems, obesity and other comorbidities							
Not at all important <i>n</i> %	2, 1.1	1, 0.6	0.808	0, 0.0	0, 0.0	2, 2.0	0.446
Not so important <i>n</i> %	9, 4.8	6, 3.4		4, 4.8	5, 3.2	5, 5.0	
Important <i>n</i> %	79, 42.0	72, 40.7		38, 45.8	63, 40.1	45, 44.6	
Extremely important <i>n</i> %	98, 52.1	98, 55.4		41, 49.4	89, 56.7	49, 48.5	
Q48. Estimate the prevalence of unnecessary treatment (e.g. ineffective surgeries and problematic opioid use) for various pain conditions across Europe							
Not at all important <i>n</i> %			0.476				0.228
Not so important <i>n</i> %	14, 8.1	13, 7.8		8, 10.0	15, 10.3	3, 3.2	
Important <i>n</i> %	70, 40.2	57, 34.1		31, 38.8	51, 34.9	41, 43.2	
Extremely important <i>n</i> %	90, 51.7	97, 58.1		41, 51.3	80, 54.8	51, 53.7	
Q55. Better understand the pathophysiology of neuropathic pain in children and adults							
Not at all important <i>n</i> %	1, 0.6	0, 0.0	0.779	0, 0.00	0, 0.0	1, 1.1	<i>p</i> < 0.01
Not so important <i>n</i> %	8, 4.8	5, 3.1		5, 6.9	1, 0.7	7, 7.9	
Important <i>n</i> %	77, 45.8	75, 46.3		42, 57.5	58, 39.5	45, 50.6	
Extremely important <i>n</i> %	82, 48.8	82, 50.6		26, 35.6	88, 59.9	36, 40.5	
<i>Second-line priorities</i>							
Q114. Better understanding, assessment and management of pain in neurological conditions (e.g. multiple sclerosis and Parkinson's disease)							
Not at all important <i>n</i> %	2, 1.3	0, 0.0	0.248	0, 0.0	1, 0.8	1, 1.2	0.103
Not so important <i>n</i> %	8, 5.3	4, 2.9		3, 5.4	3, 2.3	6, 7.2	
Important <i>n</i> %	84, 55.6	69, 50.7		37, 66.1	63, 49.2	43, 51.8	
Extremely important <i>n</i> %	57, 37.8	63, 46.3		16, 28.6	61, 47.7	33, 39.8	
Q21 Better assessment of efficacy and safety of novel candidate analgesics and co-analgesics							
Not at all important <i>n</i> %	2, 1.1	3, 2.0	0.725	0, 0.0	3, 1.9	2, 2.1	0.193
Not so important <i>n</i> %	9, 4.9	5, 3.3		4, 6.6	5, 3.2	3, 3.2	
Important <i>n</i> %	73, 39.5	65, 43.3		31, 50.8	63, 40.4	31, 32.6	
Extremely important <i>n</i> %	101, 54.6	77, 51.3		26, 42.6	85, 54.5	59, 62.1	
Q29 Explore the neurobiological mechanisms of action by which exercise and psychological therapies modulate pain							
Not at all important <i>n</i> %	4, 2.1	0, 0.0	0.293	1, 1.2	0, 0.0	3, 2.9	0.169
Not so important <i>n</i> %	18, 9.4	15, 8.6		11, 13.4	13, 8.3	8, 7.7	
Important <i>n</i> %	8, 42.4	72, 41.1		38, 46.3	63, 40.1	42, 40.4	
Extremely important <i>n</i> %	88, 46.1	88, 50.3		32, 39.0	81, 51.6	51, 49.0	

TABLE 4 (Continued)

	Male	Female	<i>p</i>	Researcher	Clinical practitioner	Researcher + clinical practitioner	<i>p</i> *
Q35 Develop novel treatment strategies for the treatment of pain comorbid with conditions including mood disorders, sleep problems and obesity							
Not at all important <i>n</i> %			0.340				0.158
Not so important <i>n</i> %	14, 7.5	7, 4.1		3, 3.7	6, 3.8	10, 10.2	
Important <i>n</i> %	81, 43.3	82, 47.4		36, 43.9	80, 51.0	40, 40.8	
Extremely important <i>n</i> %	92, 49.2	84, 48.6		43, 52.4	71, 45.2	48, 49.0	
Q90 Explore strategies of increasing long-term adherence to exercise and healthy lifestyle behaviours among patients with chronic pain							
Not at all important <i>n</i> %	4, 2.5	3, 2.0	0.568	1, 1.5	2, 1.5	2, 2.3	0.390
Not so important <i>n</i> %	13, 8.2	10, 6.8		4, 6.2	12, 9.0	5, 5.7	
Important <i>n</i> %	72, 45.3	58, 39.2		24, 36.9	56, 42.1	47, 53.4	
Extremely important <i>n</i> %	70, 44.0	77, 52.0		36, 55.4	63, 47.4	34, 38.6	

\*Analysed using chi-squared test or Fisher's exact test.

items of general, rather than specific impact. For example, improving cancer pain treatment (general) may be considered of greater urgency than applying it to specific populations (particular). Of note, questions in the lowest quartile were the only ones showing significant rating differences according to gender, as female respondents rated items related to social support, marginal groups, special populations (e.g. older adults) and patient involvement as higher priority than male respondents.

### 4.3 | Methodological aspects

There is currently no gold standard for establishing a research agenda. Different organizations have used a range of methodologies to derive strategies on specific painful conditions including spinal cord injury-related pain (Hitzig et al., 2017), HIV-related chronic pain (Merlin et al., 2023), dystonia in cerebral palsy (Gilbert et al., 2022) or neurological conditions (Boon et al., 2024). They included questionnaires to expert groups, literature reviews and consensus panel discussions, but rarely open surveys outside the expert panel. We adopted not only a multi-pronged methodology combining exhaustive literature search, organizational opinions and expert consensus, but also submitted these to the opinion of external colleagues in basic, translational and clinical sciences and industry professionals, by circulating a comprehensive survey. These combined approaches added to the validity of the Strategy. Participation in the survey was substantial, with 628 respondents out of the 1053 individuals accessing the survey page (59.6% retention). Although each specific question was answered by only approximately half of the sample (331 ± 29 responses

per question), this response rate compares favourably with other recommendations on pain priorities which used ss (Dionne et al., 2022; Gilbert et al., 2022; Hitzig et al., 2017; Maxwell et al., 2015; Merlin et al., 2023) and substantiates the robustness of the results.

### 4.4 | Strengths and limitations

The exhaustive literature assessment, analysis of research agendas from respected institutions, including the James Lind Alliance (providing a large list of patient priorities), Cochrane and IASP and supplemented with priorities emanating from the European Pain Forum and the EFIC Research Committee, represents a significant strength of the present work and one of the most comprehensive methodologies to derive an initial set of research priorities. The distillation of these into a compact set of 100 research items for rating, with the extraction of distinct themes using formal content analysis, allowed us to evaluate such 'institutional' priorities through the responses of an independent sample of individuals. While globally approving the whole set of items, the survey respondents ranked them to extract the highest priorities. Some of them align with previous suggestions in the literature, while others are new and, as discussed above, relevant to give future impetus to research.

This work also presents several limitations. The survey respondents were in their majority clinicians compared to researchers (60% vs. 40%), which may induce some response bias, although lack of significant difference in majority of items indicate that such bias was negligible. Most clinicians were pain consultants (minority were general



**TABLE 5** Relationships between lowly ranked priorities and sex and professional role of survey participants.

	Male	Female	<i>p</i>	Researcher	Clinical practitioner	Researcher + clinical practitioner	<i>p</i>
<i>Low priorities</i>							
Q38 Assess the physiological effects of race and ethnicity on pain modulation							
Not at %	9, 5.1	11, 6.6	0.567	2, 2.6	9, 5.8	9, 9.8	0.462
Not so important <i>n</i> %	49, 27.7	53, 31.6		20, 26.3	46, 29.9	30, 32.6	
Important <i>n</i> %	87, 49.2	70, 41.7		40, 52.6	68, 44.2	39, 42.4	
Extremely <i>n</i> %	32, 18.1	34, 20.2		14, 18.4	31, 20.1	14, 15.2	
Q126 Better characterize the relationship between race and ethnicity and pain and disability							
Not at all <i>n</i> %	12, 8.2	6, 4.3	0.490	1, 1.6	9, 7.3	7, 8.6	0.475
Not so important <i>n</i> %	42, 28.8	38, 27.0		19, 30.2	37, 30.1	19, 23.5	
Important <i>n</i> %	73, 50.0	74, 52.5		35, 55.6	57, 46.3	44, 54.3	
Extremely important <i>n</i> %	19, 13.0	23, 16.3		8, 12.7	20, 16.3	11, 13.6	
Q101 Identify patient subgroups who respond better to face to face or digital interventions							
Not at all important <i>n</i> %	8, 5.2	6, 4.2	0.875	3, 4.4	6, 4.9	4, 4.6	0.278
Not so important <i>n</i> %	37, 24.2	31, 21.7		12, 17.7	36, 29.5	18, 20.7	
Important <i>n</i> %	66, 43.1	68, 47.6		30, 44.1	56, 45.9	38, 43.7	
Extremely important <i>n</i> %	42, 27.5	38, 26.6		23, 33.8	24, 19.7	27, 31.0	
Q111 Examine acceptability of digital technology across diverse populations and pain conditions							
Not at all important <i>n</i> %	5, 3.5	10, 7.4	0.223	4, 6.4	8, 6.8	2, 2.5	0.608
Not so important <i>n</i> %	44, 30.3	30, 22.2		17, 27.0	37, 31.6	19, 23.5	
Important <i>n</i> %	71, 49.0	66, 48.9		31, 49.2	50, 42.7	44, 54.3	
Extremely important <i>n</i> %	25, 17.2	29, 21.5		11, 17.5	22, 18.8	16, 19.8	
Q97 Better understand how virtual reality application may exert its impact on the pain experience, to help identify treatment targets, across acute and chronic pain conditions							
Not at all important <i>n</i> %	9, 6.0	5, 3.8	0.685	2, 3.5	7, 5.7	3, 3.7	0.273
Not so important <i>n</i> %	37, 24.8	33, 25.0		22, 37.9	26, 21.0	19, 23.5	
Important <i>n</i> %	72, 48.3	71, 53.8		27, 46.6	63, 50.8	44, 54.3	
Extremely important <i>n</i> %	31, 20.8	23, 17.4		7, 12.1	28, 22.6	15, 18.5	
Q98 Examine the benefit and harms of various virtual reality applications compared to usual care across acute and chronic pain conditions							
Not at all important <i>n</i> %	9, 6.1	7, 5.3	0.428	3, 5.0	8, 6.5	3, 3.8	0.899
Not so important <i>n</i> %	44, 29.7	32, 24.2		20, 33.3	33, 26.8	21, 26.3	
Important <i>n</i> %	66, 44.6	72, 54.6		29, 48.3	60, 48.8	40, 50.0	
Extremely important <i>n</i> %	29, 19.6	21, 15.9		8, 13.3	22, 17.9	16, 20.0	
Q40 Methods to improve inclusion of older humans and animals, as well as female animals, in pre-clinical research							
Not at all important <i>n</i> %			0.033				0.583
Not so important <i>n</i> %	40, 25.3	23, 16.6		12, 17.4	32, 25.4	17, 20.5	
Important <i>n</i> %	84, 53.2	69, 49.6		35, 50.7	65, 51.6	42, 50.6	
Extremely important <i>n</i> %	34, 21.5	47, 33.8		22, 31.9	29, 23.0	24, 28.9	
Q127 Better characterize the relationship between social deprivation and social support on pain and disability							
Not at all important, <i>n</i> %	2, 1.3	3, 2.1	0.031	1, 1.6	3 2.4	1, 1.2	0.531
Not so important <i>n</i> %	31, 20.8	22, 15.7		12, 19.1	17, 13.7	20, 24.4	
Important <i>n</i> %	91, 61.1	72, 51.4		36, 57.1	77, 62.1	41, 50.0	
Extremely important <i>n</i> %	25, 16.8	43, 30.7		14, 22.2	27, 21.8	20, 24.4	

TABLE 5 (Continued)

	Male	Female	<i>p</i>	Researcher	Clinical practitioner	Researcher + clinical practitioner	<i>p</i>
Q128 Prioritize meaningful public patient and involvement in pain research through the involvement of diverse populations in the codesign of research questions and analysis							
Not at all important <i>n</i> %	6, 4.3	3, 2.24	0.028	1, 1.5	3, 2.6	4, 5.2	0.828
Not so important <i>n</i> %	30, 21.3	21, 15.7		13, 20.0	24, 20.9	12, 15.6	
Important <i>n</i> %	80, 56.7	66, 49.3		34, 52.3	64, 55.7	42, 54.6	
Extremely important <i>n</i> %	25, 17.7	44, 32.8		17, 26.2	24, 20.9	19, 24.7	
Q129 Examine the needs of under-represented, marginalized and hard-to-reach groups in pain evaluation and treatment							
Not at all important <i>n</i> %	3, 2.1	3, 2.2	0.064	0, 0.00	4, 3.3	1, 1.3	0.611
Not so important <i>n</i> %	25, 17.2	21, 15.1		12, 18.8	21, 17.1	12, 15.2	
Important <i>n</i> %	88, 60.7	68, 48.9		31, 48.4	70, 56.9	45, 57.0	
Extremely important <i>n</i> %	29, 20.0	47, 33.8		21, 32.8	28, 22.8	21, 26.6	
Q36 Assess the physiological effects of sex differences on pain modulation							
Not at all important <i>n</i> %	7, 3.8	3, 1.7	0.044	1, 1.2	4, 2.6	5, 5.1	0.446
Not so important <i>n</i> %	32, 17.3	44, 25.4		18, 22.2	32, 20.7	22, 22.5	
Important <i>n</i> %	106, 57.3	78, 45.1		37, 45.7	81, 52.3	53, 54.1	
Extremely important <i>n</i> %	40, 21.6	48, 27.8		25, 30.9	38, 24.5	18, 18.4	
Q124 Better characterize the relationship between sex and gender differences and pain and disability							
Not at all important <i>n</i> %	5, 3.4	2, 1.4	0.760	0, 0.00	3, 2.5	2, 2.4	0.569
Not so important <i>n</i> %	31, 21.0	33, 22.6		13, 19.1	29, 24.0	19, 22.6	
Important <i>n</i> %	83, 56.1	83, 56.9		42, 61.8	62, 51.2	51, 60.7	
Extremely important <i>n</i> %	29, 19.6	28, 19.2		13, 19.1	27, 22.3	12, 14.3	
Q92 Examine the effectiveness of novel treatments for chronic pain where there is insufficient evidence, for example, acceptance and commitment therapy, psychodynamic psychotherapy and emotion focused exposure							
Not at all important <i>n</i> %	4, 2.5	4, 2.7	0.073	2, 3.1	3, 2.2	2, 2.3	0.639
Not so important <i>n</i> %	26, 16.5	10, 6.9		6, 9.4	16, 11.9	12, 13.8	
Important <i>n</i> %	73, 46.2	77, 52.7		38, 59.4	67, 50.0	38, 43.7	
Extremely important <i>n</i> %	55, 34.8	55, 37.7		18, 28.1	48, 35.8	35, 40.2	
Q82 Explore if antidepressant and anti-epileptic 'withdrawal syndromes' are myths or reality?							
Not at all important <i>n</i> %	7, 4.6	5, 4.3	0.072	1, 2.3	5, 3.9	4, 5.1	0.257
Not so important <i>n</i> %	39, 25.7	16, 13.7		14, 31.8	20, 15.5	19, 24.4	
Important <i>n</i> %	77, 50.7	64, 54.7		22, 50.0	69, 53.5	40, 51.3	
Extremely important <i>n</i> %	29, 19.1	32, 27.4		7, 15.9	35, 27.1	15, 19.2	

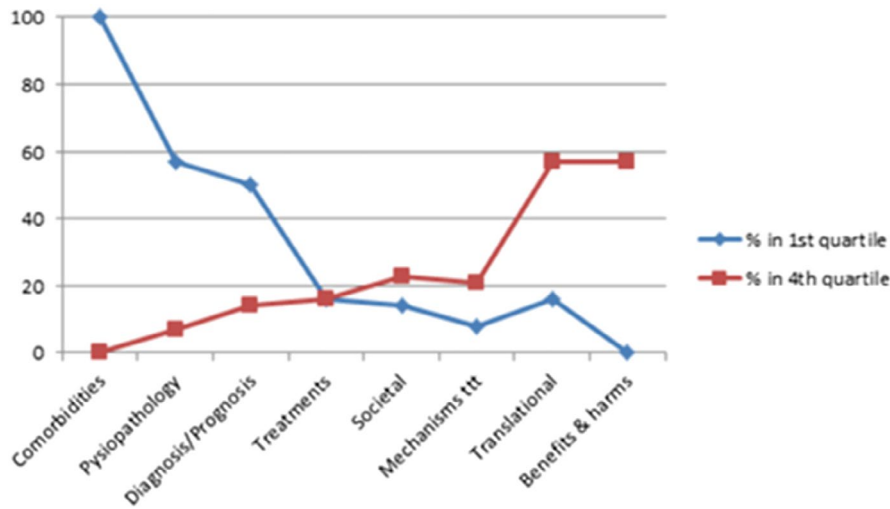
practitioners), with limited responses from allied health professionals (11% physiotherapists and 7% psychologists) which may hamper the generalization of results.

The survey was in English only. While people with a lived experience of pain were involved in the development of the Strategy (through Pain Alliance Europe) and our survey had several items put forward by patients through the James Lind Alliance literature search, they were not directly included in the survey. Therefore, results mainly reflect the priorities deemed most important by scientists and clinicians. These may differ from patient priorities.

## 5 | CONCLUSION

Better understanding pathophysiology of pain, understanding and treating comorbidities, exploring benefits/harms/costs of current therapies, developing new treatments and understanding the biopsychosocial impacts of pain emerged as the main priorities for pain research. The importance of clearly communicating the concepts of prediction, prevention, self-management and personalized pain management was also highlighted.

Careful consideration must be given to the coordinated implementation of the Pain Research Strategy for Europe



**FIGURE 8** Distribution of themes across ranking quartiles. There was a marked contrast in the presence of certain themes in the first and last ranking quartiles. Themes 1, 3 and 8, respectively on pathophysiology, new treatments and comorbidities, loaded predominantly in the top quartiles, whereas Themes 4 and 9 (Benefits/harms and translational aspects) predominated in the lowest quartiles.

developed in this study. This will provide the scientific community and funding organizations at international, European and national levels with guidance for sustained investment, fostering strategic prioritization to address the most urgent needs in pain research over the coming decade. This could be challenging given the regional differences in European countries with respect to medical, social and political emergencies, including access to resources, potential for clinical / basic research and autonomy of practice. As identified in the consensus meeting, close communication and collaboration will be needed to maximize implementation to advance research and improve the lives of those living with pain.

In the survey, research priority items were considered separately, while they are clearly inter-related in real life. Pain may be either an independent entity ('pain as a disease') or a symptom of underlying illness (Treede et al., 2019). By unravelling underlying pathophysiology, researchers can identify common pathways, risk factors and potential treatment targets. This can lead to prevention strategies using personalized medicine to optimize outcomes by ensuring that interventions are targeted and effective. Ultimately, this will improve the quality of life for those living with both chronic pain and its comorbidities, as well as reducing healthcare costs.

### AUTHOR CONTRIBUTIONS

G.P. and B.M.F. conceived the study. G.P., M.OK., L.G.L. and B.M.F. designed the methods. K.B., S.B., S.C., F.J.C., E.E., D.P.F., T.G.N., M.M., A.M., B.P. and T.R.T. commented on the methods. G.P., M.OK., B.F., E.PZ., N.S., L.G.L. and B.M.F. analysed the data. G.P., M.OK., E.PZ., L.G.L. and B.M.F. wrote the manuscript. All authors were participants in the discussion and interpretation of the results and review of the manuscript. G.P. and M.OK. contributed equally to this work. L.G.L. and B.M.F. contributed equally to this work.

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## CONFLICT OF INTEREST STATEMENT









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## DISCLAIMER

Artificial intelligence was not used in this manuscript.

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