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# Explaining persistent physical symptoms to patients in general practice: can tests to measure central sensitisation add value? A mixed-methods study

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## Abstract

**Introduction** General practitioners (GPs) often face challenges in explaining to patients with persistent physical symptoms (PPS) why their symptoms persist. Providing an explanation of the central sensitisation (CS) mechanism to patients could be helpful, yet GPs do not routinely test for signs of CS in these patients. The aim of this study was to explore the value of applying a test to assess CS in enhancing explanations provided to patients.

**Methods** In this prospective study, 25 GPs applied three tests, selected through a Delphi study, to assess CS-related symptoms: (1) the Central Sensitisation Inventory (CSI); (2) an algometer for measuring pressure pain thresholds (PPT); and (3) a monofilament for assessing temporal summation. Following the tests, both the GP and the patient completed a short questionnaire. Subsequently, GPs shared their experiences in focus groups and interviews, while a sample of patients was interviewed individually. The questionnaires were analysed quantitatively, and the focus groups and interviews were analysed qualitatively.

**Results** GPs reported that all tests were feasible to perform during consultations; testing took less than 5 min in 25% of cases and between 5 and 10 min in 60% of cases. In approximately 50% of cases, an additional consultation was required to perform the test. The results of the CSI confirmed CS-related symptoms more frequently (74%) than the algometer (46%) and the monofilament (43%). Consequently, many GPs preferred the CSI. Patients did not show a preference for any specific test; two-third found the tests valuable and approximately 50% reported that the explanation of CS was clearer when a test was used.

**Conclusions** Testing during the consultation was feasible, although an additional consultation was required in 50% of the cases. GPs preferred the CSI because its results confirmed CS-related symptoms more frequently than those from the algometer and monofilament.

**Keywords** Persistent physical symptoms, Medically unexplained symptoms, Central sensitisation, Tests, Measurement instruments, Explanation, CSI, Algometer, Monofilament

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## Strengths and limitations of this study

- This is the first study to assess the feasibility of testing for CS in general practice and its value for both GPs and patients.
- We collected both qualitative and quantitative data through questionnaires, focus groups, and interviews.
- GPs included fewer patients than we had anticipated, likely due to the impact of the COVID-19 pandemic.

## Introduction

Persistent physical symptoms (PPS) such as low back pain, headache or dizziness, and syndromes like fibromyalgia, irritable bowel syndrome and chronic fatigue syndrome, have a high prevalence in both general practice and hospital care [1–3]. PPS are physical symptoms that last for at least three months, cause distress, or interfere with daily functioning [4, 5]. A clear medical explanation for these symptoms may be lacking. However, symptoms can also persist in well-understood disorders despite adequate treatment or may not correspond to the severity of the underlying disease [6]. The societal burden of these patients – such as medical costs, disability and work absenteeism – is substantial, and their quality of life is generally low [7–11].

Patients with PPS often seek a diagnosis and recognition for extended periods, sometimes for up to two years. Understanding why their symptoms persist could help them initiate recovery earlier. Therefore, providing clear explanations may be crucial in guiding these patients [12]. GPs frequently struggle to explain to patients with PPS why symptoms persist in the absence of a specific disease or in case of an adequately treated disease [13, 14]. Explaining the central sensitisation (CS) mechanism underlying PPS may be helpful for GPs [15].

CS is defined as hyperexcitability of the central nervous system and helps explain the development and persistence of symptoms, highlighting the connection between the body and the brain [16]. An increase in receptors and neurotransmitters in the dorsal horn of the spinal cord leads to upregulation of the ascending facilitatory pathways in the central nervous system (bottom-up regulation), thereby increasing the number of signals reaching the brain. Once the brain processes these signals, descending inhibitory pain systems may become impaired (top-down regulation) [17, 18].

We found the explanation of CS to be valuable in our previous study, which focused on the experiences of GPs explaining CS to their patients with PPS [19]. Tests to measure CS may enhance the explanation, making it more convincing for both GPs and patients. Although

many tests are available, not all are suitable for use in general practice [16]. Therefore, we conducted a Delphi study to select tests that could be helpful and applicable in general practice. The panel reached a consensus on three tests that might be useful: the Central Sensitisation Inventory (CSI), an algometer to assess pressure pain thresholds and a monofilament to assess temporal summation [20].

This study examined the feasibility of applying tests to measure CS-related symptoms during GPs' consultations, assessing both the qualitative and quantitative aspects of experiences from both GPs and patients. Data on test feasibility were collected through questions about test duration and any issues encountered during performance, while experiential data from GPs and patients were gathered quantitatively through post-test questionnaires and qualitatively through focus groups and interviews. This combined approach, integrating both practical feasibility and experiential feedback, aimed to enrich the evaluation of these tests in general practice, thereby enhancing the study's overall value.

## Methods

### Study design and setting

Using a prospective design, we carried out a mixed-methods study. In this study, we evaluated with quantitative and qualitative methods how GPs and patients valued using one or more tests when explaining CS. The medical ethical committee of VUmc (METC VUmc) confirmed that the Medical Research Involving Human Subjects Act (WMO) did not apply to our study.

We conducted the study in the practices of GPs in North-Holland, the Netherlands.

GPs were provided with three CS tests: (1) the central sensitisation inventory (CSI), a questionnaire; (2) an algometer to test the pressure pain threshold; (3) a monofilament to test temporal summation.

#### 1. Central sensitisation inventory (CSI).

The CSI is a two-part self-report questionnaire [21]. Part A consists of 25 statements regarding current health symptoms, each assessed on a 5-point scale ranging from 0 to 100. Part B (which is not scored) asks whether the respondent has ever been diagnosed with one or more specific syndromes, such as fibromyalgia, chronic fatigue, or irritable bowel syndrome, and includes questions about anxiety, depression and whiplash. The CSI is designed to identify CS-related symptoms and conditions, including pain, impaired sleep, and lack of concentration and energy. It is used both as a screening tool and as a measure of treatment outcomes [22]. A cut-off point of 40 is used to differentiate between healthy controls and

patients with CS-related symptoms, and we applied this threshold in our study. This cut-off score has a sensitivity of 0.81 and specificity of 0.75 [23]. The CSI has been shown to produce reliable and valid data for quantifying the severity of various symptoms of CS [24].

## 2. Use of an algometer to assess pressure pain thresholds.

Quantitative sensory testing (QST) is commonly used to measure hyperalgesia (increased sensitivity to painful stimuli) and allodynia (the perception of pain from normally non-painful stimuli) [25]. A frequently employed method in QST is the assessment of pressure pain thresholds (PPTs) [26]. An algometer applies pressure to the body, and the test records the point at which the sensation of pressure transitions into pain, expressed in kilograms or pounds.

In our study, the algometer was applied to the forearm on the muscle belly of the extensor carpi radialis muscle, located four fingers below the lateral epicondyle of the elbow. The patient sat with the forearm supine and relaxed on a table. The algometer was placed perpendicular to the skin, with pressure increased at a rate of 0.5 kg/second. We used both digital algometers (Wagner FPX algometer) and one analogue algometer (Baseline algometer), each with a probe area of 1 cm<sup>2</sup> capable of exerting forces up to 10 kg/cm<sup>2</sup> [27]. Participants were instructed to indicate when the sensation of pressure became painful. The test was repeated three times, with a minimum interval of 30 s between applications to minimize temporal summation. The final outcome was determined as the average of the three tests.

Although PPTs in healthy controls can vary based on factors such as age (older patients generally have lower PPTs), sex (females tend to have lower PPTs), and muscle thickness (sarcopenic patients typically exhibit lower PPTs than those with greater muscle mass), we considered a PPT of  $\leq 3$  kg to be indicative of CS [25, 28, 29]. Both intra-rater and inter-rater reliability of PPTs are reported to be good to excellent, with intraclass correlation coefficients (ICCs) ranging from 0.75 to 0.99 and 0.81 to 0.90, respectively [30–32].

## 3. Use of a monofilament to assess temporal summation.

Temporal summation (TS) refers to increased perception of pain in response to repetitive noxious stimuli over time. In cases of CS, the amplification of stimuli within ascending neuronal pathways leads to the facilitation of pain and increased TS. Monofilaments, which are nylon threads of varying thickness, can be used to assess CS.

GPs already use monofilaments to assess lower extremity neuropathy in patients with diabetes. In this study we used a Semmes-Weinstein monofilament that bends into a “C” shape at 300 grams of pressure.

The procedure begins by identifying a spot on the patient's hand that has a visual analogue pain score (VAS) of 1 or 2 (on a scale of 1 to 10) while applying the monofilament. Ten stimuli of 1-second duration were applied to this spot using the monofilament, with 1-second intervals between stimuli. This procedure was repeated twice, with pauses of at least 30-seconds between applications. VAS scores were noted at both the beginning and the end of the test, and the final result was calculated as the average of these values. The patient was allowed to end the test if the pain became too intense.

In healthy controls, TS typically raises VAS values from 1 to 3 or 4, whereas in patients with CS, VAS scores increase significantly more [33–36]. A change of three or more points on the VAS scale was considered indicative of CS. While the TS protocol demonstrates high test-retest reliability across all measures, there is considerable inter-individual variation between test and retest outcomes [37–39].

## Participants

### General practitioners

We invited 30 GPs from West-Friesland in North-Holland, the Netherlands, who had previously participated in our study on explaining CS (which did not involve testing CS) [19]: 16 GPs agreed to participate. We recruited nine additional GPs who already had (some) experience with explaining CS from the professional network of researcher CdB, who is involved in the training of GP residents and has an extensive regional network. Some experience with explaining CS was required to be able to answer the central question in the focus groups: what is the added value of the tests measuring CS compared to providing only the explanation? In total, 25 GPs participated in this study.

### Patients

During consultations, GPs invited adult patients with PPS to participate in the study. We included patients who agreed to discuss their PPS symptoms with the GPs and consented to undergo one of the tests. No exclusion criteria were applied. GPs determined whether they considered the patient capable to understand the explanation, for instance, deciding whether to invite patients with linguistic challenges or low IQ to participate. When patients agreed, the GPs provided them with study information and informed consent forms. Upon deciding to participate, patients scheduled a follow-up appointment

with their GP, signed the informed consent forms, and received the explanation of CS along with one or more tests, depending on the GP's access to the testing materials.

We purposively selected 30 patients for in-depth interviews at the end of the study, of whom 17 agreed to participate. Using purposive sampling, we primarily selected patients with either high or low test scores, as well as those with conflicting opinions about the test (e.g., patients who found the test valuable but not clarifying), to enable a focused exploration of their experiences.

#### **Patient and public involvement**

Patients or the public were not actively involved in the design, conduct, reporting or dissemination plans of our research.

#### **Procedures**

After obtaining informed consent, we collected and analysed questionnaires from all participants. Focus groups and interviews were audio recorded and analysed. We collected data between December 2020 and April 2022.

CdB visited the participating GPs at their practices to provide instructions on how to administer and interpret the tests, and how to complete the informed consent forms and questionnaires. The GPs were provided with a toolbox for explaining the CS mechanism, which we had developed in a previous study. In this study, the GPs were successively provided with three different tests to measure CS, each of which they could use for 4–6 months. We considered the administration of each test to at least three patients sufficient for GPs to gain enough experience to evaluate the test, estimating that a period of 4–6 months would be an adequate timeframe for applying a test at least three times.

CdB visited most GPs three times to exchange the tests and provided instructions on their use. CdB also developed the schedule for test distribution and regularly sent emails to participants to maintain their engagement, offering additional explanatory tools, such as new metaphors and animations for patient education.

Three GPs had access to two or three tests simultaneously, allowing them to administer the tests to the same patient. GPs had the flexibility to conduct the tests before, during, or after the explanation of CS, although we did not collect data on the timing of test administration. After each test, both the GP and the patient completed a short questionnaire about the test's implementation and perceived value. These questionnaires, developed for both GPs and patients, primarily consisted of closed-ended questions (Appendix 1).

#### **Focus groups and interviews with GPs and patients**

To gather the GPs' experiences with the tests, we organized two focus groups moderated by an independent retired GP, who had both research experience and expertise in moderating focus groups. A safe and open environment was created by setting clear expectations, ensuring confidentiality, and establishing ground rules for respectful and equal participation. The moderator maintained neutrality and empathy, facilitating open dialogue and effectively managing group dynamics. We used focus groups to obtain more in-depth insights of the participants. Sharing experiences and discussion will provide more in depth insights [40].

A medical student (ZK) attended the focus groups and conducted telephone interviews with GPs who were unable to attend. Each focus group session lasted approximately 90 min.

The interview guides for both the focus groups and telephone interviews are provided in Appendix 2. We estimated that conducting two focus groups and interviews with GPs who could not attend a focus group, would be sufficient to achieve data saturation.

Further methodological details, following the COREQ checklist, are available in Appendix 3.

#### **Analysis**

We analyzed the GP and patient questionnaires using descriptive statistics in SPSS version 28 to calculate percentage-based descriptive statistics.

The audio recordings of the focus groups and interviews with the GPs and the patients were transcribed, and thematic content analysis was performed by CdB and ZK using the software MAXQDA 2020 [41, 42].

First, we familiarized ourselves with the dataset by reading and re-reading the transcripts. We then independently began coding the data, using open codes and discussing any discrepancies in our coding. Subsequently, we grouped the codes into sets which were then organized into themes. In cases where consensus could not be reached, a third researcher was available to assist. We reviewed the sets and themes to ensure they were consistent and coherent. Finally, we prepared the report and selected quotations to illustrate the identified themes.

## **Results**

#### **Applied tests for CS**

The distribution of test applications among the GPs was as follows: eight GPs employed all three available tests, six GPs applied two different tests, and seven GPs administered only one test. Notably, four GPs did

not use any tests at all. Furthermore, two GPs combined two different tests for a single patient, while one GP applied all three tests to another patient. Among the tests used, the algometer was administered in 37 instances, the monofilament in 28 instances, and the CSI in 19 instances.

The mean age of the patients was 51 years, with 75% identifying as female. Furthermore, 15 GPs participated in two focus group discussions, and telephone interviews were conducted with 10 GPs and 17 patients.

### Results GPs questionnaires

We analysed 84 questionnaires completed by the GPs. (Table 1) They mainly applied the tests to patients with moderate and severe symptoms. The GPs estimated that CS was likely in approximately two-thirds of the patients and possibly in one-third. Positive tests

results were found in 57% of cases with the algometer, 45% with the monofilament, and 63% with the CSI. In our analysis of test value as perceived by the GPs, we found they considered the test more useful when the result was positive compared to when it was negative (Appendix 4).

Additional consultations were required for 59% of the patients for the algometer test, 36% for the monofilament, and 32% for the CSI. Performance problems were rarely mentioned, except with the digital algometer, which occasionally experienced battery problems after extended periods of inactivity.

The time needed to perform the test was mostly between 5 and 10 min (60%). The test results were easy to explain. The GPs perceived the results of the algometer and monofilament to be less valuable for patients compared to those of the CSI.

**Table 1** Results of GPs questionnaires

Results GPs questionnaires	Algometer (n = 37)	Monofilament (n = 28)	CSI (n = 19)
<b>Percentage of positive tests</b>	57%	43%	63%
<b>Severity of symptoms</b>			
Mild symptoms	5%	7%	0%
Moderate symptoms	46%	32%	53%
Severe symptoms	41%	57%	42%
Unknown	8%	4%	5%
<b>Probability of CS-related symptoms</b>			
Likely	59%	64%	68%
Possibly	30%	29%	27%
Unknown	11%	7%	5%
<b>Result supported CS-related symptoms</b>	46%	43%	74%
<b>Duration test</b>			
Duration test < 5 min	35%	29%	0%
Duration test 5–10 min	43%	54%	63%
Duration test > 10 min	11%	11%	32%
Unknown	11%	6%	5%
<b>Feasibility of tests</b>			
Performance problems	19%	4%	5%
Extra consultation needed	59%	36%	32%
Result easy to explain	70%	97%	84%
<b>Value of test for GP</b>			
Result valuable for GP	49%	43%	58%
Result somewhat valuable for GP	22%	43%	11%
Result not valuable for GP	22%	11%	5%
Unknown	7%	3%	26%
<b>Value of test for patient according to GP</b>			
Test valuable for patient	38%	32%	63%
Test somewhat valuable for patient	27%	50%	5%
Test not valuable for patient	24%	14%	5%
Unknown	11%	4%	27%



### Results focus groups and interviews with GPs

We created 660 codes and 55 sets in MAXQDA from the transcripts of the focus groups and interviews with the GPs. The sets were organized into four themes. We reported the most frequently mentioned themes, sets and codes in Appendix 5.

Data saturation was sufficiently achieved in both the focus groups and interviews with GPs, as analysis revealed consistent emergence of the same themes and sets.

#### Theme 1: GPs' experiences with explaining CS and conducting tests for CS

GPs added the tests to their explanation of CS. However, combining the explanation of CS with the administration of tests was time-consuming. GPs reported that it was sometimes challenging to find time for this during busy days, with the COVID-19 pandemic further complicating scheduling. They experienced very few problems while performing the tests. A small number of GPs mentioned a lack of experience, uncertainty about test performance and interpretation, and, in the case of the digital algometer, issues such as an empty battery after extended periods of inactivity.

Two GPs indicated that, as a result of the tests, they spent less time explaining CS. Three GPs performed combinations of tests and stated that this approach added value compared to administering only one test to a patient. They reported that when two or three tests yielded positive results, the explanation became more persuasive for both the GP and the patient.

Some GPs preferred their own methods of explanation.

For certain patients, the use of metaphors, drawings and videos facilitated the understanding of CS. Overall, most patients comprehended the explanation of CS.

*GP 19: "I have always used the example of, what's it called again, of a car alarm that, ehm, goes off when the car is in danger of being stolen, but is so sensitive that for some people it will go off when a truck drives by, so to speak. That's how I always try to explain it. And well, people do seem to understand then, ehm, but I think a test like this demonstrates it very nicely, so I do see added value there."*

*GP 5: "And then you can explain that there is increased hypersensitivity. Using the model or a metaphor, whichever I prefer at that moment. And then you can make it even more concrete with a test like that and that's what I really like about these tests. Because you can explain something and they think 'OK, hypersensitivity, whatever,' but you still want to prove it to the patient."*

### Theme 2: experiences with applying the tests

#### 2.a experiences with the algometer

GPs reported both positive and negative experiences with the algometer. They appreciated the precise scale of the device, as it facilitated the explanation of hypersensitivity when a positive test result was obtained. The test was relatively easy to perform and required less than 10 min in 78% of cases. However, they expressed that they sometimes lacked experience in performance of the test and were occasionally uncertain about the reference values. They also found the pressure pain threshold (PPT) to be subjective; patients were sometimes unsure when to indicate that the feeling of pressure changed into pain.

Additionally, GPs reported occasional confusion regarding negative test results, particularly when they assumed that the patient had CS-related symptoms but the patients exhibited very high PPTs.

*GP 5: "It's not that difficult, but you need some practice to become adept at it. Because then you are able to apply more or less the same pressure every time. Instead of once in a while. So I really do need that."*

#### 2b: experiences with the monofilament

Often, GPs found the monofilament test challenging to perform. To begin the test, the GP had to identify the location on the hand where the C-shaped application of the monofilament resulted in a VAS score of approximately one, which is typically on one of the fingertips. When the fingertip was too sensitive, GPs sometimes encountered difficulties in determining the appropriate starting point on the hand and were uncertain about the amount of pressure to apply each time to achieve the C-shape with the monofilament.

While they valued the ability to measure something, they found the results less clear compared to those obtained with the algometer. Additionally, a positive result from the monofilament test helped GPs explain to patients that they had CS-related symptoms, as it indicated that they were experiencing increased pain due to temporal summation.

*GP 26: "What I noticed was that the test shows, at least to me and the patient, that things accumulate, so to speak. When you do the second and the third test, it gets painful faster and faster."*

*GP 16: "Ehm, the monofilament is little fragile and a bit, uhm, well where exactly on the fingertip do you put it?"*

## 2c: experiences with CSI

The CSI assisted GPs in initiating conversations about the symptoms associated with CS and how CS is explained. Patients reported feeling more understood as they recognized their symptoms reflected in the CSI's questions. The CSI proved beneficial in enhancing both patients' and GPs' understanding of the symptoms. However, some GPs mentioned that the CSI contained excessive wording and that the questions could be challenging for patients with low health literacy.

*GP 4: "Yes, I always feel the need to talk to people. And for that a questionnaire like this works better than a test. Well, for me anyway."*

*GP 16: "For me that's a good addition, more or less in line with my talk about sensitisation. What I really like about a questionnaire like this, ehm, uh, well, it provides deeper understanding and clarification for patients, but also for the doctor."*

## Theme 3: acceptance of CS by patients

GPs reported that some patients found it challenging to accept CS. These patients often wanted more diagnostics and proposed alternative explanations for their symptoms. While the tests sometimes facilitated acceptance of CS, there were instances where they did not.

GPs needed to believe in the explanatory model of CS to effectively convince the patients. Although some GPs questioned the model's validity, most GPs regarded CS as a useful explanation for patients with PPS.

*GP 2: "I, you can explain it, you know, with a metaphor and there are so many different metaphors. So you try to adapt to the level of the patient. What remains difficult is that many patients are not immediately open to it. Some assistance is needed there. So that's why I am really excited when, ehm, an extra test can help in that respect."*

*GP 1: "Ehm, but it did help her, because now she had an explanation for some of those symptoms. And I did say very clearly, 'We're not going to attribute everything to it, because you also have concrete things going on. So we have to be very careful. But some of your symptoms are related to this.' And she understood and she was actually also happy that she now had an explanation. That she could go home and explain to her husband why she often had these crazy pains."*

## Theme 4: effects of a positive or a negative test

A positive test result may facilitate the explanation to the patient that their symptoms are possibly related to CS. Importantly, GPs found all three tests to be more valuable when the result was positive rather than negative. They considered a positive test to be more valuable for the patient, whereas the patients' questionnaires indicated that it made no significant difference to them (Appendix 5).

When faced with a negative test result, GPs used various approaches. First, they clarified before testing that a negative test did not necessarily imply that the symptoms were unrelated to CS. Second, they emphasized that the tests were still in the research stage, which could effect the reliability of the outcomes. Third, the GPs maintained their explanation regardless of the negative test result.

However, some GPs and patients expressed confusion regarding negative test results. Some GPs adjusted their explanations, while certain patients struggled to accept that their symptoms might still be related to CS.

*GP 17: "But I could also explain it with a negative test, like well, it is research, so we are also checking whether it is useful. It could still be that you have it, and it just doesn't show up in the test, but that doesn't mean you can't still have it."*

*GP 13: "Not that I think it will make me doubt the diagnosis, but I did have a story in mind and then I couldn't explain it that way anymore. So yes, then I had to stop and think what to say instead."*

## Results of questionnaires and interviews with the patients

### Results patients questionnaires

We analysed the results of 84 questionnaires completed by patients (Table 2).

Patients reported positive test outcomes in 57% of algometer tests, 43% of monofilament tests and 63% of CSI assessments. In approximately 50% of cases, GPs required an additional consultation to perform the test. The GP incorporated the tests results in their explanations in 76% of tests involving the algometer, 89% with the monofilament, and 63% with the CSI. The majority of the patients (approximately 70%) valued the tests, and about half the patients thought the tests increased the clarity of the explanation of CS.

We examined whether these results were linked to positive or negative test outcomes. Patients' opinions about the value of the tests were not dependent on the results. However, after testing with the algometer, patients felt the explanation was clearer when the test result was positive. No such differences were found with the monofilament or CSI (Appendix 4).

**Table 2** Results of patient questionnaires

Results patients questionnaires	Algometer (n = 37)	Monofilament (n = 28)	CSI (n = 19)
<b>Result of the test</b>			
Test positive	57%	43%	63%
Test negative	43%	57%	37%
<b>Performance of the test</b>			
Extra consultation needed	57%	46%	53%
Results used in explanation by GP	76%	89%	63%
<b>Value of the test</b>			
Valuable yes	67%	75%	68%
Valuable neutral	22%	21%	21%
Valuable no	3%	4%	5%
Unknown	8%		6%
<b>Clarity of explanation</b>			
Explanation more clear	43%	64%	47%
No difference in clarity of explanation	38%	36%	42%
Explanation less clear	11%	0%	0%
Unknown	8%		11%

### Results interviews patients

Most of the patients interviewed had experienced severe symptoms over a prolonged period (Appendix 6). Seven of the seventeen interviewed patients received negative test results; however, according to the evaluation forms completed immediately after testing, all but one patient still valued the use of the test.

From the patient interview transcripts, we created 281 codes and organized them in 28 sets using MAXQDA. These sets were then grouped into three overarching themes. The most frequently mentioned themes, sets and code frequencies are provided in Appendix 7. Quotations were selected to illustrate these themes. Saturation was achieved in the 17 patient interviews, with recurrent themes and sets observed throughout.

### Theme 1: general experiences with the explanation of CS and tests

In the interviews, many patients reported having alternative explanations for their symptoms, such as attributing them to arthrosis, sarcoidosis or (poly)neuropathy. While they agreed with the GP that the symptoms could be described as PPS and related to CS, they expressed concern that the GP might conclude, without thorough investigation, that their symptoms were solely PPS.

*Patient 17302: "And they are very quick to say 'well this is what it is', you know, whereas for me it's a completely new symptom. It persists for a very long time. So to me it seems easy to say it like that, but if*

*it persists longer, I really want it to be investigated further. And you know, instead of being told again 'well it's probably that,' that is too easy. And as a patient, you experience it as very frustrating."*

Most patients understood CS and how it works; some had previously received similar explanations from other healthcare providers, such as psychologists or rehabilitation physicians. While some patients recognized the CS mechanism, and the explanation helped them feel taken seriously - especially when illustrated with drawings or metaphors - this approach was not preferred by all.

Patients emphasized the need for adequate treatment for their symptoms, noting that an explanation alone was not a solution. Many expressed interest in trajectories with psychosomatic and rehabilitation therapists.

Since the interviews took place at the end of our study, with a considerable time lapse between explanation and the test, some patients did not remember the test.

*Patient 26,102: "A better explanation about what you can do now that you have the result would help. And what might help to fight it. The videos via the link that I got from my GP helped a bit; perhaps it would also be helpful to get an explanation on a sheet of paper with a drawing."*

### Theme 2: experiences with the tests

#### 2a: experiences with the algometer

Some patients found the algometer test clear and felt it helped them better understand the mechanism of CS.



*Patient 26,102: “That I felt pain very quickly the first time, and then the 2nd and 3rd time the pain came even faster. That was eye opener for me because I didn’t expect to get the result that I got.”*

For some patients, it was challenging to determine when the pressure of the algometer became painful, and they considered the test to be subjective.

*Patient 17101: “So I think I was also pretty quick to say ‘now it’s uncomfortable’ when it might have been quite a long time before it really started to hurt. Ehm, so I felt that using only this test to explain or diagnose CS was a bit, very subjective and kind of jumping to conclusions.”*

## 2b: experiences with the monofilament

For some patients, the monofilament showed that they were more sensitive to pain.

*Patient 13,202: “The test was useful because to me it confirmed that I experience pain more quickly. Also, this test made me feel that my symptoms were taken seriously.”*

Other patients reported that they did not like the monofilament test because they did not experience any pain during the procedure.

*Patient 07202: “Well, yes it was clear to me, only I didn’t feel anything, it just felt like a tickle, so yes, then, talking about meaningful. Yes, it is valuable if it shows that I have it, then it is valuable. Yes, if you get the pain stimuli, but I didn’t have those pain stimuli at all.”*

## 2c: experiences with the CSI

In the interviews, patients reported that they valued the CSI. They found the inventory interesting and recognized the symptoms described in the questions.

*Patient 18,201: “What I experienced, was very touching, that’s why I am happy to participate. It hit the mark, this questionnaire, because it asked: ‘Do you ever experience this?’ It was all exactly spot on for how I experienced it.”*

Other patients mentioned that the test did not provide a solution for their symptoms.

*Patient 1301: “Yes, that’s what I’m saying, it was very clear and also interesting, but I thought how does this help?... It’s basically ‘just learn to live with it’ and I’ve, ehm, experienced that with my heart for years, so I, ehm, well, I just deal with it.”*

## Theme 3: acceptance of PPS and CS

Most patients accepted that they had PPS and acknowledged that they initially found this difficult to accept. They recognised a potential connection between their symptoms and CS.

*Patient 18,201: “Because it is always on your mind, and you are paying attention to it and observing it, so that really makes you hypersensitive. So I definitely believe that.”*

*Patient 07202: “Well, the story is useless for my own situation. The story itself was clear to me, only I can’t relate it to myself because I don’t recognize it.”*

## Discussion

### Summary of results

We found that the tests used to assess CS were feasible to perform during consultations. Some GPs preferred the physical tests, i.e. the algometer and the monofilament, as they provide precise, quantifiable results. Other GPs favoured the CSI because the symptom-related questions offered a useful starting point for discussing the patient’s symptoms. In 60% of cases, all three tests could be completed within 5 to 10 min. In approximately 50% of cases, an additional consultation was required to conduct the tests.

GPs considered the CSI the most valuable for the patient, as it identified CS-related symptoms more frequently than the other tests.

In the focus groups and interviews, GPs indicated that combining the explanation of CS in combination with the test results increased their confidence in consultations with patients with PPS. The tests facilitated discussions about PPS and the role of CS as a possible explanation for PPS, and GPs reported that patients were more likely to accept CS as a potential explanation for their symptoms. As a result, further diagnostic examinations were often deemed unnecessary.

Some GPs found it challenging to explain CS to patients who received negative test results, while others anticipated this issue by contextualizing the test results beforehand.

Patients did not express a clear preference for any particular test. Two-thirds of patients found the tests valuable, while around one third did not. Approximately half of the patients found the tests clarifying. In the interviews, some patients reported understanding the explanation but did not find it applicable to their situation. Although they appreciated that the GP took their concerns seriously through the explanation of CS, they remained concerned that the GP might prematurely conclude that their

symptoms were due to PPS. It was essential for patients to discuss with their GP strategies to improve their symptoms and functioning. Moreover, patients expressed disappointment that the explanation and tests did not lead to symptom improvement.

### Comparison with existing literature

To the best of our knowledge, this is the first study to explore the added value of applying tests to assess CS in general practice. We found no literature on GPs explaining CS to patients with PPS in combination with the use of tests.

Previous studies on providing explanations to patients with PPS have shown that GPs often lack the skills to effectively apply the current explanation models [43]. These models were typically communicated as possibilities and in a patient-specific way, and they were not very detailed [13]. Lundberg et al. identified four key domains of coping strategies used by GPs managing patients with PPS: (1) adopting the biopsychosocial model; (2) employing strategies to enhance communication; (3) coping with the organizational environment; (4) using strategies to cope emotionally [44].

In our study, the GPs applied the explanation of CS within the biopsychosocial model, exploring all dimensions of the patient's symptoms. Although they remained concerned about the possibility of overlooking somatic disease, they initiated conversations with patients about their symptoms and combined the explanation with one of the provided tests.

We used reference values for the algometer and monofilament from the Quantitative Sensory Testing (QST) protocol of the German Research Network on Neuropathic pain [25]. These reference values were found to be region- and age dependent, while PPTs were generally independent of gender. Geber et al. reported good test-retest and interobserver reliability for these tests when performed by trained examiners [45]. In 2022, Rankin et al. conducted a systematic review and found a high degree of variability across studies, concluding that CS was poorly defined [46].

The reference values of the German Research Network on Neuropathic pain needed to be validated for use in primary care. Den Bandt et al. assessed the value of different quantitative sensory tests in primary care, including the algometer to assess PPT and the monofilament to assess temporal summation. Their systematic review found that PPT measurements on remote parts of the body were significantly lower in people with nonspecific low back pain compared to healthy controls [47]. Their RCT in a primary care population with chronic low back pain demonstrated a significant difference in PPTs

between the CS and no-CS groups. However, the results for temporal summation were more variable [48].

In our study we observed higher rates of negative tests than expected based on the specificity and sensitivity reported in the literature for the algometer and monofilament. Although the GP assumed that CS would be present in their patients, more than expected tests appeared to be negative. Several factors may explain this. First, many GPs performed only a small number of tests, which limited their ability to apply the tests correctly. Research indicates that the tests can be reliably conducted by well-trained examiners. Second, some GPs were discouraged by negative test results and chose not to continue using the tests. Others, however, continued to use the tests and still explained CS even in cases of negative results. These GPs reported that they believed the negative results were due to improper test administration, the fact that the tests were still being applied in a research setting, or that the results were false negatives. Furthermore, the GPs were provided exclusively with the CS explanatory model, without access to alternative explanatory frameworks. Literature indicates that other phenomena, such as immune system dysfunction, autonomic system dysregulation, or somatosensory amplification, are also associated with PPS. In our study, GPs considered CS likely in 59–68% of cases and possible in 27–30% of cases. GPs might have overestimated the CS prevalence, and this might explain why so many tests were negative.

The researcher had explained the tests to each GP, and written instructions were provided; however, a well-prepared instructional video might have been helpful.

The CSI most frequently supported the presence of CS (74%). The CSI consists of 25 questions related to CS-related symptoms. Since it does not assess CS directly, some concerns remain regarding its construct validity [49, 50].

### Strengths and limitations

A strength of this study is that it is the first to provide GPs with tests to measure CS in the consultation room. Both GPs and patients completed questionnaires immediately after the testing. In focus groups and interviews, GPs shared and discussed their overall experiences in a supportive and safe atmosphere. Patients were interviewed by telephone rather than through focus groups, as the latter could have hindered open discussion due to the nature of their symptoms. We selected the patients for the interviews through purposive sampling; this yielded deeper insight into their experiences.

We estimated that every GP could perform approximately ten tests over the 1.5 years study period, and our sample of 25 GPs should have been sufficient to gather adequate data. However, fewer tests were conducted

than anticipated, which limited the GPs' experience and may have influenced their judgment. We conducted the research between December 2020 and March 2022, so this was likely due to the COVID-19 pandemic, which resulted in a shortage of time and fewer consultations with patients with PPS. Furthermore, only 8 GPs completed all three tests and 6 GPs completed two. Moreover, some GPs reported a lack of experience or negative experiences with the tests. On the other hand GPs noted that they appreciated the idea of a physical test with clear, objective results, as this was more valuable and informative for certain patients compared to verbal explanations alone. Finally, other GPs considered particularly the questions of the CSI valuable for initiating discussions with patients.

We encouraged general practitioners to include patients with mild to moderate symptoms. In practice, however, a significant number of patients with severe symptoms were included (46%). This may be because such patients are often the first to come to mind for many GPs when considering patients with PPS, and because these patients are likely to visit the practice more frequently. According to the interviewed patients, they already possessed extensive experience in diagnosis and treatment, and they were often also familiar with the concept of central sensitization. The inclusion of patients exhibiting severe symptoms may have introduced limitations to the study, as it is well-established that such individuals typically require more intensive, multidisciplinary treatment, and are consequently more challenging to manage within general practice settings.

After the tests, 80% of the patients reported a positive view of their value. However, during the interviews, many patients expressed negative opinions about the tests and the explanation. This contradiction might be attributed to our selection of patients with either extreme results or contradictory opinions. Some patients understood the mechanism of CS, but did not believe their symptoms were related to CS. In contrast, other patients strongly recognized their symptoms in the questions of the CSI and felt better understood. The considerable time gap between the tests and the interviews may have also influenced the results.

Only 17 of the 30 selected patients participated in the interviews. Selection bias may have occurred, as patients with more severe symptoms may have been more likely to participate. These patients may have had more time available due to being unable to work (full time) or engage in their hobbies. As a result, the interviews may not adequately represent the entire research population. Nevertheless, the interviews provided

deeper insight into patients with very high, low or contradictory results.

### Implications for practice and research

(Physical) Tests to assess CS are feasible in general practice, although the GP needed an extra consultation in half of the cases, but this was also due to the procedures with the informed consent forms.

The majority of GPs, approximately 70–80%, regarded the tests as (somewhat) valuable for both themselves and their patients. Approximately 70% of patients perceived the tests as (somewhat) valuable, while around 20% remained neutral in their assessment. Clarity in the explanation of results improved for about 50% of patients, whereas approximately 40% reported no significant change. Further analysis, considering whether test results were positive or negative, revealed that GPs placed greater value on positive results. Conversely, patients' perceived value of the test did not appear to be significantly influenced by the outcome. Future research should investigate methods to enhance the clarity of these tests.

The questions in the CSI may be a good starting point for a conversation about the symptoms. Finally, as patients stressed in their interviews, it is essential to provide the patient with the proper treatment to improve their symptoms after the explanation.

Future research must establish whether a combination of tests is better than one test at a time.

Future research should also establish whether GPs will consider the tests more valuable if they become more experienced in applying them. In our study, many patients had negative test results with the algometer and monofilament. It is unclear whether this has to do with test characteristics, the lack of experience in application of the test by the GP or the absence of CS.

### Conclusion

We conducted a mixed-methods study to determine whether the use of tests to assess CS provides added value compared to solely offering patients with PPS an explanation of CS from a GP. GPs found the tests feasible to perform during consultations; although approximately 50% of the patients had to return for the testing. Among the tests, GPs considered the CSI to be the most valuable for patients, as its results provided stronger support for the CS hypothesis compared to the algometer and the monofilament tests. While two-third of the patients found the tests valuable and approximately 50% clarifying, those interviewed expressed more critical views.

## Appendix 1

### Questionnaires GPs and patients

#### GP Questionnaire (please circle the correct answer)

- The most important symptoms of this patient were (more answers possible)  
 Musculoskeletal symptoms:    yes                      no  
 Fatigue:                                      yes                      no  
 Bowel symptoms:                      yes                      no  
 Other symptoms, namely:
- The symptoms of this patient with persistent physical symptoms were:  
 mild                      moderate                      severe
- I thought that the symptoms of this patient could be related to CS:  
 yes                      possibly                      no
- With this patient I used:                      algometer                      monofilament                      CSI
- The test lasted:                      0-5 minutes                      5-10 minutes                      10 minutes or longer
- The test was executed by:  
 GP/resident                      mental health nurse practitioner                      GP's assistant
- Were there any problems organizing the application of the test?    yes                      no  
 If yes, what were the problems?
- The patient had to come an extra time to do the test:    yes                      no
- The result of the test supported the suspicion of CS:    yes                      no
- The results were easy to explain to the patient:                      yes                      no
- I considered the result of the test a valuable addition to my explanation:  
 yes                      somewhat                      no
- I considered the test a valuable addition to my explanation for the patient:  
 yes                      somewhat                      no  
 Would you like to explain further or add to your answers?

#### Patient questionnaire

- At this moment, what are your most important symptoms? (maximum three)
- Which test was performed on you? (please circle the correct answer)  
 test with a pressure meter                      test with a thick thread                      questionnaire (CSI)
- Did you have to come to the practice an extra time for this test?                      yes                      no
- Did you find it valuable to do this test?    yes                      neutral                      no
- Did your GP use the results of the test in the explanation of your symptoms?    yes                      no
- What did the test add to the explanation for you?  
 It was more clear                      no difference                      it was less clear
- Would you like to further explain or add anything to your answers?

## Appendix 2

### Topic list focus groups and interviews GPs and interviews patients

#### *Topic list for the focus groups and interviews with the GPs*

Central question: what is the added value of the tests measuring CS compared to providing only the explanation?

How does the explanation with CS in patients with PPS work for you so far? What goes well? What do you find challenging? How do patients react?

Is the explanation more convincing for the GP and the patient if the test indicates sensitisation? Does it change the explanation for the GP? Does it add value to be sure that it is CS to explain it?

If the test does not indicate CS, then what? Do you explain CS, or do you go to a different explanatory model? Is this confusing for you or the patient?

Are there any differences between the three tests you have tried? Which one was most doable? Which one was most convincing? Have you also combined tests?

Would you recommend using these tests in general practice? Is there any particular test you would recommend or advise against? Or would you recommend a combination of tests? If so, which combination?

#### *Topic list interviews patients*

Can you tell us what your top three symptoms are?

What explanation do you have for your symptoms?

Was the explanation of the general practitioner about the cause of your symptoms clear? Did you understand what central sensitisation is?

What do you remember about the test your GP performed on you?

Did you find the test valuable?

Did the test make the explanation clearer?

What else could help you with the explanation of your symptoms? Think of videos, drawings or metaphors.

## Appendix 3

### Methodology focus groups and interviews according to the COREQ checklist

#### *Domain 1: research team and reflexivity*

##### Personal characteristics

The focus groups were moderated by an independent moderator, JB, who is a medical doctor and retired general practitioner, he is not an author of the article. The interviews were conducted by ZK, a medical student who is an author. JB is male, and ZK is female. JB has moderated more focus groups, including those in our previous research, and has conducted research in the past. ZK did not have prior experience with interviews.

##### Relationship with participants

There was no pre-existing relationship between the participants and the moderator or the student before obtaining informed consent. The participants were aware that the moderator was interested in the research topic and that he was a retired GP from another region. They also knew that the medical student was conducting the research phase of her medical education. No special characteristics were reported regarding the moderator and the student.

#### *Domain 2: study design*

##### Theoretical framework

The theoretical framework employed was content analysis, as mentioned in the method section under the paragraph on analysis.

##### Participant selection

Purposive sampling was used for the interviews with the patients, as described in the method section under the paragraph on participants. All participating GPs were invited to the focus groups. In cases where they were unable to attend the focus groups, we conducted telephone interviews with them. Patients were approached via email or telephone and the GPs via e-mail. In total, 25 GPs participated in the study, with 15 attending the focus groups and 10 being interviewed by telephone. 80 patients participated, we invited 30 patients for interviews, and 17 participated while 13 declined. We did not ask the patients who refused why.

##### Setting

The focus groups were conducted in a health center in the region of Hoorn. Interviews with GPs and patients were conducted via telephone. Non-participants were not present. The participating GPs were from the region North-Holland, with many of them serving as GP trainers affiliated with the GP training at Amsterdam UMC. The patients were sourced from the practices of these GPs and thus belonged to the same region. They had visited their GPs for a consultation related to PPS and were invited to participate in the study. The majority (75%) of participants were female, and the mean age was 51 years.

##### Data collection

The interview guide was provided by the authors CdB, HvdW, AB, BT and HvdH, and was not pilot tested. We did not conduct repeat interviews. All focus groups and interviews by telephone were recorded. No field notes were taken as all interactions were recorded.

The focus groups lasted for 90 minutes, while the interviews with GPs ranged from 10 to 20 minutes, and interviews with patients from 10 to 30 minutes. Regarding the interviews with patients, data saturation was discussed, and it was determined that saturation had been reached.



Transcripts were not returned to participants for comment or correction.

### Domain 3: analysis and findings

#### Data analysis

Two data coders, CdB and ZK, coded the data. No description of the coding tree is provided. Themes were derived from the data in an inductive manner. We used MAXQDA 2020 software for analysis. Participants did not provide feedback on the findings.

#### Reporting

Participants quotations are presented in the paper to illustrate the findings. Each quotation is identified with a participant number. All findings were derived from the data and were consistent, supported with quotations. Major themes are clearly described in the results section. Minor themes were not described due to word limit constraints in the article; however, they are listed in the appendices.

## Appendix 4

**Table 3** Value of test in relation to result test

Value of test in relation to result of test	Test positive			Test negative		
	yes	neutral	no	yes	neutral	no
<b>Algometer</b>						
Test valuable for GP	14	5	1	3	5	5
Test valuable for patient according to GP	11	4	4	3	6	4
Test valuable for patient	13	4	0	11	4	1
Clarity of explanation for patient*	10	6	5	4	9	2
<b>Monofilament</b>						
Test valuable for GP	8	3	0	4	9	3
Test valuable for patient according to GP	7	4	0	2	11	4
Test valuable for patient	10	1	0	11	5	0
Clarity of explanation for patient*	8	3	0	9	8	0
<b>CSI</b>						
Test valuable for GP	8	1	0	3	1	1
Test valuable for patient according to GP	8	1	0	4	0	1
Test valuable for patient	7	3	1	6	1	0
Clarity of explanation for patient*	6	4	0	3	4	0

\* Clarity explanation for patient: yes=clearer, neutral = no difference, no=less clear

## Appendix 5

**Table 4** Themes and sets from focus groups and interviews with GPs

Themes and sets GPs	Frequency codes
<b>Theme 1: GPs' experiences with explanation of CS and tests for CS</b>	
Remarks about GPs' explanation of the symptoms in general	30
Explanation of CS is challenging/time consuming	22
Explanation of CS is valuable for GP	18
GP experiences applying tests as challenging due to time and performance	16
GP does not use explanatory model CS, but own explanation for symptoms	15
Visualization and metaphors help patient to understand CS	7
Performing a combination of tests in one patient adds value	5
<b>Theme 2: Experiences with applying the tests</b>	
<b>2a. Experiences with the algometer</b>	
Algometer is valuable for the patient	31
GP has negative experience with algometer due to time and performance	27
Algometer is valuable for the GP	27
Test result of algometer is negative, not specific/sensitive enough	22
GP recommends implementing algometer in practice	14
Patient has negative experience with algometer	7
Test result of algometer is positive, valid	5
<b>2b: Experiences with monofilament</b>	
Monofilament is valuable for patient	25
GP has negative experience with monofilament due to time and performance	25
Test result of monofilament is negative, not specific/sensitive enough	24
Monofilament is valuable for GP	13
Patient has negative experience with monofilament	7
<b>2c: Experiences with CSI</b>	
CSI is valuable for patient	37
GP has negative experience with CSI due to time and performance	27
CSI is valuable for GP	25
Test result of CSI is negative, not specific/sensitive enough	16
Patient has negative experience with CSI	13
Test result of CSI is positive, valid	13
GP recommends implementing CSI in practice	7
<b>Theme 3: Acceptance of CS by patients</b>	
Patient accepts CS	16
Patient does not accept CS	16
GP has to believe in CS to convince patient	10

Themes and sets GPs	Frequency codes
<b>Theme 4: Effects of a positive or negative test</b>	
Negative test result does not confuse patient (introduction is important)	22
Negative test result confuses patient	15
Tests are in research phase	14
Negative test result confuses GP	12
Negative test result does not change explanation for GP	9
Positive test result is valuable for GP	9
Negative test result changes explanation for GP	8
Negative test result does not confuse GP	8
Test helps to motivate patient for adequate treatment	8

## Appendix 6

**Table 5** Patient characteristics purposive sampling interviews

Patient	Result test	GP values test	Patient values test	Test elucidates explanation CS for patient	Acceptance CS patient	Severity symptoms
07202	Negative	No	Neutral	Yes	No	Severe
17,201	Negative	No	Yes	Yes	Yes	Severe
15,203	Negative	Some-what	Yes	No difference	No	Severe, since 5 months
17,302	Positive	Yes	Yes	No difference	Partly	Severe, since 15 years
20,101	Positive	No	Neutral	No difference	Yes	Severe
15,201	Positive	Yes	Yes	Yes	No	Severe, since 40 years
01301	Negative	No	Yes	Yes	Yes	Severe, since + 1 year
01202	Positive	Some-what	Yes	No difference	Unclear	Mild
17,101	Positive	Yes	Yes	No difference	Yes	Severe, since 1 year
18,201	Negative	Yes	Yes	Yes	Yes	Severe, since 6 years
07201	Negative	Some-what	Yes	No difference	Yes	Severe, since 3 years
02101	Positive	Yes	Yes	Yes	Yes	Moderate, since childhood
14,102	Positive	Yes	Yes	Yes	Yes	Severe, since years
26,101	Positive	Yes	Yes	Yes	Yes	Severe
13,202	Positive	Yes	Yes	Yes	Yes	Severe, since 15 years
06201	Positive	Some-what	Yes	Yes	Partly	Moderate, since 5 years
14,101	Negative	No	Yes	No difference	Yes	Severe, since 8 years

## Appendix 7

**Table 6** Themes and sets from interviews with patients

Themes and sets patients	Frequency codes
<b>Theme 1: general experiences with explanation of CS and tests for CS</b>	
Patient has other explanation for symptoms than CS	54
Visualisation elucidates explanation CS for patient	15
Test has no additional value for patient	15
Explanation CS clear to patient	14
Test clarifies explanation CS for patient	11
Patient does not desire videos, drawings, or metaphors for explanation CS	7
Patient remembers little or nothing about explanation CS	6
Patient wants more coaching or a follow-up programme	6
Patient does not feel heard or taken seriously	6
Test does not clarify explanation CS for patient	6
Patient wants a solution for the symptoms	4
Patient does not have an explanation for symptoms	3
<b>Theme 2: experiences with tests</b>	
<b>2a: Experiences with algometer</b>	
Patient has negative experience with algometer	6
Test result of algometer is negative, not specific/sensitive enough	4
Patient remembers little or nothing about algometer	3
Patient has positive experience with algometer	3
Test result of algometer is positive, valid	1
<b>2b: Experiences with monofilament</b>	
Test result of monofilament is negative, not specific/sensitive enough	12
Patient has negative experience with monofilament	11
Patient has positive experience with monofilament	3
Test result of monofilament is positive, valid	1
<b>2c: Experiences with CSI</b>	
Patient has positive experience with CSI	4
Patient has negative experience with CSI	3
Patient remembers little or nothing about CSI	1
<b>Theme 3: Acceptance of PPS and CS</b>	
Patient accepts PPS (partly)	20
Patient does not accept CS	16
Patient wants more diagnostics	4
Patient accepts CS (partly)	3
Patient does not accept PPS	3

## Abbreviations

CS central sensitisation  
GP general practitioner  
PPS persistent physical symptoms

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not applicable.

## Authors' contributions

CdB is a GP and was a PhD student, now she has a PhD; she is the primary researcher of this project and the principal author and guarantor of this publication. ZK, a medical student, participated in the focus groups and interviews with the GPs and the patients and participated in the analysis and writing of the results and discussion section. BT, JvW, AB and HvH are members of the research group of CdB and have been contributing to the research from the start. BT, JvW, AB and HvH made substantial contributions to the design of the work, the analysis, and drafted and revised the work; they approved the submitted version and have agreed to be personally accountable for their contributions; they ensured that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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Our report adheres to Consolidated Criteria for Reporting Qualitative Research (COREQ) guidelines.

## Data availability

the datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

The study was carried out in accordance with the Declaration of Helsinki, written informed consent was obtained from all participants, and the Institutional Research Board of Amsterdam Public Health research institute approved our study (23-3-2018; WC2017-088). The Medical Ethics Review Committee of VU University Medical Center confirmed that the Medical Research Involving Human Subjects Act (WMO) did not apply to this study and that an official approval of this study by our committee was not required.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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