



# Identification of Patient Needs and Preferences in Pigmented Villonodular Synovitis (PVNS) Using a Qualitative Online Bulletin Board Study

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## ABSTRACT

**Introduction:** Pigmented villonodular synovitis (PVNS), also known as giant-cell tumour of the tendon sheath (GCTT), is a rare, benign proliferative tumour affecting the inner lining of synovial joints and tendon sheets. Information on treatment needs of PVNS patients to inform drug development is currently scarce. We conducted an exploratory qualitative study with PVNS patients to generate insights into the objective and emotional aspects related to their medical journey and experiences of living with this disease.

**Methods:** A 4-day study using an online bulletin board (OBB), an asynchronous, online qualitative research platform, was conducted with patients recruited via physician referral

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who underwent screening questions to ensure eligibility for the study and willingness to participate. The discussion was moderated, was structured and allowed open answers in response to other participants' posts.

**Results:** Eleven patients (4 from the USA, 4 from the UK and 3 from Canada; 45% female), aged 28–57 years, suffering from PVNS for 2–27 years participated in the study. Key patient insights from the study were: (1) pain was the topmost, spontaneous thought that the participants associated with PVNS, constituting a significant emotional and psychological burden; (2) surgery (arthroscopy) did not completely ameliorate symptoms associated with PVNS, as the relapse rate was high in these patients; (3) PVNS has a substantial negative financial impact on patients, their families and the healthcare system; (4) orthopaedic specialists/surgeons predominantly managed PVNS, as surgery is currently the only therapeutic option.

**Conclusion:** PVNS patients expressed an urgent need for a medical drug treatment, which can reduce pain, avoid relapses and provide an alternative to surgery, the current standard of care.

**Keywords:** GCTT; Giant-cell tumour of the tendon sheath; Online bulletin board; Patient-based evidence; Patient perspective; Pigmented villonodular synovitis; PVNS; Qualitative research; Rare disease; Rheumatology

## Key Summary Points

### Why carry out this study?

Pigmented villonodular synovitis (PVNS), also known as GCTT (giant-cell tumour of the tendon sheath), is a rare, benign proliferative tumour affecting the inner lining of synovial joints and tendon sheaths.

PVNS has no approved treatment. In most cases, surgery is the only option to remove the tumour. Other options, such as radiation therapy, targeted therapy with tyrosine kinase inhibitors and total joint arthroplasty are being investigated.

Study hypothesis was to understand the PVNS patient's emotional status and their medical journey; we conducted this exploratory qualitative research using online bulletin boards (OBBs).

### What was learned from the study?

PVNS patients expressed an urgent need for a medical drug treatment, which can reduce pain, avoid relapses and provide an alternative to surgery, the current standard of care.

In patients with PVNS, pain imposes a greater emotional and psychological burden than what was expected based on previous literature on this disease.

Surgery, the current standard of care, is reported by patients to be associated with extremely high relapse rates and does not completely eliminate PVNS; thus, patients hope for an alternative, potentially a medical drug treatment, which can reduce pain and prevent relapses.

## INTRODUCTION

Pigmented villonodular synovitis (PVNS) is a rare (prevalence: 9.2 patients/million population), benign proliferative tumour affecting the inner lining of synovial joints and tendon sheaths, usually in the knees [1–3]. PVNS is characterised by an aggressive clinical behaviour, with progressive destruction of the affected joints [4]. PVNS occurs in two forms, the localised (involving the tendons that support the joint or occurring in just one area of the joint) and diffuse (more widespread and involving an entire joint) form [5, 6]. PVNS may present with a long course of disease associated with multiple interventions, leading to loss of joint function, secondary osteoarthritis and treatment complications [7]. Currently, there is no approved medical drug treatment for PVNS; in most cases, surgery to remove the mass within or around the damaged joint is the only option. In cases of recurrent disease, other options, such as radiation therapy [8, 9], targeted therapy with tyrosine kinase inhibitors [10] or total joint arthroplasty (e.g., knee replacement) [11], are under investigation.

Patients with PVNS experience symptoms due to insidious progression of pain, swelling and stiffness in the affected joint, and it may be many months before the patient consults a doctor. Clinical features generally include swelling, with or without discomfort and mechanical derangement, such as stiffness, instability and locking [7, 12]. Whilst information on the aetiology, histopathology, pathophysiology, presentation, diagnosis, management of disease and its negative impact on patients' quality of life is available, information pertaining to the overall disease burden, detailed symptomology, patients' needs and preferences in terms of treatment/s and associated outcomes is scarce. There have been a few attempts to develop patient-reported outcome (PRO) tools in tenosynovial giant cell tumour (TGCT) [13–17]. Improved understanding of patients' experiences and unmet needs in PVNS is important for incorporating their perspectives in the development of informed, responsive PRO measures to help characterise the response

to a new drug treatment, with endpoints that matter to the patients.

Conventionally, in-depth qualitative interviews or face-to-face focus group discussions and quality of life studies have been used to gain insights into patients' perspectives, needs and experiences [13–21]. In this digital era, it is possible to engage patients virtually to understand and learn from their experiences of living with a disease [22]. This virtual interaction can be particularly important for diseases with low incidence and prevalence as these technologies can bridge geographic constraints. With the advances in web technology, online focus group discussions using conference calling, chat rooms or other online means are gaining popularity [21]. A recently released draft guidance from the Food and Drug Administration (FDA) on Patient-Focused Drug Development suggests the use of online means for qualitative research to enable participation of patients by overcoming challenges pertaining to location, disease/condition or level of impairment [23–25]. Online bulletin boards (OBBs) provide an ideal opportunity to seek information, advice and opinions from individuals experiencing the same health problems and can serve as an important source of health-related information [20, 26]. A number of studies have shown the utility of online focus group technique and asynchronous platforms (e.g., community discussion boards) to study various diseases and health-related issues in different disease conditions [27–29]; however, we had not previously used this approach with a rare disease patient population. Hence, we conducted a qualitative study using an OBB methodology to understand how PVNS patients perceive their disease and what the unmet needs or expectations are that could inform the development and design of a future drug treatment.

## METHODS

Before conducting the OBB study, we performed a literature review to understand the current level of knowledge about PVNS in published literature. Questions for the OBB study were formulated thereafter.

## Recruitment

The OBB study was conducted for 4 consecutive days in October 2015 across the US, UK and Canada. Patients suffering from non-metastatic localised or diffuse PVNS were recruited via physician referral. Recruited patients were invited to participate on an opt-in basis and received an honorarium at fair market value for their participation.

## Ethics and Compliance

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was conducted within the British Healthcare Business Intelligence Association/The Association of the British Pharmaceutical Industry (BHBIA/ABPI) guidelines following the code of conduct of the Market Research Society and EphMRA. Ethics Committee review was not required for this online patient survey research. Informed consent was obtained electronically from all individual participants included in the study. Participants' rights and privacy were protected at all times throughout the study. Participants were granted the right to withdraw from the study at any time during the study conduct and to withhold information as they saw fit. All information/data that could identify respondents to third parties was kept strictly confidential; all respondents remained anonymous by using nicknames for the study.

## Procedures

Participants were requested to log in at least twice a day for 30 min each, for 4 consecutive days. Participants were required to use self-chosen nicknames to maintain anonymity of discussion, which was structured by a trained moderator. The moderator posted questions pertaining to each day's theme on the OBB for participants to respond to. Participants were encouraged to comment on each other's posts and exchange experiences and perspectives. At the end of the 4th day, all participants were

invited to a 1.5-h follow-up telephonic discussion to address any remaining questions and to provide feedback on the OBB.

## Questions

The questions asked on each day are presented in supplementary additional file 1. The type of questions asked included mandatory questions, masked questions, open-ended questions, close-ended questions and polls. Additionally, participants were invited to upload images illustrating their feelings on the disease. Overall, during the 4 days of the OBB, the study investigators sought to:

1. Understand the disease burden of PVNS on the patient's daily living, finances and employment.
2. Understand the patient's psychological and emotional attitude towards PVNS.
3. Identify the medical journey and disease management approaches that a typical patient with PVNS goes through.
4. Solicit guidance on the optimal expected treatment outcome for short- and long-term disease management.
5. Evaluate current unmet needs, expectations, acceptable risk and value drivers of upcoming treatments.

Participants were asked their preference of drug treatment over surgery, assuming three possible outcome scenarios (Scenario 1: cure; Scenario 2: replaces surgery; Scenario 3: delays surgery by 1–2 years). Lastly, to understand patients' willingness to accept side effects as a 'trade-off' for a treatment, patients were asked to score a hypothetical side effect profile on a scale of 1–10 (1 being 'not willing to accept under any circumstances' and 10 being 'willing to fully accept') against a potential medical drug treatment. For the potential medical drug treatment, the patients were to select one of the following two scenarios: Scenario 1, 'high level of efficacy' (i.e., the medical treatment would fully cure PVNS; 100% reduction in tumour size) and Scenario 2, the medical treatment would provide 80% reduction in tumour size.

## Qualitative Analysis of Patient Responses

A combination of different qualitative analytical tools (content analysis, grounded analysis and discourse analysis) was used to analyse patients' responses [30, 31]. For themes or questions that were pre-defined, content analysis was performed to assess emerging patterns. Patient inputs obtained were coded and analysed in detail. Responses that could not fit into the pre-defined themes were analysed using grounded analysis, which helped in identifying areas for further exploration. Lastly, discourse analysis was conducted to comprehensively understand the context of patient responses and what the stated information actually meant to them; in this regard, the OBB approach provided an opportunity to follow up with either the individual participants or the group as a whole. All responses were consolidated and reported under the respective theme of each day's discussion: (1) patient knowledge and perception; (2) patient insights regarding PVNS diagnosis and management; (3) patient-reported information on PVNS symptoms, comorbidities and their impact on patient life; (4) key unmet needs and value drivers of upcoming treatments.

## RESULTS

### Participant Characteristics

The demographic characteristics of the participants were collected during the screening process and then supplemented by the spontaneous posts they made in the OBB forum (Table 1). Eleven patients (4 each from the US and UK and 3 from Canada) aged 28–57 years with localised or diffuse PVNS participated in the study. In almost all the patients (10/11), the disease predominantly affected the knees, either just the knees or knees along with other locations. At the time of recruitment, seven patients had previously undergone arthroscopic surgery and/or synovectomy, three patients were scheduled for surgery, and one patient was putting off undergoing surgery. Three of the

**Table 1** Demographic characteristics of study participants

Characteristics	Patients (N = 11)
Age (years), mean (range)	41 (28–57)
Time since diagnosis of PVNS, mean (range)	8 (2–27)
Gender, n (%)	
Female	5 (45)
Country, n (%)	
US	4 (36)
UK	4 (36)
Canada	3 (27)
Type of PVNS, n (%)	
Localised	5 (45)
Diffuse	5 (45)
Both	1 (9)
Location of PVNS, n (%)	
Knee <sup>a</sup>	8 (73)
Hip	1 (9)
Multiple locations <sup>b</sup>	2 (18)
Surgery, n (%)	
Yes <sup>c</sup>	7 (64)
No	1 (9)
Scheduled	3 (27)

PVNS pigmented villonodular synovitis

<sup>a</sup>One patient with both the knees affected

<sup>b</sup>One patient with lower body, knee, hip and ankle affected; one patient with both knees and hips affected

<sup>c</sup>Of these, three patients had multiple surgeries (total 7 surgeries), and in five patients, PVNS relapsed after 5 to 6 months, whereas the other two told there is a chance that it will relapse

seven patients had undergone surgery for their PVNS on more than one occasion.

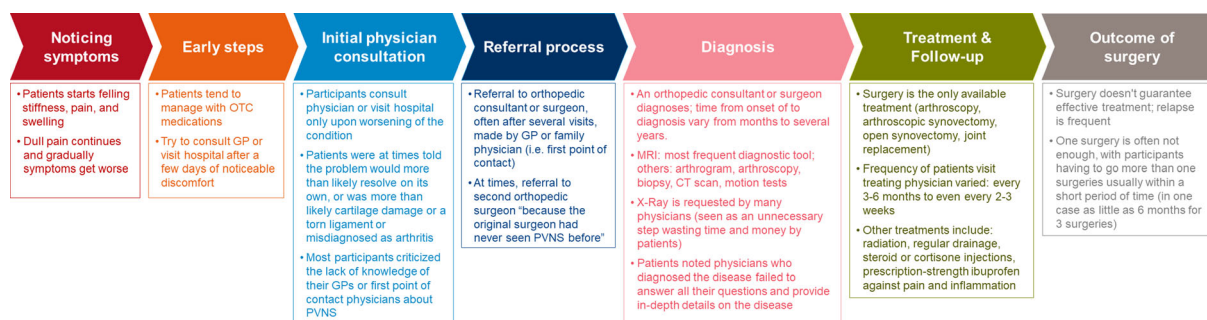
### Patient Journey

Most (9 out of 11) of the participants revealed that they were unaware of the disease prior to

diagnosis. Patients experienced symptoms such as dull pain during physical activities (jogging/doing sports) and swelling of the involved joint as early signs of PVNS, which worsened gradually. Patients tended to manage these early symptoms with over-the-counter (OTC) medications, such as ibuprofen or other painkillers; however, they felt that the usage of these medications masks the pain and resulted in the deterioration of the condition over time. As the disease and symptoms progress, patients tend to consult their general practitioner (GP) or visit a hospital after a few days of noticeable discomfort. The patients were then referred to a specialist, mostly after several GP visits, typically to an orthopaedic consultant or surgeon experienced in PVNS who would then take over the management of the patient. In some cases, the orthopaedic surgeon referred the patient to another specialist orthopaedic surgeon because of their lack of experience in treating PVNS patients. In one case, the GP referred the patient to a rheumatologist (Fig. 1).

Initially, PVNS was either misdiagnosed as osteoarthritis, rheumatoid arthritis or ‘just some fatty grizzle’ or a definitive diagnosis was not reached even after x-ray imaging. An orthopaedic consultant or surgeon usually made the final confirmatory diagnosis and took over the treatment of the disease. Apparently, magnetic resonance imaging (MRI) was the most preferred diagnostic tool for PVNS recommended by the physicians although arthrograph, arthroscopy, biopsy, computed tomography (CT) scan and a range of motion tests were also utilised. Prior to MRI, physicians sent patients to get an x-ray, which the patients felt was unnecessary and described as ‘wastage of time and money’ (presumably because they had to go through MRI afterwards anyway). Patients reported that the time from onset of disease to diagnosis was from 12 months to several years.

Only two of the total 11 participants stated that their GP had some prior knowledge of PVNS, with most rating the knowledge of their GPs about PVNS as ‘poor’. However, following referral, 8 participants thought their treating orthopaedic specialists were very knowledgeable and two quite knowledgeable. Patients noted that physicians with moderate



**Fig. 1** Patient journey. *CT* computed tomography, *GP* general physician, *MRI* magnetic resonance imaging, *OTC* over the counter, *PVNS* pigmented villonodular synovitis

knowledge about PVNS and with limited experience of actual treatment referred them to specialists who were more experienced. Post-diagnosis, internet/online searches and websites such as Wikipedia, WebMD (US patient) and/or MayoClinic (US patient) were the main source(s) of information for the patients. Patients highlighted that 'PVNS in pants', a closed Facebook community, which enabled mutual interactions regarding each other's experiences with other patients with PVNS, was extremely useful. Patients expressed the need for medical news and updates at one centralised location where non-Facebook users could access information. The frequency of follow-up visits to the physician managing their disease varied greatly and ranged from every 2–3 weeks to every 3–6 months.

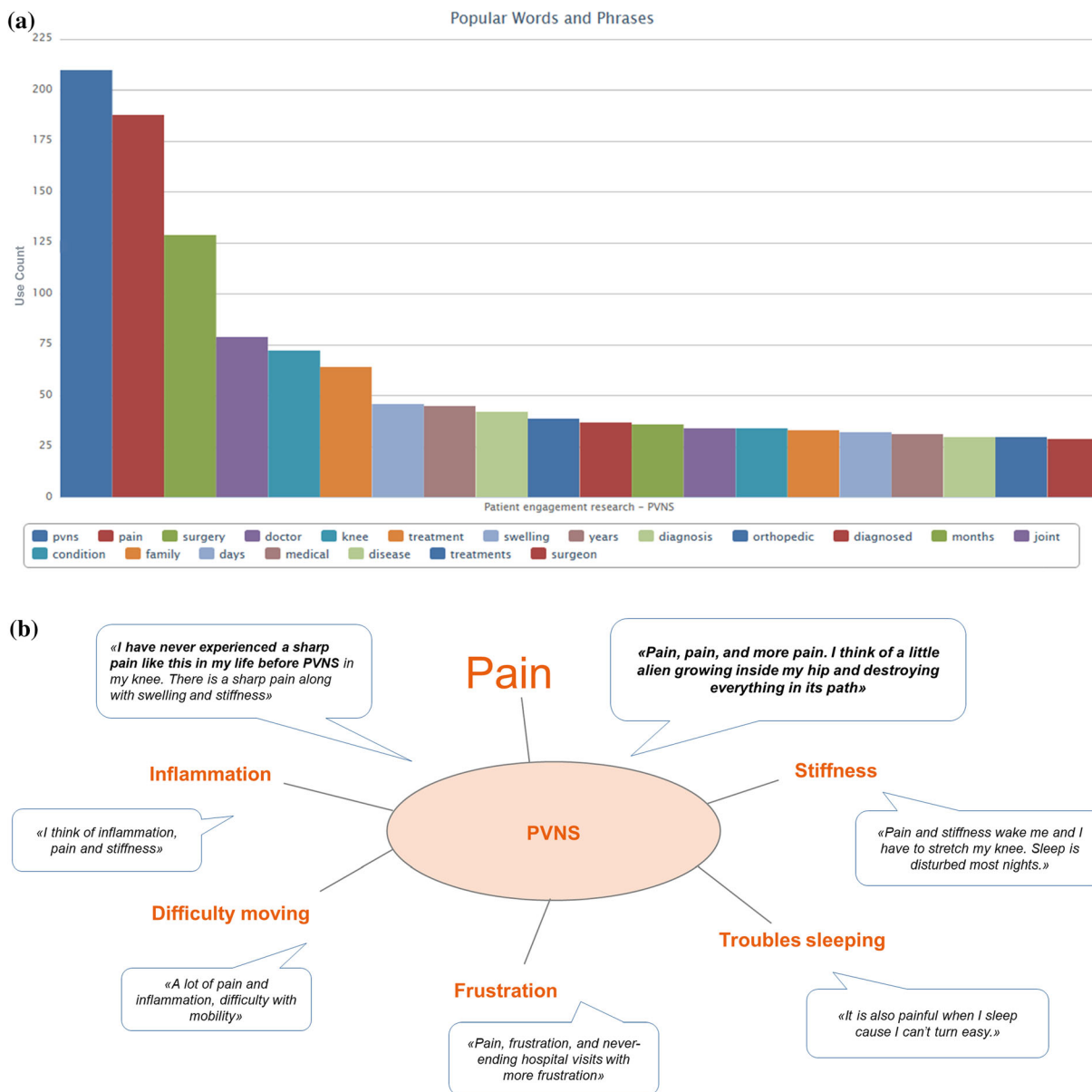
### Living with the Disease and Impact on Patients' Life

PVNS patients reported symptoms such as pain, stiffness, inflammation, difficulty in moving, frustration and disturbed sleep (Fig. 2a, b). Pain was the topmost, spontaneous thought that the participants associated with PVNS. Patients compared the severity of pain associated with PVNS with that of migraine or toothache, but more persistent and acute attacks. Patients reported that pain levels varied with joint swelling and weather conditions.

Patients reported that PVNS was affecting all their activities and making them feel older before their time. Patients expressed concerns that PVNS had changed their lives for the worse

and reported that the disease had a 'significant impact' on their physical, emotional and social well-being. When physicians measure the impact of PVNS on patient's life they usually focus on physical functioning (e.g., 'lifting, carrying groceries', 'walking several flights of stairs' and 'walking more than a mile'). Patients felt that besides physical implications, mental (e.g., feeling nervous, hopeless and worthless) and social functioning (e.g., impact of PVNS on social activities with family and friends) were also critical and very relevant. Patients felt that physical limitations carry the biggest impact as these influence the other areas. The common concerns with physical activities reported by patients included difficulties in climbing stairs, taking a bath/shower, going to the bathroom, taking dogs for walks, playing with their children and driving. The most common negative emotions expressed by patients were pain, frustration, fear, sadness and depression. Patients reported that they were no longer able to participate in family activities, sports and/or social activities because of pain and limited mobility (Table 2).

Pain and stiffness associated with the disease had a tremendous effect on patients' sleep. All participants mentioned they could not sleep through the night because of PVNS, and to get some rest, they had to rely on pain medication, muscle relaxants and/or sleeping pills on a regular basis. Lack of sleep translated into fatigue and reduced activity and productivity during the day.



**Fig. 2** Frequently mentioned words and phrases (a) and symptoms (b) described by the patients in OBB. OBB online bulletin board, PVNS pigmented villonodular synovitis

### Financial Consequences

The discussion revealed that PVNS had a significant impact on financials for the patients and their families (Fig. 3).

Of the total 11 participants, 5 mentioned that they had to change their jobs because of their disease condition and one had to re-structure his small business. All patients

mentioned that it was difficult for them to sustain 8 h of work and they required breaks more often, which shortened their workdays. The biggest issue, in their view, was the loss of wages due to changing jobs, working shorter hours and having to take time off work. For four participants, even their partner also had to take time off to drive them to appointments; therefore, the loss of earnings doubled. Due to limits

on deductibles, surgeries had to be spaced out to avoid exceeding the annual allowance (for patients from the USA). Two participants were facing insurance issues, especially those who were working as consultants or were self-employed (USA):

‘...the bills are pouring in. I’m up to \$2500 in 3 months—and that doesn’t even include the monthly premiums. Any future test/surgeries will have to be delayed until I get better insurance because I just can’t afford it’.

Participants mentioned co-payments for prescription medicine and 100% out-of-pocket expenses for OTC medications (for US and UK patients). Additional costs included medical equipment, hospital parking, gas and other associated expenses. One participant mentioned having to spend \$500 out of pocket for physiotherapy equipment, which was not fully covered by the insurance.

### Treatment, Outcomes and Unmet Needs

It was apparent that the treatment goals were similar for all the participants. Patients defined their treatment goals following their physician’s recommendations as pain relief, being able to live a normal life following the reduction of symptoms and being free of inflammation and swelling. Patients mentioned that they continued physical therapy to keep their body in shape and from deteriorating further. Most of the patients (8 out of 11) expressed that they were willing to accept joint replacement to reach their goal and to be able to live a normal life.

Patients mentioned that ibuprofen or OTC anti-inflammatories were the preferred treatment option by the GPs. Upon referral to orthopaedic surgeons, surgery was the only available treatment option offered to all the participants: arthroscopy or arthroscopic synovectomy or joint replacement (depending on the severity of the condition).

Seven of 11 patients had undergone surgery. Of these, three patients had undergone more than one surgery—a total of seven surgeries; five of these seven surgeries did not treat PVNS completely (recurrence occurred within 5–6 months). Those who had already gone through surgery experienced disappointment. Those who had not yet undergone surgery have curbed their expectations as they were told by their treating doctor that there is no guarantee of success. Pain, the long and winding path to diagnosis and the high relapse rate of surgery as well as knowing there is no guarantee of surgery success are massive burdens among both patient groups, leading to homogeneous views across the sample. Some patients also received additional radiation treatment, regular joint drainage and steroid or cortisone injections (which were perceived by patients as not efficacious).

All participants reported the lack of drug treatment and missing having an alternative option to surgery as major unmet needs. In terms of outcomes, participants wanted better pain management so that they could live a more regular life, could exercise, have social contacts and do things they love.

### Desired Properties of a Future Treatment for PVNS

Assuming three possible outcome scenarios, all participants hoped for a drug treatment to replace surgery or to prevent repeat surgeries (Table 3). The desired properties of such a drug treatment included pain relief, anti-inflammatory activity to reduce the swelling and stiffness and prevention of further joint damage. In addition, affordability and availability of the treatment to all were also important considerations.

Patients seemed skeptical as to whether a treatment providing a full cure was a realistic possibility. In a trade-off exercise, they were willing to accept side effects, as long as these side effects do not have a significant impact on



**Table 2** Impact of PVNS on patients' life (patient quotes)**Pain**

'Like feeling sore the next day after a workout—being stiff and hardly able to move. The only difference being that pain can hit other areas of the body really sharp and unpredictable. It can be severe and go on for a long period of time'  
 'Like my hip is being ripped out of the socket'

**Emotions**

'I have begged the docs to cut my leg off to just get it over and done with. But they refuse to do that'  
 'A lot of worrying and depression. I sometimes feel very low and isolated not being able to do activities that I love to do and lost friendships because I'm slowing people down and they don't have the patience for my condition'  
 'Fear about the future and increasing depression. I used to be very active in sports and this condition has made me a spectator'  
 'I sometimes worry about the future and when it will stop me doing my job. The main emotion I suppose is fear'  
 'I wanted to become a nursery nurse but I had to give it up a year after passing [my 3-year education] because I could no longer interact with the children as most of it was done sitting on the floor. Getting up and down, kneeling, crouching is a complete no-no'  
 'Sometimes the frustration makes me break down in tears. I hate being limited—I feel like I'm missing out on so much right now'  
 'I am sad by the decreased freedom of movement and mobility. Moreover, it has limited my social interaction and business travel. I spend more time in the office these days and less time seeing clients and try to avoid social activities that require movement or confined seating like in movies or sporting events'  
 'Frustration, sadness, panic, fear and the fear where I'm going to end up with this thing that seems to sometimes completely take over your whole life. I also think all the time about amputation because I'm convinced it's the only way to be free of the pain and the emotions this thing brings'  
 'I miss evening walks with my wife, bike riding with my kids and going to visit clients at their place of business'  
 'It doesn't affect my daily life—it CONTROLS it'

**Sleep and work**

'It is difficult to sustain sleep. I find I can't go more than a couple hours before I'm awakened by the sharp pains in my knees and feet. It's quite distressing and causes me to feel drowsy and fatigued throughout the day'

**Caregiver situation and fear of loss of independence in the future**

'It worries me a lot that I will lose my independence and have to depend on someone else for my needs'  
 'Down the road it will be tough on us financially if my wife had to quit [her job] to care for me but now she does double work since I am not helpful at home like I used to be'  
 'I ask my family to find a medical home that will take care of me'  
 'I depend on my husband for a lot of things. He takes days off to get me to appointments as it is half of hour of travel by car. He sometimes has to help me get into the bath as we have a shower bath and it is too high for me to get in and out. And he has to take more responsibility where our children are concerned when they go on walks and energetic activities. I do worry I will have to become more dependent on him for things and financially, keep taking time off when I've had my operations because we have three young children and it puts me out of action for weeks'  
 'I worry about the future as I live alone. At the moment I am independent. I pray I will not become a burden'  
 'My wife has been a great help to me and I have been depending on her through my condition. At home she does the lions' share of the chores. I do think about it often how dependent I might become in the future and how this will affect our financial situation if she has to cut back on her hours'

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*PVNS* pigmented villonodular synovitis

their quality of life (i.e., frequent headaches, nausea and severe diarrhoea) (Table 4).

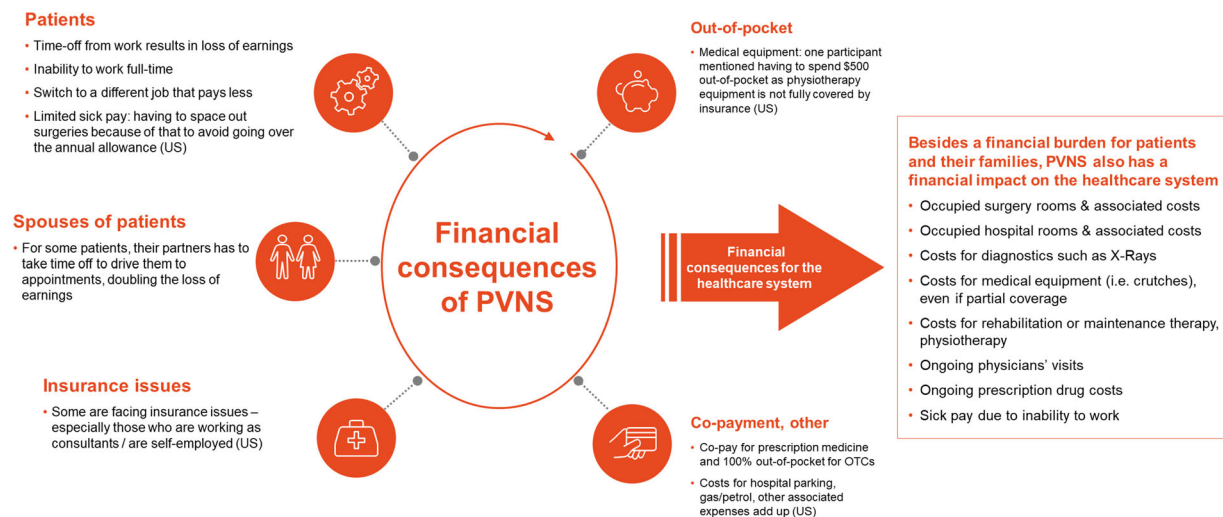
## DISCUSSION

In the changing paradigm of patient-centric drug development, patient insights are not only considered valuable at and after product launch but also rightly considered essential in the early development phase [32–34]. Engaging patients early on in the drug development process and fully understanding their perspectives on the disease and their needs, preferences and expectations related to future management strategies are critical in the early drug development lifecycle to improve the likelihood that new drugs and services better meet their needs and eventually help them lead a better life [32]. It is now acknowledged that patient research can inspire product design and development across the lifecycle. An early-on engagement of patients ensures a clear understanding of the current patient journey as well as patients' needs and beliefs, which is crucial to ensure patient-centric product development [32, 35].

In this study, we used a qualitative OBB methodology to generate patient insights into disease perception, management and unmet needs associated with PVNS [27–29]. In our

study, all the participants unanimously expressed that pain was a significant factor for emotional and psychological burden. It was also acknowledged that pain affected mobility and all activities of daily life, sleep and daytime performance because of fatigue. Some patients reported increased pain post-surgery and being pain-free was a big value driver for patients. Although studies have reported pain as a prominent symptom of PVNS, the slowness of its development, variation in its intensity and duration and its non-specificity impose additional challenges in the diagnosis [36–38]. In light of this, the patient insight from our study that pain is the topmost spontaneous thought associated with PVNS highlights the need for further research on this subject and warrants consideration in clinical management.

Another important finding that our study highlights is regarding surgery. All participating patients' main complaint was pain, whether they already went through surgery or not, as the surgical procedures did not resolve the issue and the pain usually recurred. All the participants in our study desired an approved drug treatment to replace or delay surgery, as they associated surgery with short-term relief without complete remission (relapse after approximately 6 months could potentially lead to joint destruction, necessitating joint replacement).



**Fig. 3** Economic burden: financial consequences of PVNS for patients, their families and healthcare system. *OTC* over the counter, *PVNS* pigmented villonodular synovitis

**Table 3** Patient preferences of drug treatment over surgery

Scenario 1 (Cure)	This is what patients have been awaiting for a long time. All patients hoped for such a treatment because they can avoid surgery and the effect would be permanent
Scenario 2 (Drug treatment ‘replaces’ surgery)	Patients felt that a drug treatment is always preferred over surgery as anything could go wrong during surgery and surgery does not get rid of PVNS fully
Scenario 3 (Drug treatment delays surgery by 1–2 years)	Even this scenario was interesting to patients, as long as symptoms are controlled for that year. They felt that much can change in a year with the way technology and research is advancing, and it might bridge them over until something more effective and permanent becomes available

*PVNS* pigmented villonodular synovitis

Our finding regarding the requirement of a repeat surgery due to high relapse rates is consistent with previous studies that have reported high relapse rates after surgery in PVNS [37, 39–41]. Based on the responses of our study participants, patient experiences post-surgery clearly illustrated disappointment with the results of the procedure. All but one participant in our study reported that surgery made a ‘bad situation worse’, with temporary improvement in range of motion for some and not for others.

Findings from our study also showed that PVNS has a significant negative financial impact on patients, their families, as well as the healthcare system. The topmost financial consequence for patients was the inability to work full time (taking time off or switching to a different job that paid less) because of PVNS, which caused a significant loss of earnings. Their spouses having to take time off work was an additional contributing factor to patients’ economic burden, while for the healthcare system, it was repeat costs for surgeries and hospital stays as well as other medical expenses. We believe that although our findings are based on a small qualitative research study, such information is nevertheless important because PVNS is a benign condition and payers will be interested in understanding the economic advantages in addition to the clinical benefit and improved quality of life associated with a medical drug treatment.

Differential diagnosis of PVNS versus arthritis remains challenging [38, 42, 43]. The

findings from our study highlighted the delay in diagnosis and, sometimes, misdiagnosis of PVNS. Importantly, the participants in our study attributed this delay and/or misdiagnosis, at least in part, to a lack of disease awareness among GPs. A correct diagnosis by the first physician that the patient consults would presumably prevent the chain of referrals and allow the patient faster access to appropriate care. Therefore, better education for physicians about PVNS is noted as an important need. Unless and until PVNS has caused damage to the surrounding cartilage or bone, x-ray examination is considered to add little to no diagnostic value [43]. Thus, a radiograph would only be beneficial in the diagnosis path to rule out other conditions, and MRI testing should be considered earlier for quicker diagnosis. In addition, patients should be referred to an orthopaedic specialist earlier on or upon diagnosis for immediate management to potentially limit disease progression and prevent further damage. Patients expressed that they would appreciate receiving timely information on new therapies in development and more in-depth information on the disease and of local or online support groups. These findings highlight that educational materials and awareness programs on PVNS would be beneficial not only for patients and caregivers, but also for the treating physicians. It is important to note that orthopaedic specialists or surgeons are typically the physicians treating PVNS patients, and not rheumatologists. While the rheumatologists are

**Table 4** Willingness to accept side effects as a ‘trade-off’

Hypothetical side effects	Mean rating out of 10	
	Scenario 1: Medical drug treatment with a ‘high level of efficacy’ (cure)	Scenario 2: Medical drug treatment that would achieve an 80% decrease in tumour size (replace surgery)
Headache for a with a short duration	7.7	7.6
Change of hair colour	6.9	7.1
Fatigue	6.3	7.1
Mild diarrhoea	5.9	6.6
Itchy rash	5.3	5.4
Swelling around the eyes	4.5	4.7
Nausea	4.2	4.7
Frequent headaches (with longer duration)	3.6	5.7
Diarrhoea that is ongoing for several days	2.9	3.8

Patients were asked to score hypothetical side effects they would be willing to accept as a ‘trade-off’ for a medical drug treatment that would have a ‘high level of efficacy’ (scenario 1) or a medical drug treatment that would achieve an 80% decrease in tumour size (scenario 2). 10 = ‘I am willing to fully accept this side effect’, 1 = ‘I’m not willing to accept this under any circumstances’  
*PVNS* pigmented villonodular synovitis

typically well informed about the biology and clinical aspects of *PVNS*, they are often restricted to performing non-surgical interventions. Thus, further research may be required to understand the patient journey in more detail and recognise the acceptability of future management strategies and new therapies for

treating *PVNS* by these speciality medical practitioners.

Obtaining patient insights through conventional methods, such as focus group discussion or via telephone interviews, can be a challenge in a rare disease like *PVNS*. It is well known that the rarity of *PVNS* virtually precludes the use of randomised controlled trials to evaluate the efficacy of therapeutic interventions and only observational studies are feasible [44]. Qualitative research methods have often been considered complementary to quantitative methods and prudent use of such approaches may help develop a broader understanding of clinical realities [45]. We demonstrated that the OBB, being an asynchronous, moderated, closed online community platform, offers an optimal means to uncover patient insights for qualitative patient research, with both more common and rare disease patient populations [27–29, 46].

Nevertheless, a few inherent study limitations deserve mention. The OBB involves small sample sizes and the findings might not be a true representation of the larger population. That said, qualitative research studies with small sample sizes to derive patient experiences are a scientifically valid methodology to gain patient insights around a specific research topic [47, 48]. In fact, we have noted a size of 8–12 participants as being optimal for conducting an OBB study—allowing the participants to fully engage and feel comfortable interacting and sharing with each other. Thus, owing to the rarity of the disease and the absence of available and relevant information on the impact of *PVNS* on patient lives, the insights generated from the present study can be considered a first step towards better understanding of patient needs and expectations for a new medical drug treatment that will form the basis to conduct further research. Additionally, because of the anonymous nature of the study design, socio-demographic and background data were limited to those reported by the patients during the screening process and then offered spontaneously in the chat board. Needless to say, the anonymity leads to more open-minded, honest responses, which is important for such a sensitive topic, an important factor particularly for

people experiencing a stigma due to their disease.

## CONCLUSIONS

In conclusion, in patients with PVNS, pain imposes a greater emotional and psychological burden than what was expected based on previous literature on this disease. We identified the need for physicians (particularly GPs) to be more familiar with PVNS to facilitate the diagnosis and care management strategies. Orthopaedic specialists/surgeons are the physicians mainly managing PVNS, and not rheumatologists, as was suspected prior to this research. Surgery, the current standard of care, is reported by patients to be associated with extremely high relapse rates and does not completely eliminate PVNS; thus, patients hope for an alternative, potentially a medical drug treatment, that can reduce pain and prevent relapses. Lastly, the unique insights into PVNS patients' perspectives and their views on the disease and its impact on their daily life generated from this study, particularly about future treatment attributes, can feed into early drug development for this rare disease indication as well as inform stakeholder discussions.

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**Compliance with Ethics Guidelines.** All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was conducted within the BHBI/ABPI guidelines following the code of conduct of the Market Research Society and EphMRA. Ethics Committee review was not required for this online patient survey research. Informed consent was obtained electronically from all individual participants included in the study. Participants' rights and privacy were protected at all times throughout the study. Participants were granted the right to withdraw from the study at any time during the study conduct and to withhold information as they saw fit. All information/data that could identify respondents to third parties was kept strictly confidential; all respondents remained anonymous as their answers were reported in aggregate with the answers of all other participants.

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

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