


The pandemic's effect on a patient cohort with painful polyneuropathy in 2020

A longitudinal study on pain, mood, and everyday life

Dilara Kersebaum, MD^{a,b,*} , Manon Sendel, MD^a, Sophie-Charlotte Fabig, MD^a, Juliane Sachau, MD^a, Josephine Lassen, MD^a, Stefanie Rehm, MD^a, Julia Forstenpointner, MD^a, Johanna Rügenapp, MD^a, Jan Vollert, MD^a, Philipp Hüllemann, MD^a, Ralf Baron, MD^a, Janne Gierthmühlen, MD^c

Abstract

In the early phase of the COVID pandemic 2020, we demonstrated how patients with painful polyneuropathy, against our expectations, did not experience a deterioration of their neuropathic pain. We hypothesized that our assessed measures, that is, pain intensity and characteristics, emotional wellbeing, and everyday life, would deteriorate in the further course of the pandemic according to the phases of disaster management. Thus, the aim of our study was to investigate patients repeatedly under varying pandemic conditions from March until December 2020. Sixty-three patients were investigated with validated questionnaires (brief pain inventory [BPI], neuropathic pain symptom inventory [NPSI], pain catastrophizing scale [PCS], patient-reported outcomes measurement information system [PROMIS] pain interference/sleep disturbance/fatigue/ depression/anxiety, EuroQol 5 dimensions 5 level version [EQ-5D-5L]) and a pandemic-specific, self-designed questionnaire. The data from the beginning of the pandemic with severe restrictions, during summer with loosened regulations and from December 2020 with reinstated, severe restrictions were compared with an observational design. Patients reported higher pain severity when restrictions were lower. Sleep, mood, and quality of life did not change in the course of the pandemic in the validated measures. Pain interference significantly decreased during the study independent from restrictions. Patients who reported medical disadvantages had a lower quality of life upon EuroQol 5 dimension (EQ-5D) and were significantly more worried about their health. The perception of pain intensity was dependent on pandemic severity. Sleep, mood, and quality of life did not change significantly in validated measures. Continued medical care seems decisive to prevent worsening of pain and quality of life.

Abbreviations: BPI = brief pain inventory, COVID-19 = coronavirus disease 2019, EQ-5D = EuroQol 5 dimension, PCS = pain catastrophizing scale, PROMIS = patient-reported outcomes measurement information system.

Keywords: COVID-19; neuropathic pain; chronic pain; questionnaires; emotional wellbeing; quality of life

1. Introduction

Since the onset of the severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) pandemic in early 2020, crucial aspects of the coronavirus disease 2019 (COVID-19) (e.g., transmission, pathogenesis and its management) have been examined in an unprecedented global research effort. Probably the most dramatic advance was the development of

promising vaccine candidates in record time.^[1,2] Among the multitude of pandemic- and quarantine-associated aspects that are being investigated and discussed, the psychological and social impacts are major. For instance, an increase of suicide rates, anxiety, anger, depression and substance abuse have been expected^[3-6] and shown^[7-10] to occur. A group of patients relevantly influenced by psychological and social difficulties and thus prone to be negatively affected by the pandemic are

DK and MS contributed equally to this work.

This study was supported by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Supplemental Digital Content is available for this article.

^a Division of Neurological Pain Research and Therapy, Department of Neurology, University Hospital of Schleswig-Holstein, Campus Kiel, Germany, ^b Imland Clinic Rendsburg, Department of Psychiatry, Psychotherapy and Psychosomatics, Rendsburg, Germany, ^c Interdisciplinary Pain and Palliative Care Division, Department of Anesthesiology and Intensive Care Medicine, Campus Kiel, Germany.

* Correspondence: Dilara Kersebaum, Division of Neurological Pain Research and Therapy, Department of Neurology, Universitätsklinikum Schleswig-Holstein,

Campus Kiel, Arnold-Heller-Straße 3, Haus D, Kiel 24105, Germany (e-mail: dilara.kersebaum@uksh.de).

Copyright © 2022 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Kersebaum D, Sendel M, Fabig S-C, Sachau J, Lassen J, Rehm S, Forstenpointner J, Rügenapp J, Vollert J, Hüllemann P, Baron R, Gierthmühlen J. The pandemic's effect on a patient cohort with painful polyneuropathy in 2020: A longitudinal study on pain, mood, and everyday life. *Medicine* 2022;101:50(e32054).

Received: 23 September 2022 / Received in final form: 4 November 2022 / Accepted: 7 November 2022

<http://dx.doi.org/10.1097/MD.00000000000032054>

those with chronic pain.^[11,12] Apart from the pandemic's negative psychological impact, chronic pain patients may experience another amplifier of their disease burden because the management of COVID-19 requires a high-priority use of resources (e.g. medical staff) and leads to the postponement of elective procedures. As a result, the health care of chronic pain patients might be impaired.^[13] Consequently, there has been a call to investigate the pandemic's effects on patients with chronic pain and fathom possibilities to ensure their medical care.^[11,14,15]

In a previously published study, we investigated the early influence of COVID-19 pandemic-associated restrictions and social isolation on pain, mood and everyday life in patients with painful polyneuropathy.^[16] Contrary to our initial hypothesis that the experienced pain would deteriorate due to impaired emotional wellbeing and medical care, pain intensities on average remained stable or even improved at the beginning of COVID-19 pandemic-associated restrictions. We were able to show a shift of attention from the patients' chronic pain condition towards the imminent threat of the pandemic. We thus assumed that our cohort, experiencing a life-threatening pandemic with drastic effects on everyday life, was in the so-called "heroic" phase of disaster response characterized by provisional adjustment. This would imply that the following weeks/months would entail disillusionment, resentment, uncertainty and possibly an aggravation of the experienced pain. Thus, the aim of this follow-up study was to investigate the same patient sample regarding the effects of the ongoing pandemic regulations on pain, mood and everyday life with a special focus on their possible association with loosened/stricter regulations during the course of the pandemic and throughout the year 2020.

2. Materials and Methods

2.1. Study design

Patient characteristics and recruitment have been well-described in the predecessor study^[16] which examined the effect of the first lockdown in 2020. For that analysis, patients with confirmed painful polyneuropathy who had been well-characterized clinically and with questionnaires for a former study had been contacted and informed via telephone. If willing to participate, they had received the questionnaires postally with a stamped addressed envelope for the return. For this current study, we decided to conduct follow-investigations on the very same patients throughout the year 2020. For the assessment of the longitudinal data, every patient has been contacted via telephone yet again, informed about the new objective and asked whether they wished to further participate. In case of consent, they received the questionnaires as described above. While the first paper focused on the impact of the lockdown and only included those 43 in the statistical analysis who had no relevant change of their overall health status prior to the onset of the pandemic, the current paper examines the longitudinal data of the entire cohort ($n = 63$, Fig. 1). Starting from April 3rd (i.e., 2 weeks after the pandemic-associated regulations of the German government started in March 2020), the questionnaires have been sent repetitively under varying pandemic conditions until December 2020. The exact regulations for each assessment can be found in Appendix 1, Supplemental Digital Content, <http://links.lww.com/MD/I16> (see document), an overview in Figure 2.

All patients gave their written informed consent for the participation in the study, which has been performed according to the Declaration of Helsinki. The study has been approved by the local ethics committee (AZ D453/20) and registered at the German Clinical Trials Register (DRKS00021254) which is also accessible through the World Health Organization (WHO) International Clinical Trials Registry Platform. Study

discontinuation was possible at each point in time without giving a reason. The data is available upon reasonable request.

2.2. Questionnaires

The follow-up investigations have been conducted with the same validated questionnaires that have been used and introduced in detail in our initial report.^[16]

2.2.1. Assessment of pain.

2.2.1.1. Pain intensity and characteristics. As reported in our predecessor study,^[16] the brief pain inventory (BPI)^[17] has been used to assess pain presence, frequency, current analgesic medication, and pain relief. The common interpretation of the BPI pain severity subscale to mild (1–3), moderate (4–6), and severe pain (7–10) that has been implemented and explained in the predecessor study, has been used in the current analysis as well. The severity of neuropathic pain has been assessed through the Neuropathic Pain Symptom Inventory (NPSI).^[18]

2.2.1.2. Pain interference. The Patient Reported Outcomes Measurement Information System (PROMIS) short form v1.0 – Pain Interference 6a has been used for the assessment of consequences of pain on life's relevant aspects.^[19]

2.2.2. Assessment of emotional well-being and sleep. Sleep disturbance, fatigue, anxiety and depression have been assessed through "Patient Reported Outcomes Measurement Information System"-questionnaires (PROMIS short form v1.0 Sleep Disturbance 6a,^[20] PROMIS short form v1.0 – Fatigue 4a,^[21] PROMIS short form v1.0 – Anxiety 6a^[22] and finally PROMIS short form v1.0 – Depression 6a^[22]).

2.2.3. Assessment of personality characteristics.

2.2.3.1. Pain catastrophizing. Pain catastrophizing traits were examined through the pain catastrophizing scale (PCS).^[23]

2.2.4. Assessment of quality of life. Quality of life was measured with the EuroQol 5 dimensions 5 level version (EQ-5D-5L).^[24]

2.2.5. Assessment of COVID-19 pandemic-associated changes of daily living. The patients have been asked to

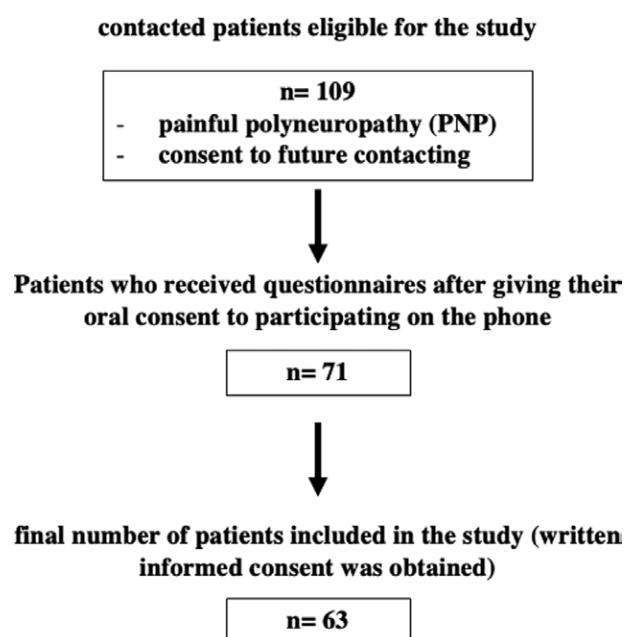


Figure 1. Patient recruitment. For more details, please view Figure 1 of Kersebaum et al^[16].

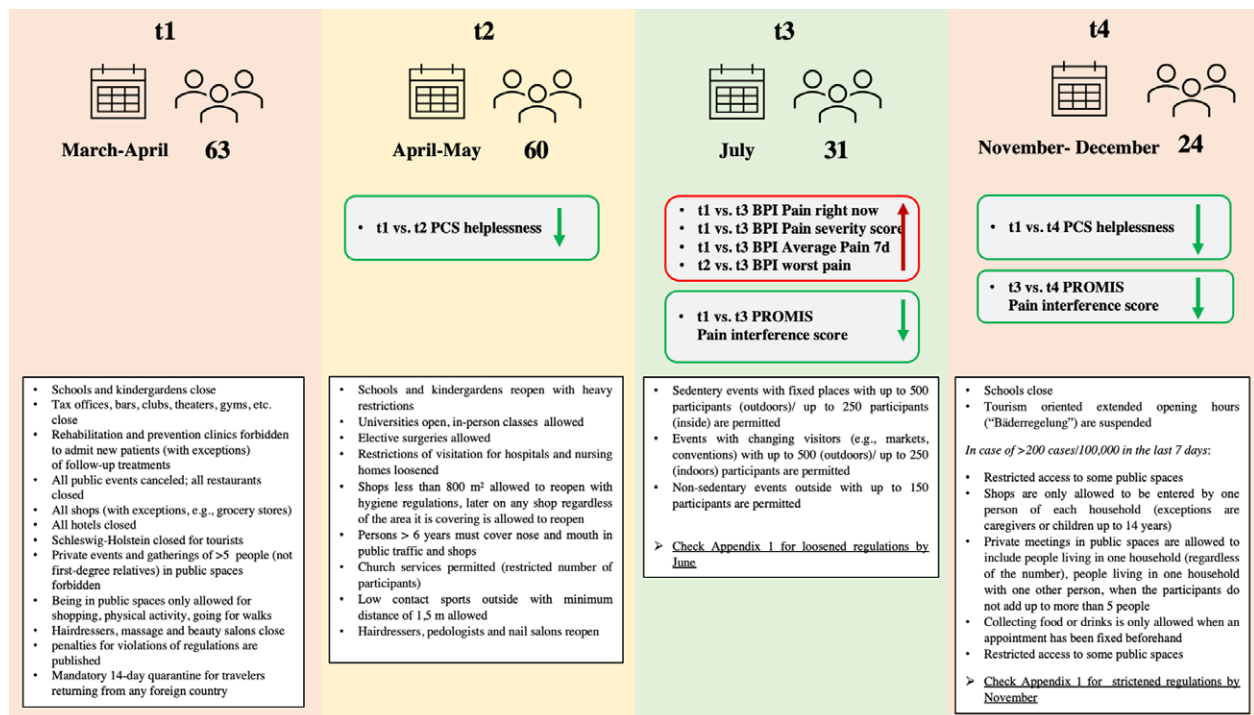


Figure 2. Patient number for each timepoint and brief overview of pandemic-associated regulations.

subjectively rate the impact of the pandemic on several aspects of their daily life. This initial version of our questionnaire has been introduced in our report about the early data.^[16] The items for the assessment of COVID-19 pandemic-associated changes of daily living have been modified and supplemented by additional questions in the course of the assessment in order to be able to adapt them to the current restrictions, if necessary (see below). These have been explained to the patients via telephone.

2.2.5.1. COVID-19 items, version 1. Changes in the daily life of our patients due to COVID-19 have been assessed through special items that, inter alia, referred to their social life, level of physical activity, medical care and asked how pain, sleep, mood have been affected (see also our initial report^[16]).

2.2.5.2. COVID-19 items, changed version 2. The second version was used at t2 and t3 and contained 20 items. The items now additionally considered were:

- Whether the subjects agreed with the pandemic-associated restrictions and felt well-informed about the reasons for their implementation,
- Whether the subjects or relatives/friends tested positive for acute respiratory syndrome coronavirus type 2 (SARS-CoV-2),
- Whether the pandemic had any positive effects for the subjects, and
- Whether the subjects felt unsettled by COVID-associated conspiracy theories.

2.2.5.3. COVID-19 items, changed version 3. The third version was used at t4 and contained 21 items now additionally assessed whether the patients were having any experiences with telemedicine since the onset of the pandemic. Appendix 2, Supplemental Digital Content, <http://links.lww.com/MD/I17> (see document) shows version 3 which also comprises the questions asked in version 2.

2.3. Analyzed timepoints

We chose to focus on 4 timepoints for our analysis: t1 (March 4, 2020, 2 weeks into heavy restrictions), t2 (April 5, 2020, lockdown), t3 (July, 2020, most restrictions loosened) and t4 (December, 2020, strict restrictions).

For details regarding restrictions in place at each timepoint see Figure 2 and Appendix 1, Supplemental Digital Content, <http://links.lww.com/MD/I16> (see document, showing the exact regulations for each assessment).

2.4. Statistical analysis

The analysis of the collected data was performed using IBM SPSS statistics for Windows (Version 25.0). Non-parametric tests were applied due to non-normal distribution and relatively small sample size. Comparisons between timepoints were conducted using Wilcoxon signed rank test. Intergroup comparisons were calculated via Mann-Whitney-U-test. For categorical variables chi-squared test was used.

All parameters were displayed as mean ± standard deviation, if not stated otherwise. *P*-values < 0.05 were considered as statistically significant.

In our previous study only patients without a change in their symptoms compared to prior to the pandemic were included. For this analysis, all participants (*n* = 63) were included. No imputation was used for addressing missing values. Data of dropouts was included until time of dropout.

2.4.1. Social change. In our first analysis of this patient cohort,^[16] we focused on the influence of social distancing and analyzed the effects of "social change." In our current analysis considering later timepoints, further pursuing this research question was not possible as every participant of our study had eventually experienced changes in their social life.

2.4.2. Medical disadvantages. As there have been reports of limitations in general healthcare due to the pandemic in Germany, we decided to compare pain, mood and quality of life

of patients who reported medical disadvantages to those who did not. The term “medical disadvantages” comprises all possible ways in which patients might have experienced problems (e.g., availability of doctors’ appointments or postponed surgeries, see also item 8 in Appendix 2, <http://links.lww.com/MD/I17>).

3. Results

In total, $n = 63$ patients were included in the analysis. Figure 2 shows the number of patients at each timepoint. Dropouts did not significantly differ from patients who completed the study in any regard. In Table 1, the characteristics of our patients are displayed. Most of our cohort has already been retired. Nine patients were still working and 7 of them reported changes due to the pandemic (e.g., switching to home office, structural changes at work). As for the education level, our patients finished $12.44 (\pm 3.96)$ years of education. Of our 63 patients, 58 replied to the question whether they lived alone ($n = 44$ no, $n = 14$ yes). Of those who answered “no,” 79.5% ($n = 35$) reported to live with their spouse, 9.1% ($n = 4$) with spouse and children, 2.3% ($n = 1$) with their parents and spouse and finally 6.8% ($n = 3$) with just their parents. One patient indicated “other.”

3.1. Pain

Patients reported a mean pain relief through medication of 43.7% (± 26.3). This did not change significantly over the course of the study.

Pain ratings are shown in Table 2. Their development throughout the year is visualized in Figure 2. Average pain, pain right now, least pain in the last 24 hours and Pain Severity Score were worse at t3 in comparison to t1, i.e. pain intensity was higher when pandemic restrictions were loosened compared to the beginning of the pandemic restrictions. The Neuropathic Pain Symptom Inventory (NPSI) total score did not differ between the different timepoints. Pain interference significantly decreased in the course of the study no matter the restrictions (Table 3, Fig. 2).

3.2. Emotional well-being, sleep, quality of life and pain catastrophizing

Scores for depression, anxiety, fatigue, sleep and quality of life rating did not change during the course of the pandemic (see Table 3). PCS helplessness score significantly decreased over the

course of the pandemic whereas PCS total score stayed consistent (Table 3).

3.3. Covid-19-associated changes of daily living

For an overview of the most relevant items, please see Table 4.

Here, quite a number of patients reported a worsening of mood and sleep at each timepoint even though the comparison of timepoints was not statistically significant. A worsening of appetite was rarely reported. In total, 24.1% of our patients lived alone, while the others reported living with family or a partner. 22% reported having a pet. As expected, social distancing was more severe during stronger pandemic restrictions, although most patients reported to have contact via telephone. Medical disadvantages were more often reported at the beginning of the corona pandemic. Patients worried more about their health when pandemic restrictions were more severe. Over the course of the first year of pandemic restrictions, few patients were confident that the situation would improve.

Some patients even noticed positive aspects during the pandemic, with the most frequent aspects mentioned being a calmer everyday life (including less traffic and noise) and more time for family, hobbies and oneself, as well as the exploration of new ways of keeping in contact via telephone and internet. While the number of patients worried about their health dropped significantly in summer, it increased with the second lockdown.

3.4. Influence of medical disadvantages

Having medical disadvantages resulted in a lower quality of life upon EuroQol 5 dimension (EQ-5D) (Table 5) by t1 and t2 and higher pain intensity and more fatigue at some timepoints (Table 5).

Patients experiencing medical disadvantages were significantly more often worried about their health (34.3% vs. 10.7%, $P < .001$) and lived alone significantly more often (75% vs. 68.9%, $P = .021$).

4. Discussion

In our predecessor study, we reported that patients experienced a shift of attention from the chronic disease towards the imminent threat of the pandemic and therefore assumed that patients might be in the “heroic/honeymoon” phase of disaster management.^[16] On that basis, we hypothesized that our assessed

Table 1

Characteristics of study cohort (n = 63).

	Characteristic	
	Age in yrs at t1 [mean \pm SD] (range)	66.62 \pm 11.27 (36–86)
	Sex [m/f] (%)	45/18 (71.43/28.57)
	Education in yrs [mean \pm SD] (range)	12.55 \pm 3.96 (5–24)
	Mean pain in the last 24 h before the pandemic [mean \pm SD] (range)	4.16 \pm 2.43 (0–10)
Analgesic medication at t1 [n, %]	No pain medication [n, %]	20 (31.7)
	Single pain medication	20 (31.7)
	Combination therapy	23 (36.5)
Aetiology of polyneuropathy [n] (%)	Idiopathic/unknown [n] (%)	43 (68.3)
	Diabetes	11 (17.5)
	Chemotherapy	3 (4.8)
	Neoplasm	2 (3.2)
	CIDP	1 (1.6)
	POEMS	1 (1.6)
	HIV	1 (1.6)
	Vasculitis	1 (1.6)

CIDP = chronic inflammatory demyelinating polyneuropathy, HIV = human immunodeficiency virus, POEMS = polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin, SD = standard deviation.

Table 2
Pain ratings upon brief pain inventory (BPI) in the overall cohort at the different time points.

	t1	t2	t3	t4	P
BPI worst pain in the last 24 h	5.37 ± 2.39	5.35 ± 2.30	6.13 ± 2.17	5.79 ± 1.98	t2 vs. t3: .009
BPI least pain in the last 24 h	2.51 ± 1.76	2.97 ± 2.41	3.00 ± 2.11	2.75 ± 1.62	t1 vs. t2: .045 t1 vs. t3: .024 t1 vs. t4: .014
BPI pain right now	3.33 ± 2.24	3.78 ± 2.41	4.23 ± 2.31	3.63 ± 2.43	t1 vs. t3: .01
BPI pain severity score	4.00 ± 1.85	4.24 ± 2.30	4.41 ± 2.13	4.20 ± 1.69	t1 vs. t3: .014
BPI average pain 7 d	4.67 ± 2.08	4.76 ± 2.1	5.13 ± 2.09	4.63 ± 1.93	t1 vs. t3: .049

The P-column indicates the significant comparisons. Other comparisons are not significant.

BPI = brief pain inventory.

Values are presented in mean ± SD. (t1: 03/04/2020, heavy restrictions; t2: 04/05/2020 lockdown; t3: 07/2020, most restrictions loosened; t4: 12/2020, heavy restrictions).

Table 3
Pain catastrophizing, emotional well-being, sleep and quality of life as assessed by validated questionnaires at the different timepoints.

	t1	t2	t3	t4	P
Emotional wellbeing and pain interference					
PROMIS depression score	50.89 ± 8.05	52.02 ± 9.18	50.62 ± 7.73	50.48 ± 8.62	ns
PROMIS anxiety score	53.30 ± 7.80	52.39 ± 8.22	50.53 ± 7.28	51.85 ± 7.47	ns
PROMIS fatigue score	52.31 ± 10.14	53.51 ± 9.83	51.41 ± 10.76	53.00 ± 9.79	ns
PROMIS pain interference score	62.84 ± 7.08	61.18 ± 7.57	60.21 ± 6.41	59.28 ± 6.96	t1 vs. t3: P = .044 t3 vs. t4: P < .001
PROMIS sleep score	53.65 ± 8.11	53.66 ± 7.88	55.23 ± 8.74	52.79 ± 8.30	ns
Pain catastrophizing					
PCS score	18.83 ± 11.77	17.00 ± 9.76	12.42 ± 9.37	11.70 ± 8.49	ns
PCS rumination score	6.13 ± 4.25	6.24 ± 4.00	4.45 ± 3.57	4.46 ± 3.80	ns
PCS magnification score	4.02 ± 2.77	3.72 ± 2.54	2.87 ± 2.57	3.08 ± 2.62	ns
PCS helplessness score	8.68 ± 5.82	7.78 ± 5.14	5.74 ± 4.31	4.74 ± 3.67	t1 vs. t2: .028 t1 vs. t4: .015
Quality of life					
EQ-5D	0.695 ± 0.168	0.718 ± 0.182	0.649 ± 0.276	0.705 ± 0.249	ns

Values are presented as mean ± SD.

EQ-5D = EuroQol 5 dimension, ns = not significant, PCS = pain catastrophizing scale, PROMIS = patient reported outcomes measurement information system.

(t1: 03/04/2020, heavy restrictions; t2: 04/05/2020 lockdown; t3: 07/2020, most restrictions loosened; t4: 12/2020, heavy restrictions).

Table 4
Results of pandemic-related questionnaire at the different timepoints.

	t1	t2	t3	t4	P
In contact with family friends (% [n out of n])	42.9 (27/63)	50 (30/60)	80.6 (25/31)	33.3 (8/24)	t2 vs. t3: .005 t3 vs. t4: <.001
In contact via telephone (% [n out of n])	90.5 (57/63)	98.3 (59/60)	100 (31/31)	100 (24/24)	ns
Medical disadvantages (% [n out of n])	44.4 (28/63)	46.7 (28/60)	35.5 (11/31)	20.8 (5/24)	ns
Worried about own health (% [n out of n])	55.6 (35/63)	53.3 (32/60)	38.7 (12/31)	75 (18/24)	t2 vs. t3: .026 t3 vs. t4: .007
Goes for walks (% [n out of n])	74.6 (47/63)	80 (48/60)	80.6 (25/31)	83.3 (20/24)	ns
Confident, situation will improve (% [n out of n])	60.3 (38/63)	58.3 (35/60)	58.1 (18/31)	29.2 (7/24)	t3 vs. t4: .033
Sleep worse (n “yes” [% out of %])	20.6 (13/63)	18.3 (11/59)	25.0 (8/32)	33.3 (8/24)	ns
Appetite worse (n “yes” [% out of %])	6.3 (4/63)	5.0 (3/60)	0	0	ns
Mood worse (n “yes” [% out of %])	47.6 (30/63)	43.3 (26/60)	34.4 (11/32)	58.3 (14/24)	ns
Pain worse (n “yes” [% out of %])	12.7 (8/63)	13.3 (8/60)	9.4 (3/32)	4.2 (1/24)	ns

ns = not significant.

measures would deteriorate in the further course of the pandemic (see phases of disaster response)^[2,5].

Due to the long-term observation of our cohort throughout the entire year, we have now been able to show that the perception of pain intensity was indeed dependent on pandemic activity, with lower pain intensity during lockdown and higher during loosened regulations, whereas domains like sleep, mood and quality of life did not change significantly in the validated measures, which is consistent with previous reports.^[2,6,27] In our cohort, the consideration of the co-factor “health care” was decisive: patients who reported medical disadvantages had a lower quality of life upon EQ-5D and were significantly more worried about their health.

Our hereby-presented follow-up data indicate a shift in summer towards a pain worsening. The worsening of the “BPI least pain” score in the assessments after t1 and the worsening of “BPI worst pain” by t3 suggests that our cohort indeed underwent the stages of disaster response in terms of pain severity/intensity and reached the stage of ‘disillusionment’. This is further supported by significantly higher average and current pain ratings and severity scores at the time of loosened restrictions (t3) when compared to the early phase (t1, ‘honeymoon’/‘heroic’ state). Apparently, with the decelerating pandemic activity and loosened regulations by t3, the perceived pandemic threat and thus distraction from the chronic pain condition was reduced whereby pain ratings increased.

Table 5
Relation of medical disadvantages to quality of life, pain and fatigue at the different timepoints.

Medical disadvantages	t1	t2	t3	t4
	n = 28	n = 28	n = 11	n = 5
EQ-5D				
Yes	0.65 ± 0.17	0.67 ± 0.21	0.52 ± 0.31	0.62 ± 0.29
No	0.75 ± 0.14	0.78 ± 0.13	0.75 ± 0.2	0.79 ± 0.17
P	.035	.030	ns	ns
BPI average pain 7 d				
Yes	5.16 ± 2.27	5.26 ± 2.08	5.53 ± 2.20	5.08 ± 2.50
No	4.07 ± 1.74	4.00 ± 1.79	4.60 ± 1.96	4.17 ± 1.03
P	ns	.030	ns	ns
BPI least pain 24 h				
Yes	2.84 ± 1.99	3.39 ± 2.75	3.13 ± 2.20	3.42 ± 1.93
No	2.14 ± 1.48	2.46 ± 1.90	2.80 ± 2.15	2.08 ± 0.90
P	ns	ns	ns	.045
PROMIS fatigue				
yes	54.96 ± 11.28	55.35 ± 11.80	53.51 ± 12.60	53.68 ± 11.58
no	50.17 ± 8.11	51.68 ± 7.19	50.09 ± 9.12	52.33 ± 8.09
P	ns	.044	ns	ns

The values are indicated as means ± SD. BPI = brief pain inventory, EQ-5D = EuroQol 5 dimension, PROMIS = patient reported outcomes measurement information system. (t1: 03/04/2020, heavy restrictions; t2: 04/05/2020 lockdown; t3: 07/2020, most restrictions loosened; t4: 12/2020, heavy restrictions).

What might seem contradictory to our hypothesis at first glance were significantly lower scores for pain interference and helplessness even at t4 (increased pandemic activity and restrictions). Since these are compatible with our patients' subjective assessment of medical care where fewer patients reported medical disadvantages, we believe the availability of pain management at any time to be responsible for this observation. Interestingly, more patients stated to worry about their health by t4 even though fewer reported medical disadvantages which we interpret to be associated with the resurgence of pandemic restrictions (mind the drastic reduction of patients who were confident the situation would improve).

This study not only reports on the course of pain assessed with validated measures throughout the first year of the pandemic, but also observes the subjectively perceived course of several pandemic-affected domains such as mood, daily life, and medical care. The biopsychosocial model of pain interference led many experts to assume that the pandemic would have a negative impact on chronic pain patients in many ways.^[11,15,28] Surprisingly neither our initial assessment, nor other studies supported this prediction unambiguously. For instance, Colloca and colleagues reported a reduction of pain severity (self-reportedly by 73%) and interference, which was in contrast with the occurrence or worsening of anxiety and depression.^[29] Other studies reported how greater pain severity/interference during social distancing was dependent, for example, on socioeconomic factors.^[30]

Our present follow-up assessment on patient's mood, quality of life and sleep showed no adherence to the stages of disaster coping in the validated questionnaires even though the subjective reports in the pandemic-items were sometimes in contrast. One explanation might be, as mentioned, that the chosen patient-reported outcome measures (PROMS) were not validated under pandemic circumstances. Another explanation is the nature of a pandemic. While a geological disaster, an earthquake for instance, can be a single event that is coped with progressively, this pandemic of a novel virus is associated with unknown factors and an unsteady course. The "impact" is persistently occurring, though with varying intensity. Remember the uncertainty when the Omicron variant first emerged: the effect of previously very successful vaccines were rendered uncertain.^[31]

While this unpredictable nature of the pandemic and uncertain course of variables such as transmission numbers, mutations and therapeutic/preventive options caused our decision to conduct multiple assessments throughout the year 2020, this

decision was associated with disadvantages, the most obvious being the patients lost to follow-up which left our already rather small cohort even smaller by t4 (reduction by almost 2/3). We presume this might be due to the circumstance that only later in the process, after the first study has been conducted, we decided to conduct follow-up investigations. Ergo, while patients had agreed to participate in the first assessment, it was not obvious for them to be part of the follow-up examinations. Also, the male population of our study is bigger than the female. Given our recruitment conditions, most likely is a coincidental distribution. Therefore, we appreciate the existence of other investigations about the effects of the current pandemic on patients with chronic pain that examined larger cohorts and seemingly produced results sometimes contradictory to ours (i.e., no relevant effect of the pandemic on the patients).^[26,27] For several reasons though, these results cannot be compared to ours. While retrospective data analysis/no use of validated questionnaires/sole assessment of pain intensity are some reasons to name, perhaps the most pivotal point to consider is the fact that they did not differentiate across pain etiologies. To our knowledge, our study is the only one examining patients with painful polyneuropathy exclusively throughout the first year of the pandemic in a longitudinal design. This characteristic is especially important as it has been shown that across pain etiologies, patients behave/respond differently in the pandemic.^[15,32,33] Thus, while the size of our cohort will not allow generalized conclusions, we believe our results provide an important and unique estimation for this patient group.

5. Conclusions

The pain perception of our patients with painful polyneuropathy was dependent on the severity-status of the pandemic. The improvement of pain during the early lockdown in 2020^[16] shifted towards a worsening as the pandemic activities grew quieter. Though sleep, mood, and quality of life did not change significantly in validated measures, patients described a worsening of mood with rising restrictions by the end of 2020. Continued medical care seems decisive to prevent worsening of pain and quality of life. We therefore support the recommendations in favor of telemedicine. Finally, we want to resume our report by appreciating the fact that despite the obvious burden and emotional distress, our patients were able to point out positive effects of the pandemic on their daily life.

Acknowledgements

This study was supported by Grünenthal GmbH Deutschland with no involvement in experimental design, conduction or interpretation of the study. We are indebted to the subjects who participated in the study for their consent and co-operation. We would especially like to thank our student assistant Swantje Jendral for her committed, outstanding support of this study.

Author contributions

Conceptualization: Dilara Kersebaum, Manon Sendel, Sophie-Charlotte Fabig, Juliane Sachau, Josephine Lassen, Stefanie Rehm, Julia Forstenpointner, Johanna Rügenapp, Jan Vollert, Philipp Hüllemann, Ralf Baron, Janne Gierthmühlen.

Data curation: Dilara Kersebaum, Manon Sendel, Sophie-Charlotte Fabig, Juliane Sachau, Josephine Lassen, Stefanie Rehm, Julia Forstenpointner, Janne Gierthmühlen.

Formal analysis: Dilara Kersebaum, Manon Sendel, Julia Forstenpointner, Jan Vollert, Philipp Hüllemann, Ralf Baron, Janne Gierthmühlen.

Funding acquisition: Dilara Kersebaum, Ralf Baron, Janne Gierthmühlen.

Investigation: Dilara Kersebaum, Manon Sendel, Sophie-Charlotte Fabig, Josephine Lassen, Stefanie Rehm, Julia Forstenpointner, Jan Vollert, Philipp Hüllemann, Janne Gierthmühlen.

Methodology: Dilara Kersebaum, Manon Sendel, Juliane Sachau, Josephine Lassen, Stefanie Rehm, Julia Forstenpointner, Johanna Rügenapp, Jan Vollert, Philipp Hüllemann, Ralf Baron, Janne Gierthmühlen.

Project administration: Dilara Kersebaum, Manon Sendel, Sophie-Charlotte Fabig, Juliane Sachau, Josephine Lassen, Stefanie Rehm, Johanna Rügenapp, Philipp Hüllemann, Ralf Baron, Janne Gierthmühlen.

Resources: Dilara Kersebaum, Manon Sendel, Ralf Baron, Janne Gierthmühlen.

Software: Dilara Kersebaum, Manon Sendel, Julia Forstenpointner, Jan Vollert, Ralf Baron, Janne Gierthmühlen.

Supervision: Manon Sendel, Ralf Baron, Janne Gierthmühlen.

Validation: Dilara Kersebaum, Manon Sendel, Jan Vollert, Ralf Baron, Janne Gierthmühlen.

Visualization: Dilara Kersebaum, Manon Sendel, Janne Gierthmühlen.

Writing – original draft: Dilara Kersebaum, Manon Sendel, Sophie-Charlotte Fabig, Juliane Sachau, Josephine Lassen, Stefanie Rehm, Julia Forstenpointner, Johanna Rügenapp, Jan Vollert, Philipp Hüllemann, Ralf Baron, Janne Gierthmühlen.

Writing – review & editing: Dilara Kersebaum, Manon Sendel, Sophie-Charlotte Fabig, Juliane Sachau, Josephine Lassen, Stefanie Rehm, Julia Forstenpointner, Johanna Rügenapp, Jan Vollert, Philipp Hüllemann, Ralf Baron, Janne Gierthmühlen.

References

- Anderson EJ, Roupheal NG, Widge AT, et al. Safety and immunogenicity of SARS-CoV-2 mRNA-1273 vaccine in older adults. *N Engl J Med.* 2020;1:12.
- Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med.* 2020;1:13.
- Holmes EA, O'Connor RC, Perry VH, et al. Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. *Lancet Psychiatry.* 2020;7:547–60.
- Brooks SK, Webster RK, Smith LE, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet.* 2020;395:912–20.
- Pfefferbaum B, North CS. Mental health and the Covid-19 pandemic. *N Engl J Med.* 2020;383:510–12.
- Bavel JJV, Baicker K, Boggio PS, et al. Using social and behavioural science to support COVID-19 pandemic response. *Nat Hum Behav.* 2020;4:460–71.
- Wang C, Pan R, Wan X, et al. Immediate psychological responses and associated factors during the initial stage of the 2019 coronavirus disease (COVID-19) epidemic among the general population in China. *Int J Environ Res Public Health.* 2020;17:1729.
- Bourion-Bédès S, Tarquinio C, Batt M, et al. Psychological impact of the COVID-19 outbreak on students in a French region severely affected by the disease: results of the PIMS-CoV 19 study. *Psychiatry Res.* 2020;295:113559.
- Rajkumar RP. COVID-19 and mental health: a review of the existing literature. *Asian J Psychiatr.* 2020;52:102066.
- Czeisler ME, Lane RI, Petrosky E, et al. Mental health, substance use, and suicidal ideation during the COVID-19 pandemic — United States, June 24–30, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69:1049–57.
- Karos K, McParland JL, Bunzli S, et al. The social threats of COVID-19 for people with chronic pain. *Pain.* 2020;161:2229–35.
- Clauw DJ, Häuser W, Cohen SP, et al. Considering the potential for an increase in chronic pain after the COVID-19 pandemic. *Pain.* 2020;161:1694–7.
- Puntillo F, Giglio M, Brienza N, et al. Impact of COVID-19 pandemic on chronic pain management: looking for the best way to deliver care. *Best Pract Res Clin Anaesthesiol.* 2020;34:529–37.
- Webster F, Connoy L, Sud A, et al. Grappling with chronic pain and poverty during the COVID-19 pandemic. *Can J Pain.* 2020;4:125–8.
- Eccleston C, Blyth FM, Dear BF, et al. Managing patients with chronic pain during the COVID-19 outbreak: considerations for the rapid introduction of remotely supported (eHealth) pain management services. *Pain.* 2020;161:889–93.
- Kersebaum D, Fabig S-C, Sendel M, et al. The early influence of COVID-19 pandemic-associated restrictions on pain, mood, and everyday life of patients with painful polyneuropathy. *Pain Rep.* 2020;5:e858.
- Cleeland CS, Ryan KM. Pain assessment: global use of the brief pain inventory. *Ann Acad Med Singapore.* 1994;23:129–38.
- Bouhassira D, Attal N, Fermanian J, et al. Development and validation of the neuropathic pain symptom inventory. *Pain.* 2004;108:248–57.
- Amtmann D, Cook KF, Jensen MP, et al. Development of a PROMIS item bank to measure pain interference. *Pain.* 2010;150:173–82.
- Buyse DJ, Yu L, Moul DE, et al. Development and validation of patient-reported outcome measures for sleep disturbance and sleep-related impairments. *Sleep.* 2010;33:781–92.
- Lai JS, Cella D, Choi S, et al. How item banks and their application can influence measurement practice in rehabilitation medicine: a PROMIS fatigue item bank example. *Arch Phys Med Rehabil.* 2011;92(10 SUPPL.):S20–7.
- Pilkonis PA, Choi SW, Reise SP, et al. Item banks for measuring emotional distress from the patient-reported outcomes measurement information system (PROMIS®): depression, anxiety, and anger. *Assessment.* 2011;18:263–83.
- Sullivan MJL, Bishop SR, Pivik J. The pain catastrophizing scale: development and validation. *Psychol Assess.* 1995;7:524–32.
- Goldberg LR. The development of markers for the big-five factor structure. *Psychol Assess.* 1992;4:26–42.
- DeWolfe DJ. (Deborah J 1949-. Training manual for mental health and human service workers in major disasters, Second Edition. 2000. <https://www.hsdl.org/?abstract&did=> [access date August 27, 2020].
- Lassen CL, Siam L, Degenhart A, et al. Short-term impact of the COVID-19 pandemic on patients with a chronic pain disorder. *Medicine (Baltim).* 2021;100:e25153.
- Fujiwara A, Watanabe K, Ida M, et al. The short-term effect of COVID-19 pandemic on disability, pain intensity, psychological status, and exercise habits in patients with chronic pain. *J Anesth.* 2021;35:862–9.
- Meyer-Frießem CH, Gierthmühlen J, Baron R, et al. Pain during and after COVID-19 in Germany and worldwide: a narrative review of current knowledge. *Pain Rep.* 2021;6:e8931–7.
- Colloca L, Thomas S, Yin M, et al. Pain experience and mood disorders during the lockdown of the COVID-19 pandemic in the United States: an opportunistic study. *Pain Rep.* 2021;6:e958.
- Hruschak V, Flowers KM, Azizuddin DR, et al. Cross-sectional study of psychosocial and pain-related variables among patients with chronic pain during a time of social distancing imposed by the coronavirus disease 2019 pandemic. *Pain.* 2021;162:619–29.
- Callaway E. Omicron likely to weaken COVID vaccine protection. *Nature.* 2021;600:367–8.
- Consonni M, Telesca A, Grazzi L, et al. Life with chronic pain during COVID-19 lockdown: the case of patients with small fibre neuropathy and chronic migraine. *Neurol Sci.* 2021;42:389–97.
- Schwab R, Anić K, Stewen K, et al. Pain experience and social support of endometriosis patients during the COVID-19 pandemic in Germany – Results of a web-based cross-sectional survey. *PLoS One.* 2021;16:e02564331–15.