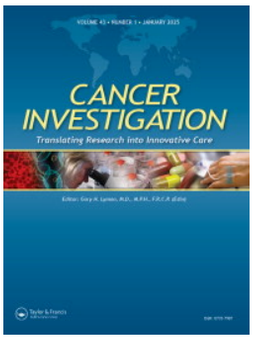

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Weather-Related Factors and Patient-Reported Outcomes (PROs) in Cancer Patients: Results from the ExPRO Study

Hanna Salm[a,b], Martin Eichler[c,d], Jeanette Bahr[b], Dimosthenis Andreou[e], Christian Schmidt[a], Sarah Uhlig[a,b] and Daniel Pink[a,b]

[a]Department of Internal Medicine C, University Hospital Greifswald, Greifswald, Germany; [b]Department of Oncology and Palliative Care, Helios Hospital Bad Saarow, Bad Saarow, Germany; [c]National Center for Tumor Diseases (NCT/UCC), Dresden, Germany; [d]Clinic and Polyclinic for Internal Medicine I, University Hospital Carl Gustav Carus, TU, Dresden, Germany; [e]Institute for Interdisciplinary Sarcoma Treatment and Research, Department of Orthopedic Oncology and Sarcoma Surgery, University Hospital Essen, Essen, Germany

ABSTRACT

Objective: The ExPRO (External factors influencing patient reported outcomes of patients with malignant diseases) study explored associations between QoL data and environmental factors on the day of questionnaire completion: mean temperature, sunshine hours, season, and lunar phase.

Methods: We undertook a cross-sectional analysis of baseline data in the prospective cohort study at two cancer centers in eastern Germany. From December 2020 to December 2021, cancer patients completed the EORTC QLQ-C30 questionnaire upon admission. Statistical analysis was performed to explore associations between QoL data and environmental factors, including temperature, sunshine hours, season, and lunar phases.

Results: We received 5040 responses (54% male). QoL scores were highest at 25-30 °C and lowest at 5-10 °C (mean 61.3 vs. 52.6, $p < 0.001$). Insomnia was highest at ≤0 °C and lowest at 25-30 °C (mean 39.3 vs. 29.5, $p < 0.001$). QoL was highest with 8 hours of sunshine and lowest with 0 hours (mean 56.9 vs. 50.9, $p = 0.003$).

Conclusion: Higher temperatures, more sunshine, and summer seasons are associated with higher QoL in cancer patients, while lower temperatures and reduced sunlight are associated with poorer QoL. These findings highlight the need to consider environmental factors in PRO assessments.

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Quality of life; symptom burden; weather; patient reported outcomes; standardized instruments

1. Introduction

The QoL of cancer patients is influenced not only by the course of their disease and potential adverse effects of their treatment, but also by external factors such as family relationships and financial risks (1). In addition, there is a common belief among both healthy and ill individuals that environmental factors, including current weather conditions (e.g., sunshine, temperature), seasonal variations, and even lunar phases, may affect their well-being, particularly in relation to sleep disturbance.

A large body of literature is devoted to the impact of climate on human health. A recent study demonstrated that weather-related changes limit social activities of patients with sickle cell disease (2). Another study reported that weather conditions affect the QoL reported by patients with trigeminal neuralgia (3). Even cancer incidence can exhibit seasonal patterns, as seen in breast cancer, where diagnoses tend to increase during spring and autumn (4). Moreover, a recent study highlighted the impact of environmental factors, such as light and humidity on breakthrough cancer pain in advanced cancer patients (5). Additionally, a study on women suggested that an increased sun exposure during summer months may lower the risk of ovarian cancer (6). Another study supports that sun

CONTACT Hanna Salm hanna.salm@stud.uni-greifswald.de Department of Internal Medicine C, University Hospital Greifswald, Greifswald, Germany

exposure, especially sun induced vitamin D, improves cancer prognosis (7).

All these results strengthen the idea that QoL in cancer patients may also show weather dependency. Given that cancer patients, especially those who are terminally ill, have impaired physiological capacity, they may be more vulnerable to weather conditions. This highlights two important considerations for research and patient care. First, in studies using self-reported QoL, prevailing weather conditions should be accounted for to ensure they do not skew the results, as weather could act as a confounding factor. Second, understanding how weather affects QoL could guide interventions to improve the well-being of cancer patients by adjusting their environment or providing targeted support during adverse weather conditions. Given the substantial global burden of cancer, expanding our understanding of all factors, including weather, that influence the QoL and symptom burden of cancer patients is critical to advancing research and enhancing patient care.

If an association between weather variables and PROs in cancer patient QoL is established, it would be beneficial to consider climatic conditions when interpreting PROs in broader research contexts. Identification of potential influencing factors and, if necessary, development of appropriate interventions are essential steps to improve the future QoL of these patients. Therefore, this investigation aims to elucidate the impact of climatic conditions on QoL in this patient population.

2. Methods

2.1. Study design and data collection

We conducted a prospective cohort study to assess QoL using the EORTC QLQ-C30 in German cancer patients. During the assessment period (December 1, 2020, to December 31, 2021), inpatients and outpatients with various types of cancer were recruited at two tertiary cancer centers in eastern Germany (Helios Klinikum Bad Saarow and Universitätsklinikum Greifswald). On the day of admission, patients received an information sheet about the study and were invited to anonymously complete the EORTC QLQ-C30 questionnaire.

Anonymous data on sex, age, and place of residence were collected alongside each EORTC QLQ-C30 form. The majority of our patients were located in the districts around Bad Saarow, east of Berlin, and Greifswald on the Baltic coast. Medical information, including treatment details and disease status, was not included.

2.2. Outcome measures

To assess QoL and symptom burden, PRO instruments have been increasingly used in clinical practice (8). PRO measures are a valid method to elicit patients' own perceptions of their well-being, providing a patient-centered view of their subjective experiences (9). The European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 Health-Related Quality of Life questionnaire is one of the most widely used PRO instruments to assess health-related quality of life in cancer patients (10).

The QLQ-C30 consists of 30 items covering five function scales (physical, role, cognitive, social, and emotional functioning), three symptom scales (fatigue, nausea/vomiting, and pain), five single-item symptom scales (dyspnea, insomnia, appetite loss, constipation, and diarrhea), a single-item scale for financial difficulties impacted by the disease and treatment, and a global health/QoL scale composed of two items. Higher scores on functioning scales indicate a higher level of functioning, while higher scores on symptom scales imply a higher symptom burden. The QLQ-C30 functional, symptom, and finance scale items are scored on a four-point scale including the following levels: "Not at all", "A little", "Quite a bit", and "Very much". The global QoL scale is composed of two items, which are scored from 1 to 7 with a score of 1 representing "very poor" and 7 indicating "excellent".

We focused on three function scales (physical, emotional, and cognitive functioning), three symptoms (fatigue, pain, and insomnia) as well as the global health/QoL score. These scales were chosen due to the relevance of these symptoms for cancer patients base on our clinical experience.

2.3. Data analysis

In preparation for statistical analysis, several steps were undertaken to manage and categorize the raw data.

2.3.1. Data management

Daily mean temperature data for the patients' districts of residence, including weekends, were obtained from https://meteostat.net, reflecting the average recorded on the specific day the QoL assessment was completed. The analysis focused on specific weather parameters: temperature, sunshine duration, and season. Each QoL assessment was associated with the prevailing weather conditions in the districts where the patients resided on that particular day. Lunar phases (full moon vs. new moon) were additionally included in the analysis.

June, July, and August were counted as summer months. December, January, and February were counted as winter months. We categorized the following groups: *Hours of sunshine* per day: 0–<=2, 2–<=4, 4–<=6, 6–<=8, 8–<=10, 10–<=12. *Temperature (C°)*: <=0, 0–<=5, 5–<=10, 10–<=15, 15–<=20, 20–<=25, 25–<=30, 30–<=35. No confounding factors were examined in this analysis.

We calculated mean scores for each subscale of the QLQ-C30 (e.g., physical functioning, emotional functioning), which were transformed into a standardized scale ranging from 0 to 100 according to the QLQ-C30 scoring manual (11). The transformation of raw scores from the QLQ-C30 subscales to a 0-100 scale follows a specific formula outlined in the scoring manual. For functional scales, where higher scores indicate better functioning, the formula is:

$$\text{Transformed score} = \left(\text{range of scores} - \text{raw score}/\text{minimum score}\right) \times 100.$$

For symptom scales, where higher scores indicate worse symptoms, the formula is slightly adjusted so that a higher score reflects greater symptom burden.

This linear transformation ensures that all scores are comparable on a 0-100 scale, where a score of 0 represents the lowest possible outcome (indicating the poorest functioning or absence of symptoms), and a score of 100 represents the highest outcome (indicating the best functioning or the most severe symptom burden).

2.3.2. Statistical analysis

We undertook descriptive analyses to summarize the socio-demographic profile of the cohort, including sex and age, as well as the weather variables and the QoL measures from the EORTC QLQ-C30 using numbers and proportions, means and standard deviations, or medians and interquartile range, as appropriate for the type of data.

We tested the association between each of the weather variables and the QoL measures including the global health/QoL and the following subscales: physical functioning, emotional functioning, cognitive functioning, fatigue, pain, insomnia. QoL scores were calculated using the R software environment, while statistical analyses were conducted using SAS 9.4 (SAS Institute).

The SAS procedure NPAR1WAY was applied. We first used the Kruskal-Wallis test to identify differences between more than two groups. Subsequently, pairwise multiple comparisons were carried out using the two-tailed unpaired Wilcoxon rank-sum test. P-values were calculated, and differences were considered statistically significant at $P < 0.05$.

2.4. Ethical approval

The study was approved by the ethics committee of the University Hospital of Greifswald (BB195/20). No identifying patient information was collected.

3. Results

We received a total of 5040 responses. The mean age was 64 years. Most patients were male (54%).

3.1. QoL by temperature (°C)

Table 1 illustrates the relationship between QoL and temperature. Regarding global health/QoL, best results were reported at 25–30 degrees, the lowest value was measured at 5–10 degrees (61.3 vs. 52.6, $P < 0.001$).

Insomnia was most pronounced at <=0 degrees and least evident at 25–30 degrees (39.3

Table 1. EORTC QLQ-C30. Mean scores (M)/standard deviations (SD) by scales/symptoms stratified by temperature.

Temperature (°C)	<=0		0–<=5		5–<=10		10–<=15		15–<=20		20–<=25		25–<=30		30–<=35		*p*-value*
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	
Function Scales																	
Physical functioning	70.1	24.5	67.6	25.5	65.3	26.4	65.1	26.0	66.9	25.4	66.4	25.8	68.8	24.2	65.7	26.5	0.084
Emotional functioning	66.1	25.4	65.7	25.1	66.1	26.2	65.2	26.1	67.9	24.4	67.4	25.5	70.0	23.0	67.5	24.3	0.202
Cognitive functioning	76.7	24.8	75.9	25.6	74.2	27.5	75.5	26.3	77.2	25.4	77.2	25.7	78.5	24.2	79.2	24.7	0.167
Symptom Scales																	
Fatigue	41.8	27.6	43.4	26.3	45.0	28.4	45.2	27.6	43.0	27.0	42.4	28.2	41.0	25.7	42.7	28.0	0.183
Pain	32.8	29.1	35.8	30.8	36.2	31.3	35.0	30.5	31.9	30.2	32.3	29.7	29.7	29.5	30.7	29.1	0.002
Insomnia	39.3	31.0	38.7	32.2	38.5	32.0	35.5	31.5	33.7	30.3	32.9	31.1	29.5	29.5	37.5	29.0	p <0.001
Global health/QoL	57.8	23.5	55.7	24.0	52.6	25.5	54.1	25.0	56.2	24.6	57.8	25.4	61.3	24.0	58.6	27.5	p <0.001

*p-values from Kruskal-Wallis Test.

Table 2. EORTC QLQ-C30.

Sunshine (h)	0–<=2		2–<=4		4–<=6		6–<=8		8–<=10		10–<=12		>12		*p*-value*
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	
Function Scales															
Physical functioning	65.0	26.1	67.5	26.3	67.3	25.7	65.5	25.2	66.0	24.8	68.2	24.3	63.2	25.8	0.30
Emotional functioning	62.9	27.1	66.7	26.1	65.8	25.1	67.1	22.0	67.5	23.8	67.0	25.0	64.5	26.2	0.15
Cognitive functioning	72.1	28.5	78.3	26.0	75.6	26.4	76.5	23.3	77.5	23.5	76.7	25.5	75.5	26.7	0.01
Symptom Scales															
Fatigue	46.2	28.0	41.8	27.4	44.7	27.8	45.0	27.2	43.9	27.4	45.8	25.5	44.9	28.7	0.02
Pain	38.6	32.2	33.3	31.0	35.2	29.9	33.5	29.2	34.2	30.6	31.3	29.5	35.5	31.6	0.04
Insomnia	41.3	33.5	34.9	32.9	39.3	30.8	34.0	28.6	33.1	30.2	34.4	29.9	32.9	31.0	p <0.001
Global health/QoL	50.9	26.3	56.0	24.8	55.6	24.3	56.3	22.3	56.9	24.4	54.8	23.4	52.9	26.0	p <0.001

*p-values from Kruskal-Wallis Test.
Mean scores (M)/standard deviations (SD) by scales/symptoms stratified by hours of sunshine (h/day).

vs. 29.5, P <0.001). Pain was most prominent at 5–10 degrees and lowest at 25–30 degrees (36.2 vs. 29.7, P 0.002). Overall, best values were obtained at 25–30 degrees, while QoL, pain and insomnia were worst at 5–10 degrees.

3.2. QoL by hours of sunshine

As shown in Table 2, insomnia was least pronounced during days with lots of sunshine, showing lowest values at 12 hours of sunshine and highest values at 0 hours of sunshine (32.9 vs. 41.3, P 0.0003). Global health/QoL was highest at 8 hours of sunshine and lowest at 0 hours of sunshine (56.9 vs. 50.9, P 0.003).

Pain was most pronounced at 0 hours of sunshine and least pronounced at 10-12 hours of sunshine (38.6 vs. 31.3, P 0.04). Cognitive functioning was lowest at 0–2 hours of sunshine and highest at 2–4 hours of sunshine (P 0.01). 10 hours of sunshine was associated with higher physical and emotional functioning; however, these results were not statistically significant.

3.3. QoL by seasons

We found no association between season and the individual scales of QoL. Global QoL was higher in summer months than during wintertime (mean 57.5; SD 25.1 vs. 53.8; SD 25.2, P <0.001).

3.4. QoL/symptom burden across lunar phases

Given that both the full moon and new moon occur approximately every 14 days, our study group for this analysis comprised 360 participants (5040/14). Neither QoL nor various symptoms were influenced by lunar phases, including insomnia (data not shown) in our study population.

4. Discussion

The collection of PRO data enables healthcare professionals to evaluate patients' health and well-being. However, the conditions under which PRO data are gathered can impact the results. Considering that PROs are typically influenced by psychological and social factors, accounting for the potential effects of external factors such as weather provides a more comprehensive understanding of PROs and QoL in cancer patients. This consideration enhances the overall interpretation of PROs and facilitates their application in research studies.

Given that climate change is likely the greatest global health threat of the 21st century, it is increasingly important to understand the potential impact of current weather conditions on the QoL. Until now, no studies have attempted to investigate the relationship between weather conditions and PROs in cancer patients. Therefore, our study aimed to determine whether such external factors influence the QoL and PRO measures in this population. Our findings indicate that QoL in cancer patients may be affected by a range of weather-related conditions.

Our results show that global health/QoL was lower in winter than in summer, with the highest scores being documented in June and July. All in all, patients' well-being was best at 25–30 degrees, whereas worse scores for QoL and symptom burden were obtained at 5–10 degrees. Surprisingly, insomnia was most pronounced below 0 degrees. Since the temperature is rather rarely below 0 degrees, this could also be related to fewer evaluations. Nevertheless, it still seems unusual that insomnia was worse in the winter than in the summer as most European households lack air conditioning and the hot temperature can have a negative influence on one's sleep (12). A possible explanation could lay in the fact that our data was collected in the height of the COVID-19 pandemic. Especially in the first few months of our study (winter 2020/2021), the pandemic was still very present, therefore we cannot exclude that patients struggled to sleep due to anxiety.

Our findings align with those of other studies indicating the impact of weather on patients' symptoms in general. For example, weather-related changes and temperature have been reported to affect the QoL of patients with trigeminal neuralgia, as previously noted (3). Nevertheless, our study was primarily centered on the weather of a specific day rather than on changes in weather.

When analyzing the possible impact of sunshine, a tendency for fewer symptoms with greater sunshine duration was observed. This trend may be explained by the role of sunlight in regulating melatonin production. Increased exposure to sunlight during the day can help synchronize the body's circadian rhythms, leading to improved sleep quality (13,14).

Previous research also indicates that there are seasonal variations for some cancer forms regarding the prognosis. Patients diagnosed during the summer and autumn have been shown to have better survival compared to those diagnosed during the winter (7,15). Furthermore, studies have demonstrated that depression is more prevalent during the winter months, while depressive symptoms decline in spring and summer time (16). In our study, patients had lower global health/QoL during the winter, when sunshine duration has a natural and rather narrow limit.

Cognitive functioning was lowest at 0–2 hours of sunshine and highest at 2–4 hours, a result that, while significant, may be due by chance. Although there appears to be a positive trend in cognitive functioning with greater sunshine, the inconsistency between lower functioning at 0 hours and higher functioning at 2 hours raises questions about the validity of this finding.

Although the daily weather varies throughout the year, the climate in our region (east and northern Germany) is generally mild compared to other countries. The effects of weather could therefore be greater in places with more extreme conditions. The following diagram, Figure 1, shows the average temperature (C°) in Greifswald, which is comparable to other neighboring counties our patients resided in.

Our investigation revealed an impact of weather conditions, while lunar phases did not display statistically significant effects. This differs from previous research indicating lunar phases influence sleep (17) and even aortic dissection (18). We did not identify significant effects of

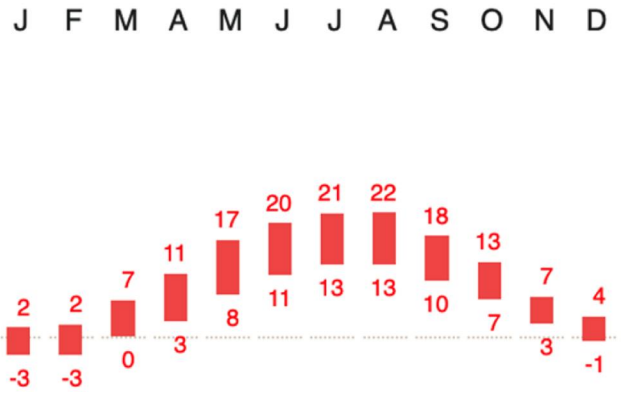

Figure 1. Average temperature (C°) in Greifswald, Germany. Source: wetterkontor.de.

lunar phases on the QoL or symptom burden of cancer patients.

4.1. Possible interventions

Based on our findings demonstrating the impact of weather conditions on QoL and symptom burden of cancer patients, several healthcare strategies could be considered for enhancement. Hospitals and healthcare facilities could educate patients on the potential effects of weather conditions and offer tailored support, such as using light therapy devices during darker months to improve sleep and mood, to more effectively manage symptoms like insomnia.

Clinical staff could provide weather-dependent recommendations to help preserve patient QoL, particularly during colder or extreme weather periods. This might involve adjusting the scheduling of appointments or activities to align with favorable weather conditions. Seasonal care plans could be developed to optimize patient support during winter months, when QoL tends to decline, by incorporating supplementary resources and tailored strategies. For example, recommendations could include scheduling outdoor activities on sunnier days to enhance mood and physical functioning, while offering indoor, low-impact alternatives during colder or harsher weather conditions.

Moreover, hospitals could adapt their architectural and design principles accordingly, as previously suggested (19,20). Specifically, integrating natural light into patient rooms can have substantial benefits for patient well-being. Studies have shown that exposure to natural light not only promotes better psychosocial health but also reduces the need for pain medication (21). Flexible room layouts and climate control systems could also be employed to address seasonal temperature fluctuations and create a more conducive healing environment.

These insights provide a foundation for further research aimed at developing targeted interventions to enhance the QoL of cancer patients based on weather conditions, thereby improving overall health outcomes. Through proactive integration of weather data and corresponding adjustments in healthcare practices, better treatment outcomes could be achieved, leading to maintainable enhancements in patient QoL.

Our study emphasizes the need to consider weather variables in data analysis to gain a deeper understanding of the interactions between environmental factors and health conditions. Future studies may develop standardized methods to adjust for weather variables to enhance the robustness of their findings and improve clinical practice. By integrating weather data into QoL research, a more comprehensive understanding of patient experiences can be achieved, enabling the development of targeted interventions.

4.2. Strengths and limitations

One strength of our study is the large number of participants we were able to recruit. Over a period of one year, we were able to collect more than 5000 questionnaires. Furthermore, weather data were collected in various residential areas making it as representative as possible for the entire study area. We acknowledge the dynamic nature of weather conditions, which can fluctuate within a single day. Furthermore, we recognize that the specific timing of participants filling out the questionnaire may not perfectly align with the moment when weather data was captured. Nevertheless, our data exhibits a discernible trend suggesting the impact of weather on PROs.

Due to the anonymous nature of data collection, medical record information such as treatment details or disease status was not included. While these factors are often considered confounding variables, in our study, they should be viewed as potential effect modifiers or mediators. However, we do not believe that clinical factors confound our analysis. Instead, a relationship may exist between weather conditions and the disease courses, as patients experiencing poorer health might be less likely to attend appointments during adverse weather, such as extreme cold or winter months. Consequently, the absence of certain clinical variables does not inherently bias our findings regarding the impact of weather on patients' QoL.

We couldn't examine potential mediating factors such as housing conditions, health literacy, or daily activities, all of which would offer

valuable insights for providing practical guidance to patients in coping with weather-related changes in QoL. However, self-reported health can offer comprehensive insights into an individual's overall health status in general (22). In addition, our analysis was based on outdoor weather data, although cancer patients likely spend most of their time indoors. However, indoor climatic conditions, including temperature, have been shown to be associated with outdoor climate conditions (23).

The study was conducted solely at two hospitals in Eastern Germany. We acknowledge that including more clinics and a wider geographical area would be necessary to achieve a more comprehensive understanding of the impact of weather on PROs. However, our data still indicate the influence of weather on PROs.

We are unable to determine the distinct number of patients who participated, as the survey was conducted anonymously, and it is possible that some patients completed the questionnaire more than once during multiple hospital admissions. While this constitutes a methodological limitation, we do not view it as bias, as there is no anticipation that multiple participations by patients are distributed unevenly throughout the year, as with singular participations.

We acknowledge that using "season" as a measure is somewhat imprecise because weather conditions can vary significantly between days, even when they fall within the same season. For example, winter-like conditions can persist at the beginning of March, despite the official start of spring. We chose seasons for practical reasons, as they provide a general framework for analyzing trends over time. However, using specific days of the year or more granular data would likely offer a more accurate reflection of short-term weather patterns. Despite this limitation, our results still suggest that seasonality plays a role in QoL outcomes.

While weather can influence symptom severity, its effects may vary depending on geography and exposure. This variability poses challenges for generalizing findings across populations and complicates comparisons. We acknowledge that incorporating weather or climate data into the interpretation of PROs may add complexity to QoL analyses. However, considering weather as a contextual factor could offer valuable insights into external influences on PROs. Although health variables should remain central, weather could enhance our understanding of patient experiences. Further research is needed to integrate this approach effectively.

Our analytic strategy was limited by the data available. We acknowledge that with multiple pairwise comparisons, some of the statistically significant findings may have occurred by chance alone. Nevertheless, a major objective of this study was hypothesis generation to guide future research, with the analysis appropriate for that purpose.

Furthermore, only selected symptoms were included to maintain clarity and specificity. While these choices allowed for a focused investigation, we acknowledge the importance of all scales in capturing the full scope of QoL in cancer patients and recommend their inclusion in future research to provide a more comprehensive understanding of the relationship between environmental factors and QoL.

5. Conclusions

This study aimed to explore the potential impact of external factors, such as weather conditions or phases, on QoL in cancer patients assessed through PROs. Our findings indicate that higher temperatures, sunny days, and summer seasons correlate positively with patients' well-being, whereas lower temperatures and reduced sunlight are associated with poorer QoL. These findings underscore the importance of contextualizing PROs with environmental conditions. Interpreting PROs should consider external environmental factors, acknowledging the context-specific nature of standardized assessments, which may vary across different geographic and climatic settings. We advocate for the consideration of potential interventions, as previously discussed, to mitigate the impact of weather-related conditions on patient outcomes. Our study serves as a hypothesis-generating investigation in a field that currently lacks comprehensive data. Future research should expand on our findings by conducting multicenter studies with even larger samples across diverse geographical regions to deepen our understanding about the complex

interactions between environmental factors and PROs in oncology.

Authors' contributions

Hanna Salm and Daniel Pink conceived and designed the analysis. Hanna Salm performed the analysis. Hanna Salm and Jeanette Bahr collected the data. Jeanette Bahr conducted the statistical calculations, which were then evaluated by Hanna Salm. Hanna Salm and all others wrote the manuscript. All authors reviewed the manuscript.

Ethical approval

The study was approved by the ethics committee of the University Hospital of Greifswald (BB195/20). No identifying patient information was collected.

Disclosure statement

All authors declare that there are no competing interests.

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