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Article in *European journal of pain* (London, England) · September 2024

DOI: 10.1100/ejpr.4735

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## ORIGINAL ARTICLE

# Geographical disparities in fibromyalgia severity: An Italian study

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## Abstract

**Background:** Geographic origin may represent a variable capable of influencing health status. This study aims to investigate the presence of differences of disease severity in Italian patients with fibromyalgia from different macro-regions.

**Methods:** This retrospective, cross-sectional study involved patients included in the Italian Fibromyalgia Registry. Three geographical macro-regions were identified, comprising patients from Northern Italy, Central Italy and Southern Italy. Clinical differences (evaluated through PolySymptomatic Distress Scale [PSD], revised Fibromyalgia Impact Questionnaire [FIQR] and modified Fibromyalgia Assessment Status [FASmod]) among the geographical macro-regions were studied using one-way analysis of variance (ANOVA) and the Scheffé's test.

**Results:** A total of 6095 patients (5719 females and 376 males) were included, with 1957 from Northern Italy, 2979 from Central Italy and 1159 from Southern Italy. All studied clinical indices showed a trend indicative of greater disease severity in Southern Italy, followed by Northern Italy and then Central Italy (mean values for PSD:  $19.97 \pm 6.20$  in Northern Italy,  $18.61 \pm 7.12$  in Central Italy,  $23.01 \pm 5.66$  in Southern Italy). These differences were statistically significant for the overall scores of all studied indices, evaluated with ANOVA (all  $p < 0.001$ ) and in the head to head comparisons, evaluated with Scheffé's test.

**Conclusions:** Geographic background is significantly associated with variations in the severity of fibromyalgia in Italian patients.

**Significance Statement:** This is the first study to demonstrate geographical origin-dependent intra-national differences in the severity of fibromyalgia. The

For affiliations refer to page 8.

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results confirm the necessity of considering fibromyalgia within the context of the biopsychosocial model and of implementing healthcare policies targeted towards the most underserved regions.

## 1 | INTRODUCTION

Fibromyalgia is a condition characterized by the predominant symptom of chronic widespread pain, accompanied by fatigue and non-restorative sleep in most patients (Sarzi-Puttini et al., 2020). The diagnosis of fibromyalgia is currently a purely clinical issue based on the severity of symptoms (Wolfe et al., 2016). Over the past few decades, several sets of diagnostic/classificatory criteria have been proposed, and depending on the set used, the prevalence of fibromyalgia may vary (Jones et al., 2015). In the general population, the prevalence ranges from 2% to 3% (Ablin et al., 2012). In certain populations, such as those with inflammatory arthritis, the prevalence rate increases to over 20% (Di Carlo et al., 2017). The variety of diagnostic and classification criteria, along with the resulting disparities in prevalence, mirror the lack of diagnostic tests and unified pathophysiological theory for fibromyalgia (Clauw et al., 2023).

Various risk factors contribute to the onset of fibromyalgia as well. The clear predominance in favour of the female sex is well-known, along with associations with potential triggers such as early psychological trauma or joint hypermobility (Ablin & Buskila, 2014; Yunus, 2001).

Numerous variables have also been studied in relation to symptom severity. In this regard, it has been demonstrated that clinical variables, such as obesity or overweight, predispose to a higher disease burden (Atzeni et al., 2021). However, an influence on symptom severity may also be exerted by socio-demographic variables, with more severe disease observed in individuals with lower educational levels or in separated or divorced males (Atzeni et al., 2022). In this sense, chronic pain conditions like fibromyalgia are currently framed within the biopsychosocial model, which is a multifactorial context where biological, psychological and social factors interact in determining a clinical phenotype (Nicholas et al., 2019).

The geographic origin of an individual is a variable that encompasses social aspects and can have significant implications for health. Italy is one of the European countries where regional health disparities are among the most pronounced: the percentages of residents reporting poor health vary from 4% in northern regions (e.g. Trentino-Alto Adige) to 10% in southern regions (e.g. Calabria and Sicily) (Franzini & Giannoni, 2010). Regarding fibromyalgia in particular, the potential presence of regional

differences in terms of symptom severity is currently an under-researched topic.

Starting from these considerations, the objective of this study is to investigate the differences in fibromyalgia severity in Italy by grouping regional data into three macro-regions, namely Northern, Central and Southern Italy.

## 2 | METHODS

### 2.1 | Setting and patients

The data analysed in this retrospective, cross-sectional study originate from a national database named the Italian Fibromyalgia Registry (IFR). The data collection period spans from November 2018 to June 2023. The IFR exclusively encompasses Italian rheumatology centers experienced in diagnosing and treating fibromyalgia, currently comprising 57 centers. To ensure certain uniformity among regions, for the objectives of this study, only Italian regions with at least 500 patients included in the IFR were incorporated into each macro-regions. This criterion was met by the Lombardy and Liguria regions for Northern Italy, the Marche, Tuscany and Lazio regions for Central Italy, and the Campania and Sicily regions for Southern Italy. In addition, all the centres included in the present study were actively enrolling patients throughout the entire study period.

The IFR includes adult patients diagnosed with fibromyalgia according to the American College of Rheumatology (ACR) 2010/2011 criteria, regardless of disease severity and ongoing therapy (Wolfe et al., 2010). The IFR is exclusively observational, focusing specifically on the collection of clinimetric data and does not encompass any interventional objectives (Salaffi, Farah, et al., 2020). The patient population included in the IFR refers to the so-called 'primary' fibromyalgia, excluding patients with rheumatological conditions (e.g. chronic inflammatory joint diseases, connective tissue diseases and vasculitis), neurological disorders (e.g. demyelinating diseases, dementias), psychiatric conditions (e.g. psychosis, severe depression) or more broadly internal medical conditions (e.g. congestive heart failure, uncontrolled endocrine disorders and ongoing malignancies) capable of interfering with clinimetric evaluation. In each centre, the fulfilment of inclusion and exclusion criteria was verified by a rheumatologist with at least 10 years of clinical experience.

All patients included in the IFR provided written informed consent. The procedures conducted within the IFR were approved by the ethical committee of the coordinating center (Regional Ethics Committee, number 1970/AV2, of the coordinating center of the IFR—Rheumatology Clinic of the Polytechnic University of the Marche), and this approval was subsequently obtained from the ethics committees of all other centres.

## 2.2 | Assessment

Upon entry into the IFR and during subsequent evaluations, anonymous collection of demographic variables such as age, gender, education level, marital status, as well as clinical metrics including the Widespread Pain Index (WPI), Symptom Severity Scale (SSS) referring to the PolySymptomatic Distress scale (PSD) from the ACR 2010/2011 criteria, the revised FIQ (FIQR) and the modified Fibromyalgia Assessment Status (FASmod) are gathered for each patient (Salaffi et al., 2013; Salaffi, Di Carlo, et al., 2020; Wolfe et al., 2010). For the purposes of this study, data from each patient's first entry into the IFR were used.

### 2.2.1 | PSD

The PSD is essentially based on the diagnostic criteria ACR 2010/2011, comprising the WPI that assesses tenderness in 19 body areas (each area registering 1 for tenderness, range 0–19) and the SSS, which evaluates the severity of non-pain symptoms like fatigue, fibro fog and cognitive disturbances (each on a scale from 0 to 3, range 0–12). The final score, ranging from 0 to 31, is not only used for diagnostic purposes but can also be employed for a clinical assessment of disease severity (Wolfe et al., 2010).

### 2.2.2 | FIQR

The FIQR investigates the severity of fibromyalgia through 21 items represented by 11-point numerical rating scales (NRS, 0–10 scales), referring to the last 7 days. Three health domains are covered, with the first nine items dealing with physical function, followed by two items covering overall general health status and the last domain focusing on 10 items referring to symptoms. The total FIQR score ranges from 0 to 100, with higher scores indicating greater disease severity. The overall score is the algebraic sum of the individual domains, where the score of the physical function domain has to be divided by three, the two items of the overall impact are considered as they are, while the

score of the symptom domain has to be divided by two (Salaffi et al., 2013).

### 2.2.3 | FASmod

The FASmod is a revised and simplified version of the Fibromyalgia Assessment Status (FAS). FASmod is made by two sections recalling symptoms over the last 7 days: the first one is represented by two 11-points NRS scales investigating fatigue and unrefreshing sleep; the second is a front-back manikin with 19 body areas, realized to analyse widespread pain, where patients are asked to rate the presence/absence of pain in each area (the presence of pain on each area is scored 1). The final score, ranging from 0 to 39, is the sum of the two NRS scales and the painful areas of the manikin (Salaffi, Di Carlo, et al., 2020).

## 2.3 | Statistical analysis

The results of the studied variables are presented as means and standard deviations (SD) and as medians and interquartile ranges (IQR), assessing normal distribution using the Shapiro–Wilk test.

To compare differences in disease severity (PSD and its subscales, FASmod, and FIQR and its subscales) among macro-regions, one-way analysis of variance (ANOVA) was employed. Meanwhile, the Scheffé's test was utilized for one-to-one comparisons between macro-regions, specifically comparing North versus Centre, North versus South and Centre versus South.

The chi-squared test was employed to compare macro-regions on variables inferred from the IFR, which are potential factors influencing disease severity. Specifically, the variables analysed were educational status (categorized as elementary school certificate, middle school certificate, high school diploma or university degree), marital status (categorized as married, divorced, widowed, single or other) and body weight (categorized as underweight for BMI <18.5 kg/m<sup>2</sup>, normal weight for BMI between 18.5 and 24.9 kg/m<sup>2</sup>, overweight for BMI between 25.0 and 29.9 kg/m<sup>2</sup> and obese for BMI >29.9 kg/m<sup>2</sup>).

Statistical significance was set at  $p < 0.05$  for all conducted analyses. Analyses have been conducted with MedCalc, version 19.6.4 (MedCalc Software, Mariakerke, Belgium).

## 3 | RESULTS

The study included 6095 patients, comprising 5719 (93.83%) females and 376 (6.17%) males, from the

following macro-regions: 1957 (32.10%) patients from Northern Italy (1862 females and 95 males), 2979 (48.88%) patients from Central Italy (2771 females and 208 males) and 1159 (19.02%) patients from Southern Italy (1086 females and 73 males). The mean age was  $54.33 \pm 11.77$  years.

The mean values ( $\pm$  SD) of the investigated clinical indices were as follows: FIQR total score  $62.64 \pm 21.43$ , FIQR physical function  $17.41 \pm 7.37$ , FIQR symptoms  $33.26 \pm 10.15$ , FIQR overall health status  $11.99 \pm 5.78$ , FASmod  $26.64 \pm 7.96$ , PSD  $19.88 \pm 6.77$ , WPI  $11.60 \pm 4.84$  and SSS  $8.28 \pm 2.95$  (Table 1).

All the clinical indices considered showed differences according to the geographical macro-region evaluated. Specifically, both FIQR (and its subscales), FASmod and PSD (including its subscales WPI and SSS) revealed higher scores, indicating greater disease severity, in Southern Italy, followed by Northern Italy and then Central Italy (Table 2, Figure 1a,b).

**TABLE 1** Demographic and clinical characteristics of the whole study population.

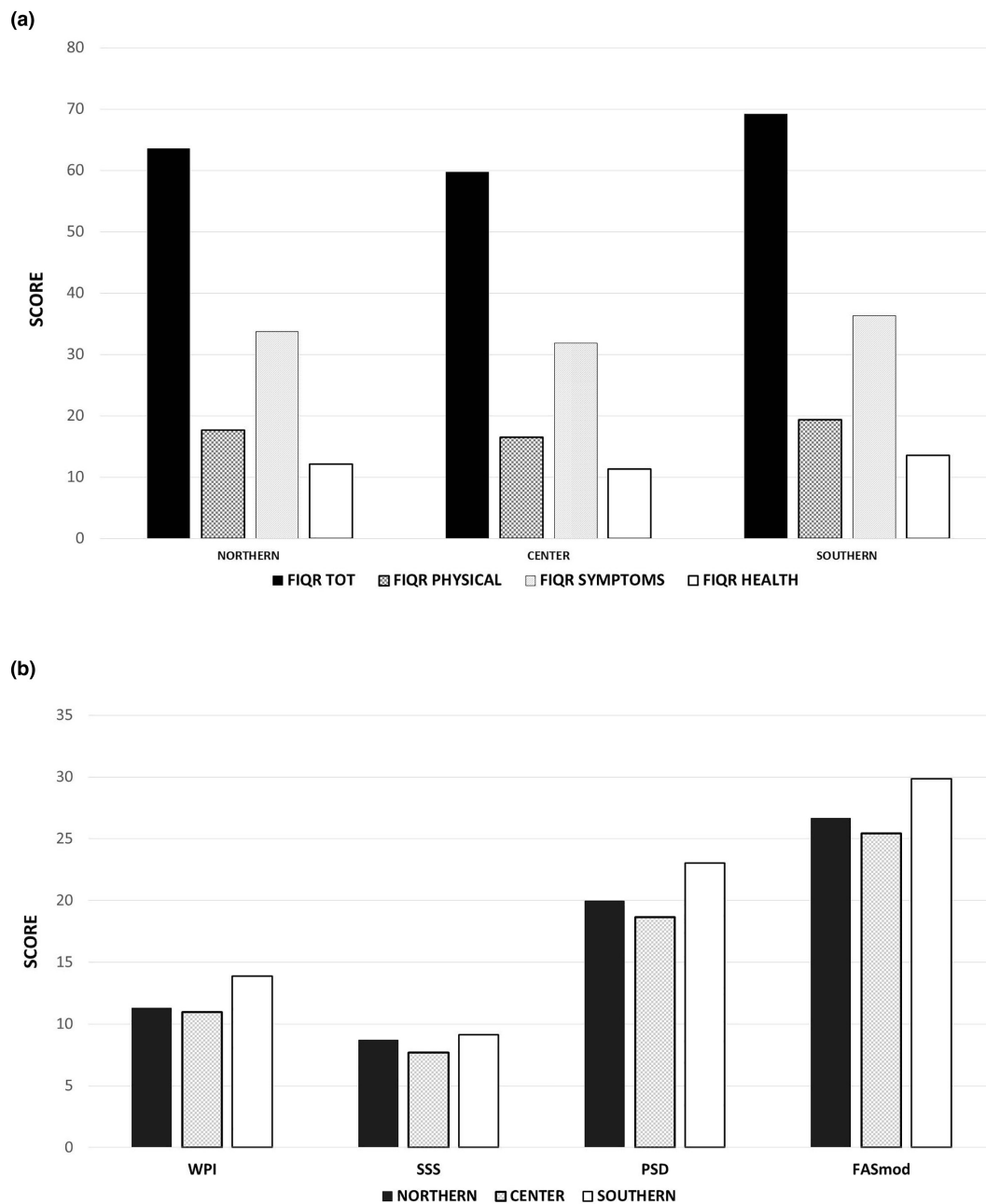
Variables	Mean (%)	SD
Age	54.33	11.77
Sex		
Female	5719 (93.83)	-
Male	376 (6.17)	-
Marital status		
Married	4603 (75.52)	-
Single	854 (14.02)	-
Widow	138 (2.26)	-
Divorced	500 (8.20)	-
Education level		
Primary school	231 (3.79)	-
Secondary school	1461 (23.97)	-
High school	2665 (43.72)	-
Degree	1738 (28.51)	-
BMI ( $\text{kg}/\text{m}^2$ )	27.85	8.89
WPI	11.60	4.84
PSD	19.88	6.77
FASmod	26.64	7.96
FIQR total score	62.64	21.43
FIQR physical function	17.41	7.37
FIQR overall health status	11.97	5.78
FIQR symptoms	33.26	10.15

Abbreviations: BMI, body mass index; FASmod, modified Fibromyalgia Assessment Status; FIQR, revised Fibromyalgia Impact Questionnaire; PSD, PolySymptomatic Distress scale; SD, standard deviation; WPI, Widespread Pain Index.

**TABLE 2** Mean values of FIQR (and its subscales), FASmod and PSD (and its subscales WPI and SSS), distributed across geographical macro-regions.

Geographical macro-regions	FIQR total		FIQR physical function		FIQR symptoms		FIQR overall impact		FASmod		PSD		WPI		SSS	
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Northern Italy	63.53 (20.08)	17.69 (7.11)	33.71 (9.25)	12.13 (5.69)	26.67 (7.33)	19.97 (6.20)	11.29 (4.77)	8.68 (2.44)								
Central Italy	59.54 (22.70)	16.48 (7.59)	31.80 (10.89)	11.29 (5.98)	25.38 (8.50)	18.61 (7.12)	10.93 (4.81)	7.68 (3.30)								
Southern Italy	69.11 (18.52)	19.32 (6.81)	36.26 (8.88)	13.57 (5.06)	29.83 (6.49)	23.01 (5.66)	13.86 (4.38)	9.15 (2.42)								

Abbreviations: FASmod, modified Fibromyalgia Assessment Status; FIQR, revised Fibromyalgia Impact Questionnaire; PSD, PolySymptomatic Distress scale; SD, standard deviation; SSS, Symptom Severity Scale; WPI, Widespread Pain Index.



**FIGURE 1** Differences in mean values of FIQR (and subscales) (a), PSD (and subscales) and FASmod (b) according to the geographical macro-regions. FIQR, revised Fibromyalgia Impact Questionnaire; WPI, Widespread Pain Index; SSS, Symptom Severity Scale; PSD, PolySymptomatic Distress scale; FASmod, modified Fibromyalgia Assessment Status.

The ANOVA has documented statistically significant differences among macro-regions. In each individual comparison between macro-regions, the differences for the studied clinical indices were significant, all with  $p < 0.0001$ , concerning Centre versus South and North versus South. The smallest difference ( $p = 0.0134$ ) emerged in the comparison of WPI between North versus Centre (Table 3).

Potential factors influencing the severity of FM, such as educational level, marital status and body weight

categories, did not show significant differences across the three macro-regions ( $p > 0.05$  for all the categorical variables).

## 4 | DISCUSSION

This study has demonstrated how geographical background is significantly associated with variations in the severity of fibromyalgia in Italian patients. To the best

**TABLE 3** One-way analysis of variance data for PSD (its subscales), FIQR, FASmod and among geographical macro-regions and significance of one-to-one comparisons (Scheffé's test) between macro-regions.

Clinimetric indices	ANOVA		Scheffé's test		
	F-ratio	p values	North versus Centre	North versus South	Centre versus South
			p values	p values	p values
PSD	187.66	<0.001	<0.0001	<0.0001	<0.0001
WPI	167.31	<0.001	0.0134	<0.0001	<0.0001
SSS	136.10	<0.001	<0.0001	<0.0001	<0.0001
FIQR	88.02	<0.001	<0.0001	<0.0001	<0.0001
FASmod	136.83	<0.001	0.0001	<0.0001	<0.0001

Abbreviations: ANOVA, one-way analysis of variance; FASmod, modified Fibromyalgia Assessment Status; FIQR, revised Fibromyalgia Impact Questionnaire; PSD, PolySymptomatic Distress scale; SSS, Symptom Severity Scale; WPI, Widespread Pain Index.

of our knowledge, the data from the IFR are the first to demonstrate a geographical characterization of fibromyalgia severity. In particular, this trend is shown: a higher disease severity in patients from Southern Italy, followed by those from Northern Italy and then individuals from Central Italy, who exhibit a less severe condition.

Fibromyalgia, like all conditions characterized by chronic pain, should be considered within the context of the biopsychosocial model. While significant efforts have been made to elucidate the neurobiological and psychological explanations for fibromyalgia, arguably less has been done to understand how social reasons impact the severity of the disease. Certainly, we are still quite far from an integrated model that can be widely applied in daily clinical practice for patients (Pontes-Silva, 2023).

The reasons for these macro-regional differences probably lie not in the biological or demographic characteristics of the patients included in the IFR, but more generally in the social and healthcare context. Geographical differences in terms of fibromyalgia severity need to be framed on multiple levels: on one hand, there are psychosocial variables capable of negatively impacting the severity of a condition primarily characterized by chronic pain; on the other hand, there are also disparities that account for significant variability in access to healthcare systems.

In recent decades, there has been an increasing acknowledgment of the influence of geographical settings on health outcomes, encompassing intricate interplays of social, genetic, environmental and behavioural processes.

Economic deprivation and the difficulties encountered in the place of living are important aspects of chronic pain. Jacobs and colleagues documented an increased severity of fibromyalgia, in terms of pain severity and interference in daily life, among African American women and

those with low income (Jacobs et al., 2023). The role of economic aspects also emerged from a study conducted in Arizona which revealed how financial constraints and concerns about one's financial situation are two determinants capable of negatively influencing the daily assessment of pain. This observation has been documented in two chronic pain conditions such as osteoarthritis and fibromyalgia (Rios & Zautra, 2011).

From a historical point of view, socioeconomic conditions within Italy have disadvantaged the Southern regions. It has been demonstrated that residing in areas characterized by increased poverty, higher unemployment rates and greater inequalities correlates with poorer health outcomes (Franzini & Giannoni, 2010).

Even socioeconomic disadvantages in childhood would seem to impact pain-related cognitions in later years. Early difficult conditions result in higher future levels of pain catastrophizing, higher perceived sensitivity to pain and greater pain-related fear (Simon et al., 2022). In fact, it is well known that, in addition to the biological component, cognitive and emotional factors significantly affect perception of pain. Race, ethnicity and culture have a crucial impact on illness beliefs, health care preferences, help-seeking behaviours and acceptance of medical interventions (Orhan et al., 2018).

A recent study, conducted using artificial intelligence techniques, has revealed that mental health factors exhibit a stronger correlation with fibromyalgia severity compared to pain factors. Consequently, it is unsurprising to find that FIQR depression scores are higher in the Southern than in the Northern and Central regions (Moreno-Sánchez et al., 2024).

Beyond how social factors can influence psychological ones, an additional issue is represented by the inter-regional diversity in healthcare access. Although in Italy, healthcare access is universally guaranteed by the National Health System, the decentralization of healthcare to

individual regions has led to significant inter-regional variability. As a result, some regions have been able to positively exploit this aspect, while others have failed to adapt to the needs of their population.

The disparities in unmet health needs are significant between the Northeast and the South of Italy, with the disadvantaged South where regional health systems are characterized by poor performance but high levels of spending (Bruzzi et al., 2022; Cavalieri, 2013). An Italian study investigated whether the probability of facing four barriers to healthcare utilization (drugs or exams costs, long waiting lists or difficult access to the healthcare service) varies among individuals with different socio-economic status and care needs, across Italian geographical areas. The study showed an increasing North–South gradient for all the considered barriers, with a higher probability of facing a barrier due to exams' costs for females and people with a low income (Matranga & Maniscalco, 2022). With regard to regional healthcare access, a study referencing the year 2013 estimated that, in the Italian context, the waiting time for access to a diagnostic test is minimal for the regions of the Northeast and maximum in the regions of the South, with the highest peaks concerning the Molise region (Landi et al., 2021).

A significant challenge that has emerged within Italy's National Health System in recent years is also the shortage of medical practitioners. The retirements have not been compensated by a sufficient number of new specialists. These shortages have had an adverse impact nationwide but have had (and continue to have) particularly serious and negative effects not only in the area of fibromyalgia care but especially in those regions of Southern Italy that were already starting from a deficit position (Pennisi et al., 2023).

What is certain is that the more vulnerable the population is from a socioeconomic standpoint, the longer the wait. Longer waits, even just for a fibromyalgia diagnosis, translate into greater disease severity. Diagnosing fibromyalgia within the first 2 years from the onset of symptoms has been shown to be associated with a reduction in the SSS and the number of tender points (Moshrif et al., 2023).

A certain role in influencing the severity of fibromyalgia can also be explained by the residential context of the patients, that is, whether they reside in a rural or urban setting. Patients living in rural areas, compared to those in urban areas, describe greater pain severity but also a greater acceptance of it and reduced levels of physical and mental fatigue (Catalá et al., 2021). These aspects could partly explain why data related to a lesser disease severity, present for all clinimetric indexes, is observed in the population of Central Italy when compared to that of Northern and Southern Italy. Compared to Central Italy, in Northern

Italy (particularly in Northwestern Italy, which includes Lombardy and Liguria) and in Southern Italy there is a higher percentage of 'urban' and 'extremely urban' municipalities (Anania & Tenuta, 2008). However, although Northern Italy and Southern Italy are more urbanized geographical areas than Central Italy, patients were not categorized on the basis of origin (urban vs. rural), so this is essentially a hypothesis that may explain some of the variability.

Investigating geographical disparities in chronic pain has significant implications for health policies. The Pain Divide study, conducted in England, demonstrated that the prevalence and impact of chronic pain are greater in the Northern regions of England compared to the South, and that in areas with a higher prevalence of chronic pain, there is significantly more prescription of opioids (Todd et al., 2018). Wide regional variabilities are also found in opioid prescriptions in the specific case of fibromyalgia. Painter and colleagues revealed that the prescription of opioids in patients with fibromyalgia is largely variable across the United States of America and is lower in those states where the prevalence of fibromyalgia and the number of general practitioners are higher, two contextual and structural variables that go beyond the physician-patient relationship (Painter et al., 2013).

Different limitations of the study need mentioning. Although a substantial number of cases were analysed, patients were compared for a limited number of variables potentially influencing disease severity (e.g. marital status, educational level, BMI category). Other variables capable of influencing the symptoms of fibromyalgia, such as disease duration, race/ethnicity, cigarette smoking, socioeconomic level and adverse childhood experiences are not included in the IFR and therefore could not be considered. Additionally, only seven out of the 20 Italian regions were included, attempting to maintain a certain level of distribution homogeneity (two Northern, three Central and two Southern regions). However, these regions were chosen based on higher patient recruitment and affiliation with high-volume reference centers.

In conclusion, this study demonstrates geographic disparity in the severity of fibromyalgia among Italian patients, where individuals from Southern Italy generally exhibit worse symptoms compared to those from the North, who in turn fare worse than those from the Central regions. These results could be explained by referring to psychosocial factors, as well as to structural variables related to the inter-regional differences of healthcare systems. Considering the high prevalence of fibromyalgia and its negative impact on function and quality of life of affected patients, the results of this study could represent a first step towards more adaptable regional health



policies tailored to the needs of each region, aimed at improving care where fibromyalgia has shown greater severity.

## AUTHOR CONTRIBUTIONS

Prof. Di Carlo, Prof. Salaffi, Prof. Atzeni and Dr. Alciati gave substantial contributions to study conception and design. All Authors gave substantial contribution in acquisition of data. Prof. Di Carlo, Dr. Farah and Prof. Salaffi gave substantial contributions to analysis and interpretation of data. Dr. Farah and Prof. Salaffi had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Prof. Di Carlo drafted the article, all Authors were involved in revising it critically for important intellectual content. All authors approved the final version to be published.

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## ACKNOWLEDGEMENTS

The Italian Fibromyalgia Registry is financially supported by the Società Italiana di Reumatologia (SIR). Open access publishing facilitated by Università Politecnica delle Marche, as part of the Wiley - CRUI-CARE agreement.

## CONFLICT OF INTEREST STATEMENT

No financial or non-financial conflicts of interest to be declared.

## DATA AVAILABILITY STATEMENT

Data will be shared upon request to the corresponding Author.

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**How to cite this article:** Di Carlo, M., Farah, S., Atzeni, F., Alciati, A., Di Franco, M., Iannuccelli, C., Bazzichi, L., Bianchi, G., Giovale, M., Tirri, R., Guiducci, S., Guggino, G., Franceschini, F., Foti, R., Lo Gullo, A., Biasi, G., Gremese, E., Dagna, L., Tirri, E., ... Salaffi, F. (2024). Geographical disparities in fibromyalgia severity: An Italian study. *European Journal of Pain*, 00, 1–10. <https://doi.org/10.1002/ejp.4735>