FIBROMIALGIA:
CLASSIFICAZIONE ED EPIDEMIOLOGIA DELLA SINDROME
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• FM
• fibromyalgia syndrome (FMS)
• fibrositis and fibromyositis terms no longer used as fibromyalgia does not appear to be an inflammatory process
• nonarticular rheumatism
• psychogenic rheumatism
FIBROMYALGIA

chronic functional illness marked by widespread musculoskeletal pain
often associated with other symptoms such as fatigue
sleep difficulties
cognitive dysfunction
depressed mood or depressive episodes

comprising 1) a history of chronic widespread pain (pain present for at least 3 months and affecting the left and right sides of the body, above and below the waist, and in the axial skeleton) plus 2) pain on digital palpation in 11 of 18 specific sites

chronic widespread pain: definition

Widespread pain is identified when all of the following are present: pain on the left side of the body, pain on the right side of the body, pain above the waist, and pain below the waist. In addition, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) has to be present.

But there were several definitions for CWP.

The prevalence of CWP varies widely depending on the definition used to identify this symptom complex. The prevalence of FMS Using CWP as a diagnostic criterion also has wide variation.

Butler S et al. Chronic widespread pain—the need for a standard definition. Pain 2016; 157: 541-3
Chronic primary pain is pain in 1 or more anatomic regions that persists or recurs for longer than 3 months and is associated with significant emotional distress or significant functional disability (interference with activities of daily life and participation in social roles) and that cannot be better explained by another chronic pain condition.

which differed from the 1990 criteria in 2 main respects: 1) the 2010 criteria operationalized the measurement of chronic widespread pain, 2) more fundamentally—they did away with the requirement for a tender point examination in favor of an assessment of fatigue, waking unrefreshed, cognitive symptoms, and somatic symptoms in general.
a patient would be classified as having fibromyalgia if a
clinician determined that they had
1) high levels of pain plus moderate levels of symptoms
or moderate levels of pain plus high levels of symptoms,
2) symptoms present at a similar level for 3 months,
3) no disorder that would otherwise explain the pain
a modified version of the 2010 criteria that relied on
1) self-reported pain
2) a simplified self-reported version of somatic symptoms
EPIDEMIOLOGY

• In 26 studies worldwide Global mean prevalence 2.7% (ranging from 0.4% in Greece to 9.3% in Tunisia)
• The mean rate: 3.1% in the Americas, 2.5% in Europe, 1.7% in Asia
• Approximately 2% of the general population in the United States suffers from fibromyalgia

• Similar prevalence rates have been reported in Canada (3.3%), Brazil (2.5%)
• and Western European countries, including Germany (3.2%), Spain (2.4%), Italy (2.2%), Sweden (2.5%), France (1.4%), Denmark (<1%) and Portugal (3.6%)

In Turkey 8.8%
In Africa (Tunisia) 9.3%
• **Who is most affected:**
• more common in females:
  4.1% in women, 1.4% in men – F/M= 3:1
• ages 20-60 years, especially middle age
The prevalence of fibromyalgia according to the ACR modified 2010 criteria was assessed in a large population survey in Germany.

Fifty-two of 2,445 participants were found to have fibromyalgia, yielding a prevalence of 2.1%.

The Prevalence of Fibromyalgia in the General Population

A Comparison of the American College of Rheumatology 1990, 2010, and Modified 2010 Classification Criteria

Gareth T. Jones,1 Fabiola Atzeni,2 Marcus Beasley,1 Elisa Flüß,1 Piercarlo Sarzi-Puttini,3 and Gary J. Macfarlane4

Objective. The American College of Rheumatology (ACR) 1990 fibromyalgia classification criteria are based on the presence of widespread pain and tenderness. In 2010, new criteria were proposed that focused more on multiple symptoms, and these criteria were later modified to require only self-report of symptoms. The current study aimed to determine the population prevalence of fibromyalgia and to compare differences in prevalence using the alternative criteria.

Methods. A cross-sectional survey was conducted. Questionnaires, including items on pain, symptoms, and rheumatologic diagnoses, were mailed to 4,600 adults in northeast Scotland. Participants who had chronic widespread pain or those who met the modified 2010 criteria, plus a subsample of other participants, were invited to attend a research clinic. Attendees completed an additional questionnaire and underwent a rheumatologic examination, and their signs and symptoms were classified according to the ACR 1990, 2010, and modified 2010 criteria. The prevalence of fibromyalgia according to each set of criteria was calculated, weighting back to the target population by age, sex, and area of residence.

Results. Of 1,604 questionnaire participants, 269 were invited to attend the research clinic, and 104 (39%) attended; 32 of these subjects (31%) met ≥1 set of fibromyalgia criteria. The prevalence of fibromyalgia according to the 1990, 2010, and modified 2010 criteria was 1.7% (95% confidence interval [95% CI] 0.7–2.8), 1.2% (95% CI 0.3–2.1), and 5.4% (95% CI 4.7–6.1), respectively. The ratio of females to males was 13.7:1, 4.8:1, and 2.3:1 of those meeting the respective criteria sets.

Conclusion. Fibromyalgia prevalence varies with the different sets of classification criteria applied. In particular, prevalence is higher and a greater proportion of men are identified with the modified 2010 criteria as compared to the criteria sets requiring clinician input. This has important implications for the use of the new criteria, both in research and in clinical practice.
Prevalence of fibromyalgia, according to the ACR criteria set used*

<table>
<thead>
<tr>
<th>ACR criteria set</th>
<th>Prevalence (95% CI)</th>
<th>Female-to-male ratio</th>
<th>% with rheumatologic diagnoses†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990 criteria</td>
<td>1.7 (0.7–2.8)</td>
<td>13.7</td>
<td>55</td>
</tr>
<tr>
<td>2010 criteria</td>
<td>1.2 (0.3–2.1)</td>
<td>4.8</td>
<td>28</td>
</tr>
<tr>
<td>Modified 2010</td>
<td>5.4 (4.7–6.1)</td>
<td>2.3</td>
<td>45</td>
</tr>
</tbody>
</table>

* ACR = American College of Rheumatology; 95% CI = 95% confidence interval.
† Proportion of respondents who had a positive response to the question “Have you ever been told by a healthcare provider that you have any of the following diseases: osteoarthritis, rheumatoid arthritis, osteoporosis, lupus, scleroderma, ankylosing spondylitis, gout, or fibromyalgia?”
• Of 4,600 questionnaires distributed to adults, in Northeast Scotland
• 1,604 (36.3%) of the remaining 4,417 eligible invitees returned a completed questionnaire.
• The median age of the respondents was 55 years (interquartile range [IQR] 44–65 years),
• 55% were female,
• Of the questionnaire respondents, 269 were invited to attend the research clinic for a clinical examination;
• 104 of them (39%) attended, and 32 of those (31%) were found to meet at least 1 set of criteria for fibromyalgia: 11 participants met the ACR 1990 criteria, 7 met the ACR 2010 criteria, and 27 met the ACR modified 2010 criteria.
Compared to the ACR 1990 criteria, which was used as the gold standard, the ACR 2010 criteria had a sensitivity of 55% and a specificity of 99%; in contrast, these values for the modified 2010 criteria were 64% and 78%, respectively.
**Conclusion.** Fibromyalgia prevalence varies with the different sets of classification criteria applied. In particular, prevalence is higher and a greater proportion of men are identified with the modified 2010 criteria as compared to the criteria sets requiring clinician input.
Identifying the symptom and functional domains in patients with fibromyalgia: results of a cross-sectional Internet-based survey in Italy

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Objective: The aims of this cross-sectional study were to investigate the usefulness of using an Internet survey of patients with fibromyalgia in order to obtain information concerning symptoms and functionality and identify clusters of clinical features that can distinguish patient subsets.

Methods: An Internet website has been used to collect data. Fibromyalgia Impact Questionnaire Revised version, self-administered Fibromyalgia Activity Score, and Self-Administered Pain Scale were used as questionnaires. Hierarchical agglomerative clustering was applied to the data obtained in order to identify symptoms and functional-based subgroups.

Results: Three hundred and fifty-three patients completed the study (85.3% women). The highest scored items were those related to sleep quality, fatigue/energy, pain, stiffness, degree of tenderness, balance problems, and environmental sensitivity. A high proportion of patients reported pain in the neck (81.4%), upper back (70.1%), and lower back (83.2%). A three-cluster solution best fitted the data. The variables were significantly different ($P<0.0001$) among the three clusters: cluster 1 (117 patients) reflected the lowest average scores across all symptoms, cluster 3 (116 patients) the highest scores, and cluster 2 (120 patients) captured moderate symptom levels, with low depression and anxiety.

Conclusion: Three subgroups of fibromyalgia samples in a large cohort of patients have been identified by using an Internet survey. This approach could provide rationale to support the study of individualized clinical evaluation and may be used to identify optimal treatment strategies.

Keywords: fibromyalgia, Internet, FIQR, FAS, cluster analysis, SAPS, pain
**Criteria**

A patient satisfies modified 2016 fibromyalgia criteria if the following 3 conditions are met:

1. Widespread pain index (WPI) ≥ 7 and symptom severity scale (SSS) score ≥ 5 OR WPI of 4–6 and SSS score ≥ 9.
2. Generalized pain, defined as pain in at least 4 of 5 regions, must be present. Jaw, chest, and abdominal pain are not included in generalized pain definition.
3. Symptoms have been generally present for at least 3 months.
4. A diagnosis of fibromyalgia is valid irrespective of other diagnoses. A diagnosis of fibromyalgia does not exclude the presence of other clinically important illnesses.

**Ascertainment**

1. **WPI**: note the number of areas in which the patient has had pain over the last week. In how many areas has the patient had pain? Score will be between 0 and 19.

   - Left upper region (Region 1)
   - Jaw, left
   - Shoulder girdle, left
   - Upper arm, left
   - Lower arm, left

   - Right upper region (Region 2)
   - Jaw, right
   - Shoulder girdle, right
   - Upper arm, right
   - Lower arm, right

   - Axial region (Region 5)
   - Neck
   - Upper back
   - Lower back
   - Chest
   - Abdomen

2. **Symptom severity scale (SSS) score**

   - Fatigue
   - Waking unrefreshed
   - Cognitive symptoms

   For each of the 3 symptoms above, indicate the level of severity over the past week using the following scale:
   - 0 = No problem
   - 1 = Slight or mild problems, generally mild or intermittent
   - 2 = Moderate, considerable problems, often present and/or at a moderate level
   - 3 = Severe: pervasive, continuous, life-disturbing problems

   The symptom severity scale (SSS) score: is the sum of the severity scores of the 3 symptoms (fatigue, waking unrefreshed, and cognitive symptoms) (0–9) plus the sum (0–3) of the number of the following symptoms the patient has been bothered by that occurred during the previous 6 months:
   - Headaches (0–1)
   - Pain or cramps in lower abdomen (0–1)
   - And depression (0–1)

   The final symptom severity score is between 0 and 12.

   The fibromyalgia severity (FS) scale is the sum of the WPI and SSS.

   *Not included in generalized pain definition.*
### 2016 Changes to modified ACR fibromyalgia diagnostic criteria

This revision makes the following changes to the fibromyalgia criteria shown in Table 3.

1. Changes criterion 1 to “widespread pain index (WPI) ≥ 7 and symptom severity scale (SSS) score ≥ 5 OR WPI 4–6 and SSS score ≥ 9” (WPI minimum must be ≥ 4 instead of previous ≥ 3).
2. Adds a generalized pain criterion (criterion 2), and one that is different from the 1990 widespread pain definition. The definition is: “Generalized pain is defined as pain in at least 4 of 5 regions. In this definition, jaw, chest, and abdominal pain are not evaluated as part of the generalized pain definition.”
3. Standardizes and makes 2010 and 2011 criterion (criterion 3) wording the same: “Symptoms have been generally present for at least 3 months.”
4. Removes the exclusion that regarding disorders that could (sufficiently) explain the pain (criterion 4) and adds the following text: “A diagnosis of fibromyalgia is valid irrespective of other diagnoses. A diagnosis of fibromyalgia does not exclude the presence of other clinically important illnesses.”
5. Adds the fibromyalgia symptom (FS) scale as a full component of the fibromyalgia criteria.
6. Creates one set of criteria instead of having separate physician and patient criteria by replacing the physician estimate of somatic symptom burden with ascertainment of the presence of headaches, pain or cramps in lower abdomen, and depression during the previous 6 months.

Forms and pain maps to aid in ascertainment are available at [this link](https://medicine.umich.edu/sites/default/files/content/downloads/MM%20w%20SSI%202016.pdf) (Michigan Pain Map) and [this link](https://www.arthritis-research.org/sites/default/files/editor/FM%20Diagnostic%20Criteria%20Survey%20Questionnaire%2020%282013%29.pdf) (National Data Bank for Rheumatic Diseases (NDB) fibromyalgia diagnosis form).

The fibromyalgia symptom (FS) scale is also known as the polysymptomatic distress (PSD) scale.
These criteria can continue to serve as diagnostic criteria when used in the clinic, but also as classification criteria when used for research.

The requirement for generalized pain (pain in 4 of 5 regions) to insure that regional pain syndromes are not captured by the criteria.

The return to original 1990 recommendation that “fibromyalgia remains a valid construct irrespective of other diagnoses”
• **Associated conditions:**
• **associated symptoms and presentations**
  – *noncardiac chest pain*
  – *heartburn*
  – *palpitations*
  – *irritable bowel syndrome (IBS)*
    • *dysmenorrhea*
    • *interstitial cystitis-Painful bladder syndrome*
    • *endometriosis*
    • *vulvar vestibulitis*
    • *vulvodynia*
  – *chronic prostatitis*

• **psychiatric disorders**
  – *anxiety disorder, such as generalized anxiety disorder*
  – *mood disorder, such as depression*
  – *posttraumatic stress disorder (PTSD)* may be common in fibromyalgia patients
    • *questionnaire study of 77 fibromyalgia patients*
    • *57% had PTSD symptoms*
    • *prevalence of PTSD higher than general population but no control group studied*

Frequency of concomitant fibromyalgia in rheumatic diseases: Monocentric study of 691 patients

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Abstract

**Objective:** Fibromyalgia (FM) is a confounding factor for diagnosing and assessing rheumatic disease activity. This study sought to assess the extent of this syndrome in rheumatism patients at a French rheumatology department.

**Method:** This monocentric epidemiological study enrolled all patients consulting due to rheumatoid arthritis (RA), spondyloarthritis (SpA), or connective tissue disease (CTD). FM diagnosis was confirmed or excluded according to the rheumatologist opinion and the 1990 American College of Rheumatology (ACR) criteria.

**Results:** We enrolled 691 patients, including 451 women (65.3%), with a mean age of 55.8 years (18–93). Of the enrolled patients, 325 presented with RA, 298 SpA [59 psoriatic arthritis (PsA), 137 ankylosing spondylitis (AS), 64 non-radiographic SpA (nr-SpA), and 38 peripheral SpA], and 71 CTD. The rheumatologist established FM diagnosis in 97 patients (14%), while 55 (8%) fulfilled the 1990 ACR criteria. The frequency of FM was lower in RA patients (4.9% by 1990 ACR criteria; 7.7% by expert opinion) compared to SpA (11.1% by 1990 ACR, \( p < 0.05 \); 17.5% by expert opinion, \( p < 0.003 \)) and CTD (11.3% by 1990 ACR, non-significant; 28.2% by expert opinion, \( p < 0.001 \)). In the SpA subgroups, FM was more common in the nr-SpA than in PsA or AS (23.9%, 9.6%, and 6.4%, by 1990 ACR, \( p = 0.001 \); 37.3%, 13.5%, and 7.2%, by expert opinion, \( p < 0.001 \)).

**Conclusion:** FM-like symptoms are commonly associated with rheumatic diseases. The frequency of FM is particularly high in non-radiographic axial SpA, thus raising questions about the specificity of the Assessment of SpondyloArthritis International Society (ASAS) classification criteria.
FM is diagnosed

• In rheumatoid arthritis (6.6–22.4% of patients), with an incidence of 7%, maximal in the first year following RA diagnosis
• in ankylosing spondylitis (4–15% of patients)
• in systemic lupus erythematosus (SLE) (6.2–24% of patients)
• in Sjögren’s syndrome (12–30%)
Demographic and clinical characteristics of the population.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years ± standard deviation (min–max)</td>
<td>55.8 ± 15.5 (18–93)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>451 (65.3)</td>
</tr>
<tr>
<td>Duration of disease, years</td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>11 (5–20)</td>
</tr>
<tr>
<td>(min–max)</td>
<td>(0–58)</td>
</tr>
<tr>
<td>Rheumatoid arthritis, N</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>325</td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>236 (72.8)</td>
</tr>
<tr>
<td>Rheumatoid factor, N (%)</td>
<td>216 (66.7)</td>
</tr>
<tr>
<td>Anti-CCP, N (%)</td>
<td>222 (68.5)</td>
</tr>
<tr>
<td>Spondyloarthritis, N</td>
<td>298</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>152 (51.0)</td>
</tr>
<tr>
<td>Psoriatic arthritis, N (%)</td>
<td>59 (19.8)</td>
</tr>
<tr>
<td>AS (New York criteria), N (%)</td>
<td>137 (45.9)</td>
</tr>
<tr>
<td>SpA, non-radiographic (axial ASAS), N (%)</td>
<td>64 (21.5)</td>
</tr>
<tr>
<td>MRI arm</td>
<td>35 (54.7)</td>
</tr>
<tr>
<td>Clinical arm</td>
<td>29 (45.3)</td>
</tr>
<tr>
<td>SpA, peripheral (peripheral ASAS), N (%)</td>
<td>38 (12.8)</td>
</tr>
<tr>
<td>Connective tissue disease (CTD), N</td>
<td>71*</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>65 (91.6)</td>
</tr>
<tr>
<td>Systemic lupus erythematosus (SLE)</td>
<td>28 (39.4)</td>
</tr>
<tr>
<td>Sjögren’s syndrome (SS)</td>
<td>27 (38.0)</td>
</tr>
<tr>
<td>Scleroderma (Scl)</td>
<td>14 (19.7)</td>
</tr>
<tr>
<td>Myositis</td>
<td>6 (8.45)</td>
</tr>
</tbody>
</table>

ASAS, Assessment of SpondyloArthritis International Society; AS, ankylosing spondylitis; CTD, connective tissue disease; SLE, systemic lupus erythematosus; SS, Sjögren’s syndrome; Scl, scleroderma; SpA, spondyloarthritis; MRI, magnetic resonance imaging.

* Four patients had two CTD associated (2 SLE + SS, 1 SS + Scl, 1 SLE + myositis).
Frequency of fibromyalgia according to 1990 ACR criteria and physician opinion.

<table>
<thead>
<tr>
<th></th>
<th>ACR 1990 criteria</th>
<th>Physician's diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis (%)</td>
<td>4.9(^a)</td>
<td>7.7(^b)</td>
</tr>
<tr>
<td>Spondyloarthritis (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nr-axial SpA</td>
<td>23.9</td>
<td>37.3</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>9.6</td>
<td>13.5</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>6.4</td>
<td>7.2</td>
</tr>
<tr>
<td>Peripheral SpA</td>
<td>5.3</td>
<td>28.9</td>
</tr>
<tr>
<td>Connective tissue diseases (%)</td>
<td>11.3</td>
<td>28.2</td>
</tr>
<tr>
<td>All rheumatic diseases (%) (95% CI)</td>
<td>8.0 (6.1–10.2)</td>
<td>14.0 (11.5–16.8)</td>
</tr>
</tbody>
</table>
In clinical practice

FM is a confounding factor in rheumatic disease cases in terms of both diagnosis and disease activity assessment.

Firstly, distinguishing FM from rheumatic disease can be challenging, particularly in non-radiographic axial spondyloarthritis (nr-axial SpA), due to the widespread, primarily axial pain, fatigue, and sleep disorders that are common clinical features of both conditions, as well as the enthesitis sites potentially overlapping with FM tender points.

Secondly, concomitant FM disrupts disease activity and functional impairment assessment of RA and spondyloarthritis (SpA). It leads to overestimations in the 28-joint Disease Activity Score, as well as the BASFI and BASDAI indices, and causes non-justified therapeutic intensification with more frequent use of biological therapy.
CONCLUSIONS

FM is:

• More prevalent in women
• In patients over 50 years
• In subjects with low education level, with low socioeconomic status, living in rural areas and possibly in obese women
• Comorbid with many diseases, usually called “functional” disorders, such as chronic fatigue syndrome, irritable bowel syndrome, depression, anxiety, panic attacks, post-traumatic stress disorder
• Associated with headache, including episodic and chronic migraine and chronic tension type headache

Queiroz LP Curr Pain Headache Rep 2013; 17:356
CONCLUSIONS 2

Fibromyalgia occurs frequently among persons with musculoskeletal disorders and may be seen with almost any other medical condition, as well as in persons with psychological disorders. If such patients have symptoms consistent with fibromyalgia and satisfy fibromyalgia criteria, they may be diagnosed as having fibromyalgia using fibromyalgia criteria: the current criteria definition of fibromyalgia does not exclude patients with coexistent conditions.