The study of the descriptive epidemiology of chronic widespread pain (CWP) in several countries is of interest, as the occurrence of this condition varies among different populations. However, reports of pain prevalence are not consensual: it is clear that chronic musculoskeletal pain is frequent all over the world, varying from 4.2% to 13.3%. The reasons for the prevalence differences in CWP might include genetic and/or environmental factors.

Multifactorial aetiopathogenesis of CWP and fibromyalgia syndrome (FMS) certainly includes genetic susceptibility and environmental influences. The risk factors for the occurrence and maintenance of CWP/FMS include female gender, increasing age, family history of chronic pain, several causes of distress, obesity and poorest mental and/or physical status. On the other hand, risk factors that negatively influence the outcome of CWP/FMS are: high levels of psychological distress, presence of somatisation, presence of fatigue, poor sleep, higher number of painful sites and pain intensity, poorest mental status and functional capacity, presence of co-morbid conditions and highest number of primary-care consultations. Mild alcohol consumption and individualised social support seem to have a protective effect on the outcome of CWP/FMS.

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Descriptive epidemiology

Introduction

Chronic widespread pain (CWP) and fibromyalgia syndrome (FMS), from a rheumatological perspective, are viewed as generalised musculoskeletal pain syndromes. From the broader epidemiological perspective of chronic pain, there is accumulating evidence that multiple chronic musculoskeletal pain sites, irrespective of formal definitions of ‘widespreadedness’, are an important measure of the population burden of pain and pain-related disability [1]. This represents a shift towards thinking of multiple-site chronic pain as a continuum of experience, often established early in adult life, and away from the categorical view of widespread pain. To paraphrase Croft [2], the question is “How much of it have you got?” rather than “Have you got it?”. A large Norwegian cohort study tracked the number of musculoskeletal pain sites in participants over a 14-year period from 1990 to 2004 and found that the number of sites reported was stable over time (68.8% of those who reported five or more sites at baseline reported the same number of sites 14 years later) [3]. Furthermore, this was seen consistently across age groups, suggesting that the persistence of relatively stable multi-site musculoskeletal pain is established early in adult life. From the perspective of measuring and reducing the global burden of musculoskeletal pain, the number of pain sites, a continuous measure with strong prognostic capacity for pain-related disability, may prove to be suitable as a marker of individual and population risk analogous to blood pressure [4].

Intriguingly, recent developments in the conceptualisation of FMS show a similar line of thought, with a shift away from a category-based definition towards a continuum-based approach [5]. Twenty years after the American College of Rheumatology (ACR) first published fibromyalgia classification criteria, new ACR preliminary diagnostic criteria have been developed [5]. The fundamental change in the new criteria is that they allow fibromyalgia to be characterised as part of a dynamic continuum of chronic widespread musculoskeletal pain that takes into account changes in the ‘widespreadedness’ of pain in a quantitative manner as well as taking into account changes in concomitant symptoms (e.g., fatigue and loss of restorative sleep) and their level of severity. With the removal of the sometimes controversial requirement for tender points as a diagnostic criterion [6], there is now the potential for wider use of the new criteria in surveys and in future rounds of estimating the global burden of disease.

With a better understanding of the important role of central pain processing in CWP and in FMS, the gaps between the ‘fibromyalgia literature’ and the ‘chronic pain literature’ are rapidly narrowing. However, this article is based on what has gone before, and so necessarily focusses on studies of CWP and FMS that have used the 1990 ACR criteria.

Case definition

For many common musculoskeletal conditions, there are significant variations in case definitions that have been used in epidemiological studies that estimate population burden. This is as true for commonly occurring conditions, such as low back pain, as it is for generalised musculoskeletal pain conditions.

Incidence versus prevalence: selecting the most appropriate measure

In epidemiological studies of disease occurrence, two commonly used measures are incidence (first-ever occurrence or onset of a condition) and prevalence (presence of a condition), which may be measured at one point of time, or over a defined period of time. Generalised musculoskeletal pain conditions are characterised by a gradual onset, are often established by early adult life and follow a complex episodic course with remittance and recurrence of pain symptoms. It is therefore debatable whether measures of incidence do, in fact, capture initial onset of the condition or the onset of a new episode of an already prevalent condition. Therefore, prevalence is the preferred measure in the context of generalised musculoskeletal pain conditions.
Morbidity

Generalised musculoskeletal pain syndromes are commonly associated with an array of symptoms and conditions. Some of these – pain at multiple sites, fatigue, sleep disturbance, mood disturbance and cognitive symptoms (e.g., impaired concentration and memory) – are also found in other musculoskeletal conditions and a range of syndromes characterised by the co-occurrence of multiple symptoms, such as chronic fatigue syndrome and irritable bowel syndrome [7,8]. The new ACR diagnostic criteria for FMS incorporate specific measures of persistent common symptoms and symptom severity for fatigue, lack of restorative sleep, cognitive problems and somatic symptoms in general [5].

Generalised musculoskeletal pain syndromes can have a profound effect on health-related quality of life (HRQoL); compared with the general population, those with CWP or, particularly, FMS report lower scores on the Short-Form (36) Health Survey (SF-36) [9].

A notable feature of the effect of generalised musculoskeletal pain syndromes on HRQoL is the global impact on physical and psychological well-being and functioning, seen consistently across studies [10].

Mortality

CWP/FMS is associated with neuroendocrine disturbances, smoking, poor exercise capacity and increased body mass index. Therefore, there are a priori grounds for considering whether these conditions contribute to increased mortality. There are studies that have shown a statistically significant but small relationship between different forms of widespread pain and increased risk of cancer mortality [11,12]; however, others have not [13].

A new Danish study examined mortality in a cohort of FMS patients seeking care between 1984 and 1999 through linkage to the Danish Mortality Registry [14]. While there was no overall increase in mortality, there was an elevated risk of cause-specific mortality in females for three causes of death: suicide (10-fold increase in mortality risk), liver cirrhosis/biliary tract disease (sixfold increase in mortality risk) and cerebrovascular disease (threelfold increase in risk). Recently, a large prospective data linkage study found that, for chronic pain more generally, socio-demographic factors appeared to explain the relationship between pain and mortality [15]. However, severe pain (defined by high levels of pain intensity and substantial pain-related disability) was associated with an increased risk of all-cause mortality even after adjusting for socio-demographic factors.

Geographical variation

Geographical differences in occurrence of chronic widespread pain

What is the importance of epidemiological studies of rheumatic diseases?

The study of the descriptive epidemiology of rheumatic diseases in several countries and areas around the world is of interest, as the occurrence of these diseases varies among different populations. Geographical, ethnic and racial factors can be determinant for their frequency and expression. In contrast to industrialised countries, the prevalence of rheumatic diseases in developing countries is largely unknown. The investigation of the epidemiological profile of rheumatic diseases in these countries can reveal the role of environmental and lifestyle factors characteristic of this populations, providing insights into the disease aetiology.

Why study CWP ‘and’ Fibromyalgia?

CWP is the cardinal symptom of the FMS, one of the most common reasons for referral to a rheumatologist.

Prior to 1990, several diagnostic criteria for FMS and CWP were available [16]. In 1990, the ACR established the classification criteria for CWP [17], which is defined as pain above and below the waist, involving both sides of the body and lasting for at least 3 months, and for FMS, which includes CWP and the observation of pain brought on by pressure at specific anatomic sites. Previous studies did not use consistent criteria for this syndrome and, in particular, definitions of widespread pain differed.
Therefore, we should not neglect the fact that minor differences in the definition of widespread pain can be reflected in the disease prevalence estimates [18].

Although CWP is the cardinal feature of FMS, the relation between these two clinical expressions of chronic pain is by no means clear. Neither CWP nor FMS appears as confined conditions, as with time, patients frequently move across different categories of pain syndromes [19]. This supports the concept that chronic pain conditions may constitute a continuum of pain distribution from localised to widespread, rather than different entities. About 20% of the population with CWP also has 11 of 18 tender points [7], and in 70–80% of the patients who later develop FMS, the disease starts with localised and intermittent pain. The number of painful sites usually increases slowly over the years, before the patient finally develops the full-blown picture of FMS [20]. It is not clear why some people with widespread pain also have a compatible FMS examination and others do not.

Very few studies have estimated the prevalence of CWP in the general population and there are currently no published robust international epidemiological data even though the classification criteria can be easily applied to an epidemiological context [21–23,26–32] (Table 1).

Valuable information about the epidemiological aspects of CWP can be obtained by reviewing studies on FMS. FMS appears to have a worldwide distribution, particularly in the Western world, where differences in frequency can be found between various geographical regions [21,26,29,33–44] (Table 2).

Reports of pain prevalence are not consensual, at least in part, as a consequence of the different definitions of pain used in individual studies, but also likely due to study methodologies and populations. Despite these facts, it is clear that musculoskeletal pain is frequent all over the world.

**Prevalence of CWP and fibromyalgia**

Recent studies have reported that CWP is common in the general population and its prevalence, varying between 4.2% and 13.3%, is quite high in the USA, UK, Canada, Israel and Russia (Table 1). Population-based studies of CWP performed in the USA and UK suggest that approximately 5–11% of the population has this symptom at a given time [22,23,27]. In adolescents, there is paucity of data. Mikkelsson et al. [25] studied 1756 third- and fifth-grade schoolchildren and found widespread pain in 7.5% (Table 1), but further investigations of CWP in children and adolescents are clearly warranted.

Recently, Macfarlane et al. [45] conducted a study that compared the occurrence of CWP and analysed the potential aetiology behind differences in prevalence in Europe. The authors demonstrated that there is higher prevalence, particularly in Eastern Europe, which is due to adverse psychosocial factors including poorer psychological health and physical morbidities. The major limitation of this study is that it only included men and, it is known that CWP is more frequently diagnosed in middle- and older-age females [36].

Geographical variations have also been observed among patients with FMS. FMS is recognized as a common condition in the clinic and a major cause of morbidity worldwide. FMS has a different prevalence depending on the studied population and the diagnostic criteria used, ranging from 0.7% (Denmark) to 2.4% (Spain) (Table 2).

In the first study that determined FMS prevalence in the general population of five European countries, using an identical methodology, Branco et al. [46] found overall prevalence of FMS in the

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country</th>
<th>Age group</th>
<th>Prevalence (%) total</th>
<th>Prevalence (%) women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forseth et al. [21]</td>
<td>1992</td>
<td>Norway</td>
<td>20–50</td>
<td>NI</td>
<td>15.3</td>
</tr>
<tr>
<td>Croft et al. [22]</td>
<td>1993</td>
<td>England</td>
<td>18–79</td>
<td>11.2</td>
<td>15.6</td>
</tr>
<tr>
<td>Wolfe et al. [23]</td>
<td>1995</td>
<td>USA</td>
<td>18+</td>
<td>10.6</td>
<td>NI</td>
</tr>
<tr>
<td>Jacobsson et al. [24]</td>
<td>1996</td>
<td>USA (Pima)</td>
<td>35–70</td>
<td>0.0</td>
<td>NI</td>
</tr>
<tr>
<td>Mikkelsson et al. [25]</td>
<td>1997</td>
<td>Finland</td>
<td>Pre-adolescents</td>
<td>7.5</td>
<td>NI</td>
</tr>
<tr>
<td>White et al. [26]</td>
<td>1999</td>
<td>Canada</td>
<td>18+</td>
<td>7.3</td>
<td>NI</td>
</tr>
<tr>
<td>Hunt et al. [27]</td>
<td>1999</td>
<td>England</td>
<td>18–65</td>
<td>4.7</td>
<td>5.3</td>
</tr>
<tr>
<td>Buskila et al. [28]</td>
<td>2000</td>
<td>Israel</td>
<td>18+</td>
<td>9.9</td>
<td>14.0</td>
</tr>
<tr>
<td>Lindell et al. [29]</td>
<td>2000</td>
<td>Sweden</td>
<td>20–74</td>
<td>4.2</td>
<td>NI</td>
</tr>
<tr>
<td>Bergman et al. [30]</td>
<td>2001</td>
<td>Sweden</td>
<td>20–74</td>
<td>11.4</td>
<td>NI</td>
</tr>
<tr>
<td>Storzhenko et al. [31]</td>
<td>2004</td>
<td>Russia</td>
<td>27–75</td>
<td>13.3</td>
<td>NI</td>
</tr>
<tr>
<td>Mas et al. [32]</td>
<td>2008</td>
<td>Spain</td>
<td>20+</td>
<td>8</td>
<td>NI</td>
</tr>
</tbody>
</table>

NI: Not indicated.
Italian (3.7%), Portuguese (3.6%), German (3.2%), Spanish (2.3%) and French (1.4%) general populations comparable to those already published. Of note, this study provided the first evidence of FMS prevalence in France and Portugal. In this survey, the estimated prevalence of FMS in the general population was age-related, reaching a peak prevalence in the group of 75–84 years. However, it is likely that these results could be overestimated in the elderly because ageing is associated with frequent co-morbidities that may result in widespread pain and/or fatigue. In this study, besides gender and age, the likelihood of having FMS did not appear to be affected by other socio-demographic variables.

What are the reasons for the different prevalence rates of FMS and CWP between various geographical regions?

Any ethnic differences in widespread pain prevalence may be a result of psychosocial or cultural differences, as well as genetic predisposition and the physical or social environment. If psychological and psychosocial factors influence the reporting of symptoms, and subjects at higher risk can be identified by past health and illness attitudes and beliefs, then it would be surprising if there were not differences in prevalence between countries because such risk factors or markers are likely to differ between populations of countries with distinct cultures [45]. On the other hand, unfavourable climatic conditions and variations in sunlight exposure and vitamin D status may also influence musculoskeletal pain.

White and Thompson [41] conducted a very interesting study in a community of Amish adults in Southwestern Ontario, having as a priori assumption that, if litigation and/or compensation availability have major effects on FMS prevalence, then FMS prevalence in the Amish should approach zero. The question was “Is it possible that individuals in this culturally isolated society express their FMS differently?” Strikingly, the authors found that FMS prevalence in the Amish was clearly greater than zero (7.3%). Somewhat surprisingly, FMS prevalence was higher in this population than in any other previously reported population. In accordance with this hypothesis, Jacobsson et al. [24] verified that no subject in the Pima Indians reported chronic generalised musculoskeletal pain. The extremely low prevalence of CWP among Pimas also contrasts with the prevalence of inflammatory rheumatic diseases observed in these Native Americans; the reasons for these prevalence differences in two isolated communities might include genetic and/or environmental factors.

Risk factors

Pain as a continuous spectrum of distribution from no pain, through chronic local and regional pain, to CWP and FMS is one of the possible ends of the chronic musculoskeletal pain continuum [30].

### Table 2

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country</th>
<th>Age group</th>
<th>Prevalence (%) total</th>
<th>Prevalence (%) women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mäkelä and Heliövaara [33]</td>
<td>1991</td>
<td>Finland</td>
<td>30+</td>
<td>0.8</td>
<td>1.0</td>
</tr>
<tr>
<td>Forseth and Gran [21]</td>
<td>1992</td>
<td>Norway</td>
<td>20–49</td>
<td>NI</td>
<td>8.6–10.5a</td>
</tr>
<tr>
<td>Lydell and Meyers [34]</td>
<td>1992</td>
<td>South Africa</td>
<td>35+</td>
<td>NI</td>
<td>3.2</td>
</tr>
<tr>
<td>Prescott et al. [35]</td>
<td>1993</td>
<td>Denmark</td>
<td>18–79</td>
<td>0.7</td>
<td>1.3</td>
</tr>
<tr>
<td>Wolfe et al. [36]</td>
<td>1995</td>
<td>USA</td>
<td>18+</td>
<td>2.0</td>
<td>3.4</td>
</tr>
<tr>
<td>Lindell et al. [29]</td>
<td>1996</td>
<td>Sweden</td>
<td>20–74</td>
<td>1.3</td>
<td>NI</td>
</tr>
<tr>
<td>Farooqi and Gibson [37]</td>
<td>1998</td>
<td>Pakistan</td>
<td>15+</td>
<td>0.1–3.2b</td>
<td>NI</td>
</tr>
<tr>
<td>Clark et al. [38]</td>
<td>1998</td>
<td>Mexico</td>
<td>9–15</td>
<td>1.2</td>
<td>2.5</td>
</tr>
<tr>
<td>White et al. [26]</td>
<td>1999</td>
<td>Canada</td>
<td>18+</td>
<td>3.3</td>
<td>4.9</td>
</tr>
<tr>
<td>Carmona et al. [39]</td>
<td>2001</td>
<td>Spain</td>
<td>20+</td>
<td>2.4</td>
<td>4.2</td>
</tr>
<tr>
<td>Cardiel and Rojas-Serrano [40]</td>
<td>2002</td>
<td>Mexico</td>
<td>16+</td>
<td>1.4</td>
<td>NI</td>
</tr>
<tr>
<td>White and Thompson [41]</td>
<td>2003</td>
<td>Amish, Canada</td>
<td>18+</td>
<td>7.3</td>
<td>10.4</td>
</tr>
<tr>
<td>Senna et al. [42]</td>
<td>2004</td>
<td>Brazil</td>
<td>16+</td>
<td>2.5</td>
<td>3.89</td>
</tr>
<tr>
<td>Haq et al. [43]</td>
<td>2005</td>
<td>Bangladesh</td>
<td>15+</td>
<td>3.2b</td>
<td>NI</td>
</tr>
<tr>
<td>Salaffi et al. [44]</td>
<td>2005</td>
<td>Italy</td>
<td>18+</td>
<td>2.22</td>
<td>NI</td>
</tr>
</tbody>
</table>

NI: Not indicated.

a Minimum and maximum prevalences.

b Urban districts.

The extremely low prevalence of CWP among Pimas also contrasts with the prevalence of inflammatory rheumatic diseases observed in these Native Americans; the reasons for these prevalence differences in two isolated communities might include genetic and/or environmental factors.
Risk factors for the occurrence of CWP and FMS

In this section, we will discuss relevant, modifiable and non-modifiable factors that initiate and maintain CWP and FMS.

Non-modifiable risk factors

Gender and age. The development of CWP and FMS is influenced by both gender and age. Clearly, women report CWP and comply with ACR FMS criteria more often than men [27]. For both genders, CWP and FMS tend to increase with age [47]. The higher female prevalence of CWP and FMS can be explained by an increased sensitivity to pain or a willingness to seek health care. The role of hormonal factors frequently mentioned in women with CWP has not been demonstrated in a population-based study [48]. A probable cause of the ageing increase of CWP and FMS prevalence results from the persistence over time of chronic pain.

Familial aggregation and genetic susceptibility. CWP and FMS are much more prevalent in relatives of patients who suffer from these clinical entities [49]. This familial aggregation may result from a genetic susceptibility and/or from family environment. Evidence from twin studies estimates an overall heritability for CWP of 48–54% with no difference between genders [50]. Results of human leucocyte antigen (HLA) association with FMS were inconclusive [51]. Hence, other genetic markers have been studied and two recent large reviews of the published studies on genetic predictors of CWP, including polymorphisms in genes coding for catechol-o-methyltransferase activity and μ-opioid receptors among a number of others, concluded that no definitive pain susceptibility gene has yet been identified [52,53].

More recent studies not included in those reviews suggested that: (1) among a Turkish population the high-activated genotype of monoamine oxidase A may be pathogenic in FMS [54]; (2) functional single nucleotide polymorphisms (SNPs) in guanosine triphosphate cyclohydrolase and μ-opioid receptor were not associated with CWP [55] and (3) adrenergic receptors gene polymorphisms are related to the risk of developing FMS [56]. Therefore, further investigations in different ethnic groups with larger sample size are needed to confirm or contradict these observations.

Modifiable risk factors

Stressful life events. History of CWP and FMS patients is frequently characterised by long-term emotional problems and/or physical burden.

Early life stress may play a role as a CWP/FMS initiating risk factor. Although this hypothesis could not be confirmed in a prospective study that assessed the relationship between court-documented abuse in childhood and pain in adulthood [57], another prospective survey using data from the 1958 British Birth Cohort Study has shown that both physical and social adversities prior to the age of 7 years are associated with an increased risk of CWP at 40 years of age [58] (Table 3). Childhood maltreatment is, in general, an FMS risk factor but some forms of abuse (e.g., sexual assault) did not show any relationship with pain in adulthood.

However, experiences of physical and sexual assault in adulthood showed a strong association with FMS existence [59]. The vast majority of studies that seem to support emotional trauma and sexual abuse as risk factors of CWP/FMS used self-report questionnaires or interviews to assess abuse history. Thus, results of retrospective studies on the role of victimisation and CWP/FMS must be analysed with criticism because the poor recall can overestimate that apparent relationship. A case–control study among Spanish women showed a strong association between FMS and psychological distress but the authors were not able to conclude whether FMS is a consequence of this psychological distress or vice versa [60] (Table 3).

A postal questionnaire survey completed by 4971 Finish hospital employees (4250 women and 541 men) was used to prospectively examine the association between occupational stress and the development of FMS. This study outcomes support the possibility that stress at work along with the
Aetiological factors results in the onset of FMS [61]. Socioeconomic adversity can also influence the reporting of CWP [62]. (Table 3).

Pain-prone lifestyle. Some FMS patients at least seem to have a particular lifestyle stress – often since adolescence – by mental and/or physical auto-overexertion, perfectionism traits and self-sacrificing behaviour [63].

A recent study showed an association between premorbid psychosocial risk factors with the new onset of CWP, which is related with poor mental scores. This demonstrates for the first time that psychosocial risk markers for the onset of CWP act as independent risk markers for poor mental health-related quality of life (HRQoL) observed in subjects with CWP. Authors also described in these patients poorest physical HRQoL independently of prior poor psychosocial status [64] (Table 3). In a population-based prospective study, three psychosocial factors independently predicted a moderate increased risk to develop CWP: health-seeking behaviour, somatisation and poor sleep. Subjects with these three factors together had a highest increased risk of developing CWP [65]. Disturbed sleep is often reported by FMS patients. Insomnia and non-restorative sleep are some of the described patterns. Although postulated as a possible cause of FMS, the alpha–delta sleep pattern is not specific of this condition [66]. CWP can occur without any sleep disruption and alpha–delta anomaly can be present without the development of pain.

Physical trauma and recurrent pain episodes. In a retrospective case–control study, physical trauma 6 months prior to CWP onset has been significantly associated with FMS. Trauma was defined as a fracture, surgery, miscarriage or childbirth and traffic or other type of accident, for which the subject received medical care [67]. A prospective study found that FMS was 13 times more common in individuals who had prior cervical spine injury compared with those with lower limb fractures [68].

<table>
<thead>
<tr>
<th>Reference</th>
<th>Design</th>
<th>Risk factors</th>
<th>Odds ratio (95% CI)</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kivimäki et al., 2004 [61]</td>
<td>Prospective</td>
<td>Workplace bullying, High workload, Low decisions latitude</td>
<td>4.1 (2.0–9.6), 2.1 (1.2–3.9), 2.1 (1.1–4.0)</td>
<td>Finland</td>
</tr>
<tr>
<td>Atherton et al., 2004 [69]</td>
<td>Prospective</td>
<td>Low levels of Vit D (in women but not in men)</td>
<td>1.57 (1.09–2.26)</td>
<td>Great Britain</td>
</tr>
<tr>
<td>Jones et al., 2009 [58]</td>
<td>Prospective</td>
<td>Children hospitalized following road traffic accident, Children residing in institutional care, Children experienced maternal death, Children experienced familial financial hardship</td>
<td>1.5 (1.05–2.1)</td>
<td>Great Britain</td>
</tr>
<tr>
<td>Ruiz-Pérez et al., 2009 [60]</td>
<td>Case–control</td>
<td>Age (women), Employed, Housewives, Psychological distress</td>
<td>1.06 (1.03–1.09), 4.97 (1.45–17.02), 3.47 (0.98–12.22), 4.62 (2.68–7.97)</td>
<td>Spain</td>
</tr>
<tr>
<td>Macfarlane et al., 2009 [62]</td>
<td>Prospective</td>
<td>Lowest social class, Obesity, Mental health</td>
<td>2.9 (1.8–4.6), 1.4 (1.16–1.69), 2.74 (2.28–3.29)</td>
<td>Great Britain</td>
</tr>
<tr>
<td>Nicholl et al., 2009 [64]</td>
<td>Prospective</td>
<td>Poorest mental status, Poorest physical status</td>
<td>2.3 (1.6–3.2), 8.0 (5.4–11.8)</td>
<td>Great Britain</td>
</tr>
</tbody>
</table>

* Studies on FMS risk factors.
Other causes for musculoskeletal pain (e.g., low back pain, shoulder pain, osteoarthritis and rheumatoid arthritis) are also associated with the development of CWP.

Other. Further, other putative CWP/FMS risk factors have been described, including lower education levels, unemployment, divorce, obesity, low levels of vitamin D in women and certain infections (e.g., human immunodeficiency virus, Lyme disease and hepatitis C virus) [69,70,26].

Outcome risk factors

The medical research to address the prognosis of CWP and FMS is limited. In the community, CWP has, in general, a relatively good prognosis. At hospital care level, the outcome of CWP and FMS is not so favourable.

Patients with high levels of psychological distress, fatigue and highest primary-care consultation consumption are more likely to have persistent pain symptoms [71,72]. McBeth et al. found that in almost half of the cases of CWP, pain symptoms will resolve over 1 year. These authors described for the first time that individuals, who present psychological features associated with somatisation, are more likely to have persistent symptoms [73].

A population-based prospective study has demonstrated that sleep is associated with the resolution of CWP. In fact, self-reported restorative sleep was independently related with the resolution of CWP and the return to musculoskeletal health [74]. Bergman et al., in a 3-year follow-up (1995–1998), showed that the persistence of CWP was predicted by the higher number of painful regions (odds ratio (OR) = 7.56, 95% confidence interval (CI) 2.17–26.30) and being an immigrant in Sweden (OR = 3.22, 95% CI 1.33–7.77). In contrast, the author found a protective effect on alcohol consumption on a weekly basis (OR = 0.42, 95% CI 0.21–0.85) and having individualised social support (OR = 0.49, 95% CI 0.28–0.85) [47].

FMS patients with mild symptoms at clinical onset have a better prognosis. The global severity of FMS correlates with pain intensity, mental status and functional capacity of the patient [75]. Co-morbid conditions (e.g., joint hypermobility, metabolic disorders, hypothyroidism and vitamin D deficiency) can be both precipitating and perpetuating/aggravating factors of FMS [76]. Furthermore, somatic hypervigilance and dysfunctional cognitive coping strategies, such as catastrophising, can generate increased stress status with the correspondent higher intensity and persistence of pain. Another important stress-generating factor, which interferes with FMS recovery, is the very common situation of not being generally accepted by the others as suffering from a real and legitimate illness with the correspondent lack of familial, social and work support [63].

What are the time trends of chronic widespread pain?

The number of studies on the temporal evolution of CWP that enable its adequate assessment is limited. Nevertheless, this is a very important issue that requires further investigation. It has not been determined whether the prevalence of CWP is increasing or decreasing in the population in general, and which are the changes, if any, seen over time among regions, countries and communities. The lack of knowledge in this area regarding FMS is similar. As we referred above, it is impossible to establish a comparison between the available studies, as the methodologies and criteria used to identify CWP were different within each study. Further, studies present CWP prevalence over a specific period of time, often scarcely identified, rather than the prevalence established in a particular time point.

As earlier mentioned, CWP is not a clinically stable entity, and the differences found by the various authors may result mainly from the different definitions used rather than from the substantial variations of its prevalence over time. The exception to this rule derives from the UK where two surveys were conducted in different but adjacent geographic areas over a 7-year period, and more importantly, with a similar definition to CWP. The prevalence of CWP was similar for both surveys, with a proportion of approximately 13% of the studied population [22,27]. Further, in a more recent survey conducted in the UK, using a similar definition of CWP, this entity was identified in 15% of the 6500 adults studied.
Clinical variations in CWP status may, in turn, be one of the possible explanations for the stability of its prevalence, as the individuals, who became pain free, are counterbalanced by those with initial or recurring pain [71].

The findings of Hardt et al. in a large US epidemiological survey that included 10,291 respondents, who participated in the 1992–2002 National Health and Nutrition Examination Survey (NHANES), suggest that the prevalence of chronic, regional and widespread pain is lower than previously reported [77]. By contrast, Harkness et al. describe the results of two cross-sectional surveys conducted 40 years apart in the northwest of England. The authors found large differences in the prevalence of musculoskeletal regional and widespread pain between the two surveys, being much higher for both genders presently than 40 years ago, which is unlikely to be due only to the study design [78].

ACR 1990 classification criteria for FMS were rapidly adopted as specific diagnostic criteria for this condition and, thus, the establishment of FMS as an individual syndrome promoted the diffusion of its knowledge among rheumatologists and primary-care physicians (general physicians, GPs). This increased awareness may, at least partly, explain the relevant increases seen in FMS incidence both in rheumatology consultations in Canada, and GP consultations in Sweden. FMS was the only rheumatologic disorder, believed by the majority of 89 inquired Canadian rheumatologists, to have increased in proportion over the last 5 years in their practices [79]. Swedish GPs referred that pain was a relevant cause for the increase seen in their consultations for the last 10 years, and FMS was, among all pain causes, the condition with increased number of consultations [80]. Wolfe states that, in the medicolegal setting, FMS achieved levels almost epidemic both in terms of legal complaints, resulting mainly from accidents, and at the US Social Security setting, due to disability claims and payments to workers [81]. Almost a quarter of FMS patients in the US received some form of payment due to disability or accidents [82]. The high prevalence of FMS and the claiming capacity of patients may partially justify those phenomena.

In contrast with CWP, FMS is a more stable clinical disorder, in which patients still present symptoms over time, and remissions are rare [83]. All studies published on FMS evolution are unanimous regarding the lack of progression over time of this condition to other diseases or syndromes, including inflammatory arthropathies and systemic rheumatic diseases [84]. These clinical characteristics may contribute to the increase over time of FMS prevalence. The General Practice Research Database (GPRD) collects since 1987 data routinely recorded by the GPs of the UK, and contains over 35 million patient-years of data, representing 5% of the UK population. Gallagher et al. studied both fatigue symptoms and diagnosis recorded by the GPRD from 1990 to 2001. The incidence of the different fatigue symptoms barely changed throughout the study period, but the annual incidence of FMS has grown remarkably since 1997. The authors concluded that this is likely to reflect fashions in diagnostic labelling rather than true changes in incidence [85].

Difficulty in obtaining this information: what are the weakness of the data reported above?

The global burden of generalised musculoskeletal pain syndromes, including CWP/FMS, is not known at this time, as population-level data on the prevalence and impact of these syndromes is not available in several regions of the world, notably in developing countries. In part, this weakness is a problem shared by musculoskeletal pain conditions as a group, as is highlighted in the other articles in this issue. However, in the case of CWP/FMS, there have been additional challenges in defining population burden because of the 1990 ACR criteria relating to presence of tender points on examination. This requirement introduced practical difficulties in the context of large-scale population studies and probably contributes to the geographical variation described in the section titled ‘Prevalence of CWP and Fibromyalgia’.

Our knowledge of trends over time in the occurrence of CWP/FMS at the population and individual level is even more limited. The recent publication of the new ACR criteria for FMS removes the tender points requirement and provides a measure based on a continuum of symptoms rather than a distinct cut-off point (i.e., what is termed fibromyalgianess) [5]. This offers exciting new opportunities for longitudinal studies in this area, and should lead to better global estimates of the burden of generalised musculoskeletal pain syndromes in the future.
Practice points

- The prevalence of musculoskeletal pain varies greatly across studies. This is probably due to different definitions of pain and study methodologies and designs, making it difficult to draw comparisons.
- The prevalence of CWP in developing countries is largely unknown.
- CWP/FMS are puzzling conditions still without biomedical explanation.
- The majority of studies designed to identify individuals at higher risk to develop CWP/FMS are cross-sectional, and for this reason cannot differentiate the temporal relationship from the identified putative influencing factors and symptoms’ onset.
- Despite the more consistent and recent data from well-designed studies, there are still some methodological problems, which make it difficult to draw definite conclusions.
- Physical, emotional and sexual trauma can play an important role in the occurrence and perpetuation of CWP/FMS, as well as in the degree of associated disability.
- Although there are no solid data on CWP time trends, its prevalence seems to have stabilised in the last decades.

Research agenda

- International epidemiologic data of CWP is needed, using similar study methodologies and populations to determine the prevalence of this condition all over the world.
- More accurate definitions of CWP/FMS are needed to achieve significant advances in medical research.
- Future research must be conducted with prospective cohort studies to determine whether the identified related factors truly predict CWP/FMS onset, or can be only seen as associated features.
- Research is needed to determine whether interventions tailored to change risk factors effectively improve CWP/FMS outcome.
- Collaborative well-designed studies are needed to assess the course of CWP/FMS over time to optimise the management of patients, and to rationally and economically plan the necessary health-care resources.

References

[2] Croft PR. The question is not “have you got it?” but “how much of it have you got?”. Pain 2009;141:6–7.


Gürsoy S, Erdal E, Sezgin M, et al. Which genotypes of MAO gene that the patients have are likely to be most susceptible to the symptoms of fibromyalgia? Rheumatol Int 2008;28:307–11.


