



# Severity of symptoms persists for decades in fibromyalgia—a 26-year follow-up study

Risto Isomeri<sup>1</sup> · Marja Mikkelsen<sup>2,3</sup> · Markku Partinen<sup>4,5</sup> · Markku J. Kauppi<sup>2,3</sup>

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## Abstract

The aim of this study is to find out the outcome of 28 patients who got the diagnosis of primary fibromyalgia (pFM) 26 years ago. In 1986, 56 patients with widespread pain were examined and filled in a base questionnaire (BQ). Of them, 42 fulfilled the Yunus criteria for pFM. Twenty-six years later, addresses of 38 patients were found, and an extensive follow-up questionnaire (FupQ) was mailed to them. Of them, 28 (74%) answered the FupQ. This included nine identical questions with the BQ and questions concerning changes in their symptoms and quality of life (QoL). Three patients (11%) had healed from fibromyalgia (FM), and 23% reported having one or several symptomless periods lasting at least 1 year. In others ( $n = 25$ ), all but pain and ache showed slight deterioration. Despite the aging and FM, the level of functional ability evaluated by Stanford Health Assessment Questionnaire (HAQ) remained at the same level (BQ 0.41 vs. Fup 0.44,  $p = 0.82$ ). The sum score of reported symptoms ( $n = 21$ ) did not change significantly (10.8 (SD 2.9) vs. 11.1 (SD 4.1),  $p = 0.75$ ). Experienced sleeplessness increased most significantly (27 vs. 65%,  $p = 0.0034$ ). Exercising did not have a significant influence on the changes of the measured parameters. However, the three healed patients exercised regularly. Symptoms of FM have persisted in most patients for decades without significant deterioration of self-reported functional ability. About one fourth of patients had experienced long symptomless periods during their illness. Three patients (11%) reported that they have healed from FM.

**Keywords** Fibromyalgia · Follow-up · Musculoskeletal pain · Pain · Prognosis

## Introduction

*Fibromyalgia* (FM) represents one of the syndromes in which central sensitization (CS) plays a great role [1, 2]. The syndrome seems to be persistent, but also remissions have been seen in follow-up (Fup) studies [3].

There are quite few long-term *follow-up studies* (FupS) concentrating on the clinical course of FM and lasting 6 years or more [3–10]. Symptoms usually persist but patients learn to cope with them and become slightly better [4–5, 7–8]. Fluctuation of symptoms was found in the longest FupS. Sometimes, the participants did not fulfill the FM criteria as 44% of patients, initially criteria-positive, failed to meet criteria at least once during 11–16.5-year Fup time. At the end of the study, 25% of patients had at least moderate improvement of pain but 36% of patients felt their situation worsen [9]. Active training and participation in patient education programs seem to give better prognosis [6].

The longest reported Fup periods have been 19 and 35 years. Of these studies, the first one concentrated on working ability [11] and the second one on mortality [12]. Thus, there is a need for reports of the very long-term outcome of FM.

*The aim of this study* was to find out and describe the outcome of 28 patients who got the diagnosis of primary fibromyalgia (pFM) 26 years before the study, in 1986.

✉ Risto Isomeri

<sup>1</sup> Helsinki, Finland

<sup>2</sup> Päijät-Häme Central Hospital, Keskussairaalankatu 7, 15850 Lahti, Finland

<sup>3</sup> Faculty of Medicine and Life Sciences, Tampere University, Tampere, Finland

<sup>4</sup> Helsinki Sleep Clinic, Vitalmed Research Center, Helsinki, Finland

<sup>5</sup> Department of Clinical Neurosciences, University of Helsinki, Helsinki, Finland

## Material and methods

In 1986 at the Rheumatism Foundation Hospital (RFH), Heinola, Finland, we collected data from 56 patients with widespread pain (WSP). They fulfilled a questionnaire with 25 questions and were clinically examined by a rheumatologist or a physiatrist (RI) including the tender point (TP) count. Of them, 42 fulfilled the diagnosis of primary fibromyalgia (pFM) according to Yunus 1981 [13].

The structured questionnaire included questions about concomitant diseases, social situation, work, and about patient's symptoms and factors which relieve or worsened them (e.g., effects of weather changes, sauna, medication, given physiotherapy, and their self-treatment methods). The baseline questionnaire (BQ) included pain rating in 100 mm visual analog scale (VAS), Stanford Health Assessment Questionnaire (HAQ) [14], and a Finnish questionnaire to evaluate depression briefly by Rimon (RBDS) [15]. After the baseline study visit in RFH, the patients continued their treatment and controls with their local doctors.

The FupS was done as a postal questionnaire 26 years after the baseline examination. We asked the addresses of the 42 patients with definite FM from the Finnish population registry. We got the addresses of 38 patients; the four missing patients had either emigrated from Finland or died. The follow-up questionnaire (FupQ) was mailed to those 38 patients in November 2012 and a second mailing was done in February 2013 for those who had not responded to the first contact.

The FupQ included 52 questions. Nine questions were identical with the base questionnaire (BQ). These were marital status, other diseases, factors affecting negatively on life, 25 different symptoms, pain rating in 100 mm VAS (last 3 months), RBDS, HAQ, and effects of weather changes and sauna on the patient's symptoms and general feelings. In seven questions, we asked the patients to estimate with a five-point Likert scale the changes in their FM symptoms and general feelings during the 26-year Fup time. The patients were asked to focus their interest only towards FM symptoms, when they were answering these questions. Furthermore, their body mass index (BMI) was calculated from their self-reported height and weight. They filled in the Fibromyalgia Impact Questionnaire (FIQ) [16] and EuroQol-5 D [17]. In EQ-5D, we used only 200 mm line with 1–100 scale.

The study plan was accepted in the Regional Ethics Committee of the Expert Responsibility Area of Tampere University Hospital on September 4, 2012.

## Statistical analysis

Statistical comparison of changes in outcome measurements was performed by using the Fisher-Pitman permutation test for paired replicates and exact McNemar test. Confidence

intervals for the means changes were obtained by bias-corrected bootstrapping (5000 replications). Correlations were estimated with Spearman's correlation coefficient method. Statistical analyses were performed using the Stata statistical software, release 13.0 (StataCorp, College Station, TX, USA).

## Results

We got relevantly filled FupQ from 28 of the 38 patients (74%). The symptoms of the patients had lasted on average 6 years before the baseline examination when the diagnosis of pFM was conducted in the RFH in 1986 (Table 1). The TP count of the FupQ group was 11.5 (SD 3.3) at baseline. This did not significantly differ from those patients ( $n = 14$ ) which did not respond the FupQ. In 1986, when patients were examined, the minimum TP count needed for diagnosis of FM was 5 points by Yunus criteria 1981. WSP consistent with the criteria of ACR-90 diagnosis [18] was reported in the Fup stage by 26 (93%) patients. The FIQ mean total score was 43 (SD 13).

One or several *symptomless periods* lasting more than 1 year were reported by 6/26 (23%) of patients who answered the question. Three of them (11%) answered that they had

**Table 1** Demographic and clinical characteristics of 28 FM patients at the follow-up

Variable	Measurement $N = 28$
Female, $n$ (%)	26 (93)
Age, years, mean (SD)	70 (9)
Living alone, $n$ (%)	4 (14)
FM symptoms, years, mean (SD)	32 (7)
Body mass index, mean (SD)	27.8 (3.7)
Widespread pain *, % (95% CI)	93% (76–99)
EQ5D **, mean (SD)	59 (22)
FIQ, mean (SD)	
FIQ total score	43 (13)
Physical function	1.8 (1.9)
Feel good	4.2 (2.9)
Work missed	2.2 (3.1)
Job ability	6.9 (1.5)
Pain	6.8 (1.5)
Fatigue	5.1 (2.3)
Morning tiredness	5.3 (2.3)
Stiffness	5.9 (2.1)
Anxiety	3.9 (3.0)
Depression	3.6 (3.0)

\*Like in ACR—90 criteria

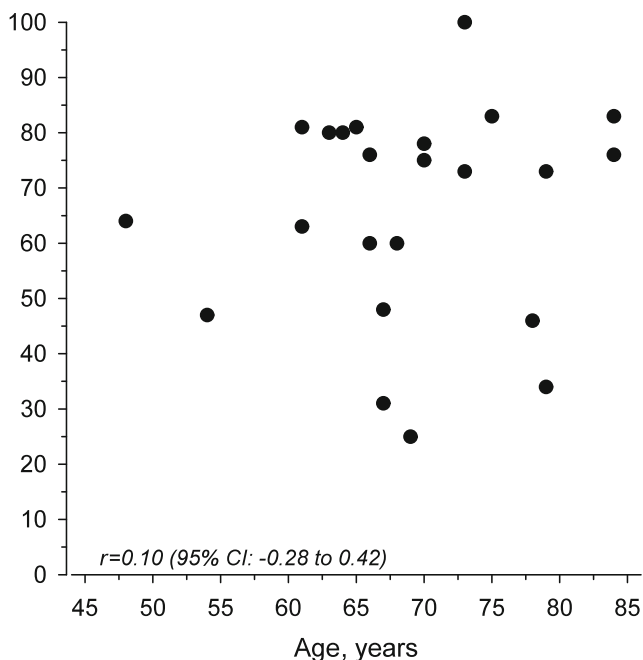
\*\*Scale 0–100 (0 = the worst health, 100 = the best health)

healed from fibromyalgia. The symptomless period of these patients had been 25, 10, and 2 years before the FupS.

Pain and ache during the last 3 months measured by 100 mm VAS was in the Fup 61 mm. Reported pain (Fig. 1) did not correlate with the patients age nor with their BMI. Altogether, 48% reported restless legs syndrome (RLS) symptoms weekly.

The number of symptoms did not change significantly between the baseline and FupS. The sum score of reported 21 symptoms was in the beginning 10.8 (SD 2.9) and at the end 11.1 (SD 4.1),  $p = 0.75$ . The frequencies of the following symptoms showed significant changes at Fup: less pain during nighttime in the Fup (BQ% vs. FupQ%) 62 vs. 27% ( $p = 0.035$ ), more abdominal irregularities in the Fup (31 vs. 65%,  $p = 0.035$ ), and more sleeplessness (27 vs. 65%,  $p = 0.0034$ ). The most common symptoms which were reported by the same patient both at the baseline and at Fup were morning stiffness ( $n = 23$ ), influence of weather changes on symptoms ( $n = 23$ ), pain during movements ( $n = 18$ ), numbness and tightness of muscles ( $n = 15$ ), and general fatigue ( $n = 13$ ).

In identical questions (BQ vs. FupQ), significant differences were not found in the following: pain by VAS was 52 vs. 61 mm, RBDS 8.6 vs. 6.8, HAQ 0.41 vs. 0.44, the worsening effect of weather changes 89 vs. 96% and sauna 71 vs. 80% (Table 2). The age of patients did not associate in the Fup with RBDS ( $p = 0.36$ ), HAQ ( $p = 0.087$ ), or FIQ ( $p = 0.78$ ). The experienced level of function (HAQ) also did not associate with pain VAS ( $p = 0.56$ ) or with the FIQ total scores ( $p = 0.097$ ) in the Fup.



**Fig. 1** Pain measured by visual analogue scale (VAS) by the patients' age at follow-up

Figure 2 shows changes in the main symptoms and in the quality of life. In general, all but pain and ache showed slight deterioration, but a lot of symptom specific variance did occur. The age or baseline TP count of patients did not associate significantly with these changes. The amount of reported exercise by the patients did not explain the differences between these groups (improved, unchanged, worsened), either. The three “healed” patients did not answer these questions.

The following diagnoses of other major illnesses were conducted for the patients during the follow-up time: osteoarthritis ( $n = 13$ ), chronic back pain (6), hypothyreosis (6), cardiac disease (6), bronchial asthma (6), diabetes mellitus (3), breast cancer (2), rheumatoid arthritis (1), ankylosing spondylarthritis (1), and Sjögren's syndrome (1). No one reported depression.

Regular exercise was practiced by 21/24 (88%) of patients answering the question. Nine out of twenty (45%) participants reported exercising at least three times a week. In the Fup, the exercise did not explain the variance of the following measurements: pain VAS, RBDS, HAQ, or FIQ. It also did not explain the changes in symptoms and quality of life or the amount of symptomless periods during the 26-year period reported by the patients. Those three patients who had reported having healed from FM stated exercising regularly at least 1–2 times a week.

The use of pain medication had decreased with 31% of patients, remained unchanged with 8%, and increased with 61%. The patients reported that the three best pain medications were paracetamol (35%), ibuprofen (35%), and a combined preparation containing 500 mg paracetamol + 30 mg codeine (9%). The four best drugs improving sleep were zopiclone (31%), amitriptyline (15%), zolpidem (15%), and a preparation containing 12.5 mg amitriptyline + 5 mg chlor-diazepoxide (15%). Vitamins, mineral supplements, and natural health products were used by 22/28 (79%) patients. Self-care (yoga, exercise, etc.) was practiced by all patients ( $n = 28$ ). The best self-treatment methods were exercise 18/27 (66%), winter swimming 4/27 (15%), and relaxation methods 2/27 (7%).

## Discussion

This prospective study examined the long-term outcome of patients with pFM diagnosed 26 years ago. The follow-up rate was rather good (74%) for such a long Fup. FM persisted in most of the patients, while three (11%) reported that they had healed from FM. In addition, about quarter reported that they had had at least one symptomless period lasting at least 1 year or more.

Those patients ( $n = 25$ ) whose symptoms continued reported slight deterioration of symptoms, but they were also 26 years older than at baseline (Fig. 2). However, less night

**Table 2** Changes in symptoms and measurements between baseline and follow-up contacts

Symptom or measuring	Baseline <i>n</i> = 28	Follow-up <i>n</i> = 25	Significance
Pain, VAS (SD)	52 mm (20)	61 (21)	NS
Sleeplessness	25%	68%	<i>p</i> = 0.0034
Negative effect of sauna (L4 + 5)*	71%	80%	NS
Effect of weather changes (L4 + 5)*	89%	96%	NS
RBDS (SD)**	8.6 (4.6)	68 (4.4)	NS
HAQ (SD)***	0.41 (0.36)	0.44 (0.49)	NS

\*Measured by Likert scale 1–5; L4 = gets worse slightly, L5 = gets a lot worse

\*\*Rimon's brief depression scale (see text)

\*\*\*Health Assessment Questionnaire (see text)

pain was reported in the Fup, whereas sleeplessness and abdominal irregularities were more common in the Fup. The level of functional ability evaluated by HAQ remained at the same level at the baseline and the Fup. This means that although the symptoms persist, the worsening of self-evaluated functional ability did not occur. The patients were 26 years older in the Fup, and thus, the good HAQ result was a positive surprise. Functional ability, analyzed by FinnFIQ, was better in this study than in a previous Finnish study [16]. Patients may adapt to their symptoms in a long run.

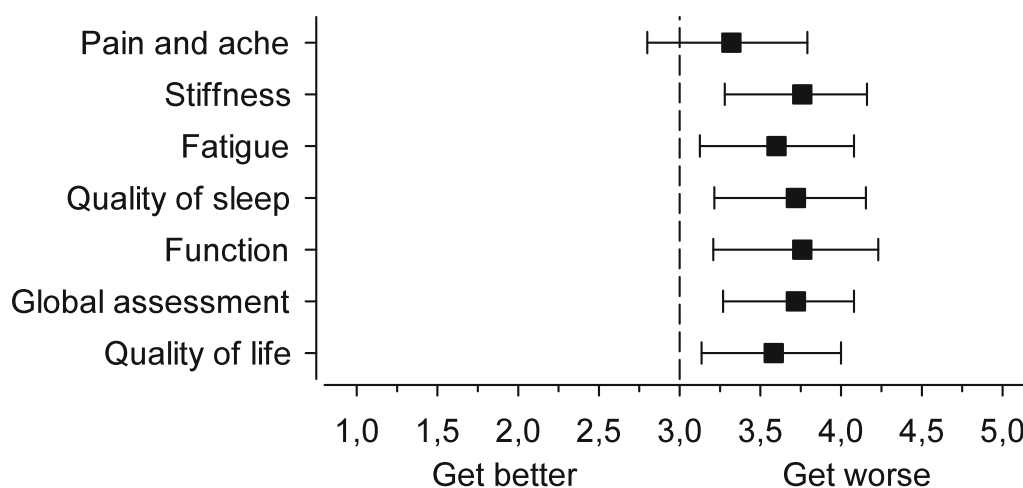
As in our study, FM has been rather persistent in other FupS, too. Bengtsson et al. [3] found that only 1 of 55 patients had healed at 8-year follow-up. Wallit [9] reported that 10% of patients were almost symptom-free at a 16.5-year follow-up, which is comparable to our result (11%).

In general, symptoms of FM may fluctuate [9], which may cause false positive results in short-term outcome studies [19]. The fluctuation was seen also in our 26-year FupS as every fourth reported at least one ore more pain-free periods. This strengthens the importance of long follow-up studies.

Deterioration of symptoms was more common in our study than in previous long-term clinical studies (over 6 years) [3–10]. However, the sum score of symptoms did not show worsening. This supports the previous findings that various symptoms persist [5, 7, 8, 20]. On the other hand, it should be remembered that country-specific issues, such as different compensation systems, may influence the patient's outcome [21].

Almost half of the subjects reported symptoms of RLS, but only one had that diagnosis. In a previous study, the prevalence of RLS was 33% among FM patients [22], whereas it varies from 2 to 15% among the normal population [23]. The symptoms of RLS should be asked from FM patients and evaluate whether diagnostic examinations are needed. Treatment of RLS, when needed, could improve sleep and quality of life [22].

The effect of weather changes on the patients' symptoms was very high in our study [24, 25]. Few studies have shown correlation between air pressure and FM symptoms [24, 26], and those whose symptoms have persisted less than 10 years show stronger reactions [27].



**Fig. 2** Reported changes in symptoms during 26-year follow-up

The worsening effect of sauna to FM symptoms has been reported by clinicians in Finland [28], where most people enjoy sauna (temperature 70–100 °C) regularly. Sauna is a heat stress for the body, and stress may modulate symptoms in FM [29].

Exercising is important to FM patients [30]. In addition to diminishing pain, cardiovascular fitness training showed activation on brain areas responsible of pain modulation [31]. Most of the patients (21/24) in our FupS reported that they exercise regularly. This may have kept their self-reported functioning (HAQ) at the same level as at baseline, although their symptoms showed slight worsening. However, more than half had increased their use of pain medication from the baseline. Probably, the medication relieved not only FM symptoms but also pain caused by age-related degenerative changes.

Although the strength of our study is the long follow-up, our study has several weaknesses. The number of patients was small, and they represent secondary or tertiary care population. The diagnostic criteria of FM have changed during the follow-up although as many as 93% fulfilled the criteria for WSP (ACR-90) at the follow-up. On the other hand, the baseline FM diagnoses were solid (confirmed by the same experienced clinician [RI] who performed the FuoQ), and most of the patients replied to the FupQ.

We conclude that this study shows that in most cases the FM symptoms persist for years and even decades. However, the symptoms fluctuate and patients may have long symptomless periods and 11% even reported that they have healed from FM. We did not find any explanations to the poor or good outcome, but most of our patients performed physical exercise regularly.

When a patient with FM asks about her/his future, we have to tell that the symptoms are likely to remain, but will probably fluctuate so that even long symptomless periods may take place. Healing of the problem is possible, however rather uncommon. Patients should be encouraged to engage in physical exercise, since it will keep on the physical ability to do daily life activities (HAQ remained here unchanged), although physical exercise will probably not make the symptoms disappear.

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**Compliance with ethical standards** All persons who participated in this study gave their informed consent prior to their inclusion in the study. The study plan was accepted in the Regional Ethics Committee of the Expert Responsibility Area of Tampere University Hospital on September 4, 2012.

**Disclosures** None.

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