



## Clinical pain research

## Mortality rate and causes of death in women with self-reported musculoskeletal pain: Results from a 17-year follow-up study

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## H I G H L I G H T S

- This is a prospective study with 17 years follow-up of an adult female cohort.
- Chronic pain, especially widespread pain, constituted a risk factor for death.
- Feeling anxious, frightened or nervous was associated with increased mortality.
- There was an increase in all-cause mortality.

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## A B S T R A C T

**Introduction:** Chronic musculoskeletal pain represents a significant health problem among adults in Norway. The prevalence of chronic pain is reported to be 35–53% in cross sectional studies of both genders. For many years, it has been a common opinion among medical doctors that chronic pain may indeed reduce a person's quality of life, but not affect life expectancy. However, over the previous two decades, reports about mortality and cause of death in individuals with chronic pain have been published. So far, several studies conclude that there is an increased mortality in patients with chronic pain, but it is not clear what causes this. Increased occurrences of cardio-vascular death or cancer death have been reported in some studies, but not verified in other studies.

**Aims of the study:** The aims of this study were to estimate the mortality rate in females with different extent of pain, to identify potential risk factors for death and to investigate if the causes of death differ according to prior reported pain.

**Methods:** This is a prospective population-based study of all women between 20 and 50 years registered in Arendal, Norway, in 1989 ( $N=2498$  individuals). At follow-up in 2007, 2261 living females were retraced, 89 had died.

All subjects received a questionnaire containing questions about chronic pain (pain  $\geq 3$  months duration in muscles, joints, back or the whole body) as well as 13 sub-questions about pain-modulating factors, non-specific health complaints and sleep problems, by mail in 1990, 1995 and 2007. Only subjects who answered the questionnaire in 1990 were included in the analyses. Of the deceased, 71 had answered the questionnaire in 1990.

A multivariate model for cox regression analysis was used in order to clarify if chronic pain, sleep problems, feeling anxious, frightened or nervous and number of unspecific health were risk factors for death.

The causes of death of 87 of the deceased individuals were obtained by linking the ID-number with the Norwegian Cause of Death Registry.

**Results:** The ratio of deceased responders was 2% (14/870) among those with no pain versus 5% (57/1168) among those with chronic pain at baseline. When separating into chronic regional pain and chronic widespread pain, the mortality rate was respectively 4% and 8% in the different groups. Age adjusted

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Abbreviation: NHC, non-specific health complaints.

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hazard ratio for mortality rate in individuals with initially chronic pain was [HR 2.5 (CI 1.4–4.5)] compared to pain free individuals. In the multivariate analysis, having chronic pain [HR 2.1 (1.1–4.2)] and feeling anxious, frightened or nervous [HR 3.2 (1.8–5.6)] were associated with increased risk of death. There was no difference in death from cardiovascular disease or malignancies between the groups of pain free individuals vs. the group of individuals with chronic pain.

**Conclusion:** The mortality rate was significantly higher for individuals with chronic pain compared to pain free individuals, adjusted for age. In addition, feeling anxious, frightened or nervous were risk factors for death. There was an increase in all-cause mortality.

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## 1. Introduction

Chronic musculoskeletal pain is a common complaint in the grown up population. The prevalence of chronic pain (CP = pain  $\geq$  3 months) is reported to be 35–53% in cross sectional studies of both genders [1–5] and 40–57% in females only [6–8]. The prevalence of chronic widespread pain (CWP) in different European countries is estimated to be 11–13% [1,3,5,9].

Over the previous two decades, reports about mortality and cause of death in individuals with CP have been published. Two studies have reported no difference in mortality rate between individuals with CP and individuals with no pain (NP) [10,11], while others have reported increased mortality in individuals with CP, especially CWP [12–17]. The increased mortality rate is reported to be significant at all age groups until 65 years [12].

In several studies reporting increased mortality in individuals with CP, the main causes of death are cardiovascular disease and cancer [12–15,17]. However, in one other cohort study, a significantly increased risk of developing cancer among individuals with CP was not found [18].

The aim of this study was to estimate the mortality rate in females with different extent of pain, to identify potential risk factors for death and to investigate if the causes of death differed according to the prior reported pain.

The course of chronic musculoskeletal pain and general health complaints for the survivors in this cohort is described elsewhere (*Scandinavian Journal of Pain*, Volume 3, Issue 4, Pages 210–217).

## 2. Methods

### 2.1. Design

The present study is a questionnaire based prospective cohort study of adult females focusing on self-reported chronic musculoskeletal pain and general health complaints.

The cohort consists of all women born 1st of January 1940 to 31st of December 1969 registered in Arendal municipality, Norway, in 1989, a total of 2498 women. In 1989, Arendal was a small municipality covering 12.2 km<sup>2</sup> located on the coast of South Norway. At 1st of January 1990, the total population consisted of 12,216 inhabitants, 5836 men and 6380 women. The rate of unemployment was 3.1%. The subjects received a questionnaire by mail in 1990, 1995 and 2007. Two reminders were sent out on each occasion.

In 1990, a representative sample of 217 of the 1168 women who had reported CP underwent a structured interview and a clinical examination in order to clarify if the ACR-90 classification criteria for FM [19] were fulfilled. In 1995, 214 of these women were re-examined. In addition, 100 women who had reported NP in 1990 but CP in 1995 (converters) and 100 women who had reported NP in both 1990 and 1995 (controls) went through the same procedure.

### 2.2. Material

In 1990, 82% (2038 of 2498) of the women returned the questionnaire. The further follow-up response rates were 78% (1894 of 2435) in 1995, and 73% (1654 of 2261) in 2007. Eighty-nine

women from the cohort died during the follow-up. Of these, 71 had returned the questionnaire properly filled in in 1990 and were included in the analysis. Eighteen of the 71 deceased individuals had been examined in 1995. By linking the ID-number from those who died with the Norwegian Cause of Death Registry, we received the causes of death of 87 of the deceased. Cause of death was categorized as “cardio vascular”, “malignancy”, “suicide/accidental”, “others” and “unknown”.

### 2.3. Screening questionnaire

The questionnaire consisted of two parts (*Appendix 1*). Part one dealt with pain issues. There were four sub-questions about pain and/or stiffness in muscles, joints, back and total body during three continuous months or longer in the last year. A positive responder had at least one affirmative answer in the first part, while a negative responder had none. Chronic regional pain (CRP) was defined as pain in solely muscles, joints or back or in any combination of two of these areas, while CWP was defined as pain in muscles *and* joints *and* back or any combination involving pain in the whole body (Article in press, expected publication October 2012 in *Scandinavian Journal of Pain*).

The second part of the questionnaire consisted of 13 sub-questions about non-specific symptoms, sleep problems and pain-modulating factors that are often reported by individuals with CWP [1,3,19,20]. Four questions were related to pain, of which three were about modulating factors for pain (physical activity, weather changes or feeling nervous, anxious, mentally stressed or depressed) and one about having pain at night. The remaining nine questions were two questions about disrupted sleep and non-restorative sleep and seven non-specific health complaints (NHC); fatigue, feeling anxious or nervous, regular headache, rumbling stomach, alternately hard/loose stools, numbness/tingling in the skin, or joints/muscles feeling swollen. The questions could be answered ‘yes’ or ‘no’, and a time frame was not specified.

### 2.4. Variables

#### 2.4.1. Age

Age was categorized into three groups based on year of birth; 1940–1949, 1950–1959 and 1960–1969.

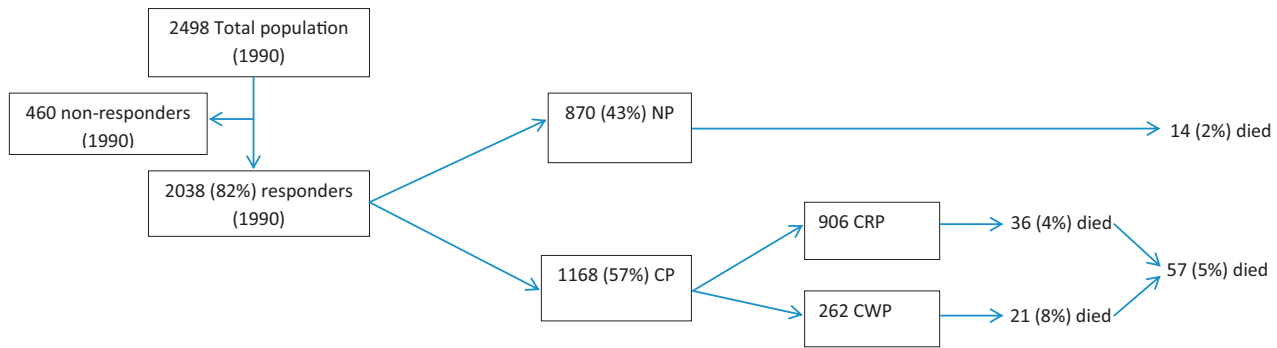
#### 2.4.2. Pain

Pain at baseline was categorized into three; no pain (NP), chronic regional pain (CRP) and chronic widespread pain (CWP). However, in some of the analyses, pain was presented as dichotomous variable with “no pain” and “any kind of chronic pain” as the two possible values.

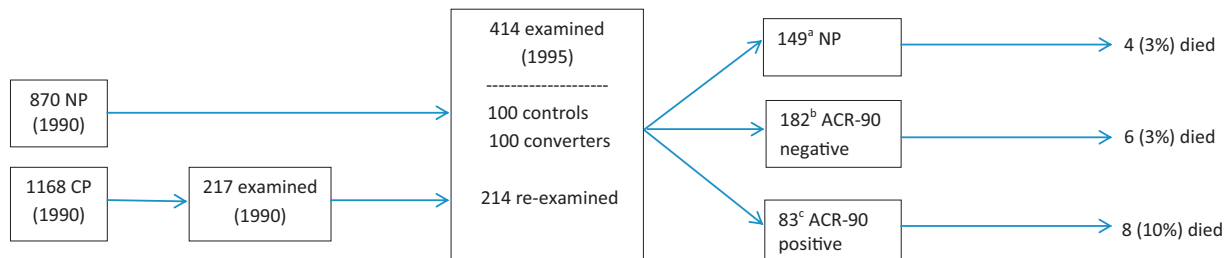
#### 2.4.3. Sleep problems

The questions about disrupted sleep and non-restorative sleep are presented as two dichotomous (yes/no) variables. In an earlier publication, disrupted sleep was found to be a risk factor for pain development and pain persistence (Article in press, expected

A. Flowchart, the total population.



B. Flowchart, the examined sub group.



**Fig. 1.** Response rate, numbers of individuals in different pain category, numbers of occurred deaths by 2007. NP=no pain, CP=chronic pain, CRP=chronic regional pain, CWP=chronic widespread pain. Re-examined=subjects who underwent a clinical examination in both 1990 and 1995. Controls and converters underwent a clinical examination 1995. Controls=100 subjects who reported NP in both 1990 and 1995 on the questionnaire. Converters=100 subjects who reported NP in 1990, but CP in 1995 on the questionnaire. <sup>a</sup>149 NP=100 controls+49 subjects who reported CP in 1990, but NP in 1995. <sup>b</sup>182 CP, ACR-90 not met=182 subjects who reported CP, but who did not meet the ACR-90 criteria for Fibromyalgia. <sup>c</sup>83 CP, ACR-90 met=83 subjects who reported CP and who met the ACR-90 criteria for Fibromyalgia.

publication October 2012 in Scandinavian Journal of Pain). Consequently, sleep problems was considered a possible confounding factor and thus applied as a separate variable.

#### 2.4.4. Non-specific health complaints

There are seven questions covering the most common NHC on part two of the questionnaire; fatigue, feeling anxious, frightened or nervous, regular headache, rumbling stomach, alternately hard/loose stools, numbness/tingling in the skin, or joints/muscles feeling swollen. The biological association between such symptoms and CP is not well understood, but the association between FM and both somatic symptoms and mental illness has partly been described [21]. None of these symptoms were thought to have a causal relationship with death. However, we wanted to investigate if an increasing number of symptoms were associated with increased risk of death as this might express poorer general health.

#### 2.4.5. Short form 36

In 1995, the 414 examined women were asked to fill in Short form-36 (SF-36). SF-36 is a generic questionnaire that provides information about eight different aspects of health, and it is widely used in health surveys. The items of the SF-36 are grouped into eight subscales: physical functioning (10 items), role limitation due to physical problems (4 items), role limitation due to emotional problems (3 items), bodily pain (2 items), social functioning (2 items), mental health (5 items), vitality (4 items), and general health perception (5 items). The raw scores were coded and recalibrated following the standard guidelines, and the items were then summed and transformed to the eight 0–100 scales (0 = worst health, 100 = best health) [22].

#### 2.5. Statistical analyses

Response rate, proportion of subjects with NP, CRP and CWP and deaths are presented as numbers (*n*) and percentages (%). Mortal-

ity rate is expressed as number per 1000 person years at risk for death. The follow-up period was from 1st of January 1990 to 31st of December 2006. Person-years at risk were computed among survivors and decedents from inclusion to death, to time of emigration or to the end of follow-up, a maximum of 17 years.

Cox regression was used to determine the risk estimates for death. The underlining time scale was years of follow-up. Initially, a stepwise cox regression was performed to clarify if any of the seven NHC on the screening questionnaire were significantly associated with death. Only feeling anxious, frightened or nervous reached the 0.05-level of significance, thus we chose to use this item as a separate variable in the further analyses. The other six NHC were summarized to a single count variable (0–6). In addition, analysis of the association between death and CP stratified by the three age categories was performed. The final model included age, pain category at baseline, sleep problems, feeling anxious, frightened or nervous and NHC.

Mean SF-36 scores from the follow-up in 1995 were analyzed by independent *t*-test comparing the mean score in the eight different subscales in those who died vs. those who were still alive in 2007.

The frequencies of the causes of deaths are presented by numbers (*n*) and percentages (%) within each pain category.

The analyses were performed using the SPSS 16.0 statistical package.

#### 2.6. Ethics

The project was approved by the Regional Committee of Medical Ethics.

### 3. Results

Response rate, proportion of subjects with NP, CRP and CWP and deaths are presented in Fig. 1.

**Table 1**

Mortality rate. Risk factors for death; adjusted for age only and adjusted for age, chronic pain, sleep problems, feeling anxious, frightened or nervous and number of non-specific health complaints in a multivariate model. A total number of 2038 subjects were included in 1990, of these, 71 died during follow-up.

Exposure 1990	Deaths (n)	Person years	Mortality rate (pr. 1000 person years)	Hazard ratio for death adjusted for age 95% CI	Multivariable model <sup>a</sup> 95% CI	Multivariable model <sup>b</sup> 95% CI
Pain free (n = 870)	14	14,697	1.0			Reference category
Chronic pain						
Total (n = 1168)	57	19,396	2.9	2.5 (1.4–4.5)	2.1 (1.1–4.2)	
Chronic regional pain (n = 906)	36	15,092	2.4			2.0 (1.0–4.0)
Chronic widespread pain (n = 262)	21	4304	4.9			3.3 (1.4–8.0)
Sleep problems						
Yes (n = 980)	46	16,327	2.8	2.1 (1.3–3.4)	0.9 (0.5–1.8)	0.9 (0.5–1.8)
No (n = 1012)	23	16,974	1.4			
Missing (n = 46)	2					
Anxious, frightened or nervous						
Yes (n = 371)	33	6103	5.4	3.8 (2.3–6.2)	3.2 (1.8–5.6)	3.1 (1.8–5.5)
No (n = 1505)	33	25,252	1.3			
Missing (n = 162)	5					
Non-specific health complaints <sup>c</sup> (0–6) (n = 2028)	70			1.2 (1.1–1.4)	1.0 (0.8–1.2)	1.0 (0.8–1.2)
Missing (n = 10)	1					

<sup>a</sup> Multivariable model; “no pain” and “all kinds of chronic pain” are possible values for pain.

<sup>b</sup> Multivariable model; “no pain”, “chronic regional pain” and “chronic widespread pain” are the possible values for pain.

<sup>c</sup> Non-specific health complaints (NHC) was assessed by the exact number of complaints (minimum 0 to maximum 6) and analyzed as a covariate in the statistical model. The person years and mortality ratio are therefore not given for each specific number of complaints.

The proportion of deceased responders was 5% (57/1168) in the pain groups (CRP + CWP) and 2% (14/870) the NP group. The proportion was even higher in the CWP than in the CRP group, respectively 4 and 4%. These numbers correspond to the findings in the examined samples. The clinical examination of 414 selected women in 1995 revealed that 20% (83 of 414) met the ACR-90 criteria for FM at that point of time. At follow up 12 years later, the ratio of deceased responders was 10% in the FM group, 3% in CP not fulfilling criteria for FM and 3% in NP individuals.

In this population, 99% had a follow-up time of 6 years or more. Among the 71 deceased, 64 (90%) had a follow-up time of 6 years or more.

### 3.1. Mortality rate

In the analysis stratified by age, there was an association between CP and death in all three age categories,  $p$ -value < 0.1 (data not shown).

The age-adjusted mortality rate in individuals with initially CP was significantly higher than in individuals with NP, 3/1000 vs. 1/1000 person years, [HR 2.5 (1.4–4.5)] (Table 1, Fig. 2). This increased mortality rate was still persistent even after adjustment for sleep problems, feeling anxious, frightened or nervous and number of health complaints in addition to age in the multivariate model, [HR 2.1 (1.1–4.2)] (Table 1).

### 3.2. Risk factors for death

Pain at baseline [HR 2.1 (1.1–4.2)] and feeling anxious, frightened or nervous [HR 3.2 (1.8–5.6)] were the variables associated with death in the multivariate model, while sleep problems and NHC (0–6) did not reach a level of significance (Table 1).

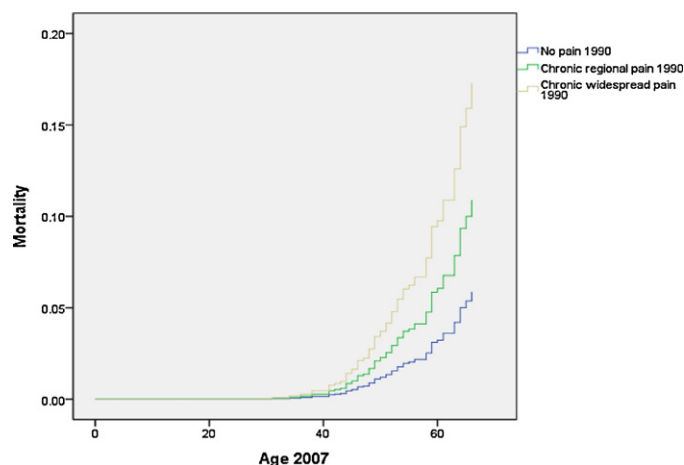
In this study, the mortality rate was highest among women either having CWP (based on the questionnaire), 5/1000 person years, or meeting the ACR-90 criteria for FM (based on clinical examination), 9/1000 person years. To ascertain the association between increasing amount of pain and increased risk of death, a cox regression with NP as a reference category was performed. Individuals with CRP had a slightly increased risk of death [HR 1.9

(1.0–3.7)], while individuals with CWP had even higher risk [HR 2.8 (1.3–6.1)]. Among the examined individuals, the numbers of deceased who were pain free ( $n = 4$ ) or who full filled ( $n = 8$ ) or did not full fill ( $n = 6$ ) the ACR-90 criteria for FM were quite low. We decided that we did not have a sufficient data set to perform an age adjusted cox regression on this specific data set.

Table 2 presents the mean SF-36 scores in 1995 of the later on deceased women ( $n = 15$ ) compared to those who were still alive ( $n = 376$ ) at the closure of the study (2007). The mean score was significantly lower for all subscales of SF-36 in the deceased compared to the women still alive, indicating a lower quality of life at an early stage in the deceased women.

### 3.3. Causes of death

The causes of death of 87 of the 89 deceased respondents in this study are presented in Table 3. There were no significant differences in cause of death between the individuals with and without CP. However, the proportion of “other” and “unknown”



**Fig. 2.** Mortality in individuals with no pain 1990, chronic regional pain 1990 and chronic widespread pain 1990 at different ages.

**Table 2**  
Mean SF-36 scores in 1995.

	Dead in 2007 (n = 15) Mean (SD)	Alive in 2007 (n = 376) Mean (SD)	Mean difference 95% CI	p-Value	Age adjusted mean difference, 95% CI
PF	69.7 (27.2)	85.4 (18.0)	15.7 (6.2–25.2)	0.04	15.7 (2.3–29.1)
RP	56.7 (39.5)	76.5 (34.0)	19.9 (2.1–37.6)	0.03	19.2 (1.4–37.0)
BP	52.9 (25.4)	69.1 (25.9)	16.3 (2.9–29.6)	0.02	15.7 (2.3–29.1)
GH	55.3 (22.0)	72.8 (22.7)	17.5 (5.8–29.2)	0.004	16.5 (4.8–28.1)
VT	43.0 (20.8)	54.4 (23.1)	11.4 (–0.5 to 23.3)	0.06	11.3 (–0.6 to 23.2)
SF	61.7 (29.7)	84.7 (22.2)	23.1 (11.4–34.7)	<0.001	22.5 (10.8–34.1)
RE	48.9 (35.3)	71.3 (34.0)	22.4 (4.8–40.0)	0.01	21.5 (3.9–39.1)
MH	63.7 (21.9)	78.3 (16.7)	14.5 (5.8–23.3)	0.001	14.5 (5.7–23.3)

PF: physical function; RP: role physical; BP: bodily pain; GH: general health; VT: vitality; SF: social function; RE: role emotional; MH: mental health.

causes was higher among the deceased respondents with CP, 36% ( $n = 20/56$ ), compared to only 7% ( $n = 1/14$ ) among those with NP. “Other causes” were lung disease ( $n = 5$ ), infection ( $n = 5$ ), live ( $n = 3$ ), endocrine ( $n = 2$ ), kidney ( $n = 1$ ), neurological ( $n = 2$ ), gastrointestinal ( $n = 1$ ) and rheumatic ( $n = 1$ ). All women who committed suicide had reported to be anxious, frightened or nervous in 1990.

#### 4. Discussion

In this adult female population, the mortality rate during 17 years follow-up was significantly higher for those with CP and for those feeling anxious, frightened or nervous than for individuals without such complaints at baseline. There were no differences in incidence of death by cardiovascular disease, cancer or suicide/accident among those with CP and those who were pain free. However, one third of those with CP died from “other” or “unknown” causes, while the figure for women without CP was 7%.

##### 4.1. Mortality rate in individuals with CP vs. without CP

The present study is a large, population based survey with a response rate of 82% at baseline. The mortality rate in females with CP was higher than in pain free women in this study; 3/1000 per person years versus 1/1000 per person years. This concurs with other studies who also found a higher mortality rate among individuals with CP than among pain free individuals [14,15]. However, there are differences in the magnitude of the mortality rate, which might be caused by gender and age differences in the samples studied. The Norwegian Central Bureau of Statistics report a higher mortality is in men than in women in all age groups, and as expected, higher mortality with increasing age. The present study population consists of females who are quite young; 20–50 years at baseline and 37–67 years at the end of the study. We will expect lower mortality rate than in studies with both genders represented and including individuals with higher age.

**Table 3**  
Causes of death for individuals with no pain (NP) or chronic pain (CP) at baseline and for non-responders. *p*-Values presented for differences in causes of death in NP-group vs. CP-group.

	No pain 1990 n (%)	Chronic pain 1990 n (%)	p-Value	Non-responder 1990 n (%)
Cardiovascular disease	5 (36%)	11 (19%)	0.20	2 (12%)
Malignancy	6 (43%)	20 (36%)	0.62	7 (41%)
Suicide/accident	2 (14%)	5 (9%)	0.55	3 (18%)
Other causes <sup>a</sup>	1 (7%)	15 (27%)	0.12	4 (24%)
Unknown causes <sup>a</sup>	0	5 (9%)	–	1 (6%)
Total	14 (100%)	56 (100%)	–	17 (100%)

<sup>a</sup> When merging “other causes” and “unknown causes”, the differences between NP and CP reaches a *p*-value of 0.05.

Moreover, there seems to be an increased risk of death with increasing pain extension, as the mortality rate for individuals with CRP in the present study was 2/1000 per person years, [HR 1.9 (1.0–3.7)] and 5/1000 per person years, [HR 2.8 (1.3–6.1)] for individuals with CWP compared to pain free individuals. It is though important to notice that the confidence intervals are quite wide and partly overlapping. These findings are in line with several earlier reports [12–17].

There are no obvious biological explanations for a higher mortality rate in individuals with CP. Most likely, there are different explanations as CP is a heterogenic group with different causes of pain and assumingly represents unlike subgroups with unequal risks for mortality. Unfortunately, the present study suffers from lack of information about possible co-morbidity. Moreover, the duration of the pain condition at baseline is unknown which may have an influence on the risk for mortality. One option is that longer duration of pain may represent a higher mortality rate. In addition, it is possible that there is delay in both patients and doctors when individuals with CP get other severe diseases involving pain.

The fact that more individuals with CP have a more unhealthy way of living, being less physical active and more smoking and belonging to a lower social class [23] might be important confounders for the association between CP and increased risk of death. Unfortunately, we have not registered such information, but for the studies that have been able to adjust for these factors, the results have been inconsistent [12–14]. However, as several studies including the present one, have found increased mortality rate in individuals with CP, this should lead to an increased focus on risk factors for death in general in follow-up of these patients.

##### 4.2. Other risk factors for increased mortality

Besides pain, feeling anxious, frightened or nervous was the only other examined factor that was associated with increased risk of death. This supports findings from another study which reported increased mortality in individuals with pessimistic, anxious and depressive personality traits [24]. This knowledge may be of



importance since as many as 28% of women with CP reported feeling anxious, frightened or nervous while only 9% of those without pain did the same. It is plausible that feeling anxious, frightened or nervous may lead to CP and also the other way around. It is important to be aware of this phenomenon in clinical practice. Physicians should be encouraged to conduct a thorough clinical assessment and answer the patients' questions in a way that they feel reassured that their condition is treated in the best way.

Unfortunately we did not inquire about feeling depressed in the screening questionnaire. Often depression and anxiety co-exists. It would also be of interest to investigate whether depression could be an independent risk factor.

The subjects examined in 1995 ( $n = 414$ ) filled in SF-36. During 12 years follow-up, 18 women in this group deceased. There are a significantly lower score in all eight subscales at baseline for those who died during follow-up. Even though this is a quite small sample, the results strongly suggest lower quality of life at baseline for the deceased.

#### 4.3. Causes of death

In the present study, cardiovascular death was only half as common in subjects with initially CP as in initially pain free subjects, 19% versus 36% respectively. This finding does not concur with McBeth et al. demonstrating cardiovascular death to be more common in subjects with pain [15]. Neither malignancies were more frequent in the deceased respondents with pain in this study, also in contrast to McBeth et al. reporting hormone related cancer (breast/prostate) to be increased [13]. As described earlier, adjusting for life style factors in analysis on cardiovascular death have given contradictory results [12–14]. In one study, the association between CWP and cardiovascular death was insignificant after correction for the confounding factors [12]. Interestingly, however, in other studies the association remained significant after correction for the same factors [13,14].

Data processed by The Norwegian Central Bureau of Statistics show that cardiovascular death dominates after the age of 80 and cancer death dominates before the age of 80 in Norway. This coincides well with our somewhat unexpected finding of a lower proportion of cardiovascular death than cancer deaths.

Whereas the increased mortality for females with CP was an increase in all-cause mortality, we found that 25% of women feeling anxious, frightened or nervous died from suicidal or accidental death. Indeed all who died from suicide/accident had reported feeling anxious, frightened or nervous at baseline. In other studies, it has been seen that have found anxiety is a risk factor for suicide [25,26].

Two studies have reported increased risk of suicidal/accidental death in individuals with FM [16,27]. In neither of those, the overall mortality rate in patients with FM was increased; however, the risk of suicide or accidental death was increased for these patients. Such association was not found in this present study, it was rather individuals feeling anxious, frightened or nervous who were over-represented among those who committed suicide.

"Other" and "Unknown" as the cause of death were over-represented among individuals with CP at baseline. We suggest that this might be a consequence of that individuals suffering from CP could be more difficult to diagnose with new conditions than pain free individuals, and also that the delay might lead to death from conditions that possibly could be treatable in an earlier stage.

However, there are some methodological considerations that have to be made.

Firstly, it is possible that subjects who died during the first years of follow-up, died of already existing diseases which also resulted in pain. In the present study, only 5/71 died during the first 2 years,

and therefore we have assumed that this does not affect our results significantly.

Secondly, the fact that death certificates are the only source of information on the underlying cause of death in the majority of deaths in Norway represents an uncertainty in such studies. One Norwegian study reports that more than 90% of cases were based on information from death certificates [28]. However, when they compared the death certificates with autopsy reports in the cases where both existed, they found a change in cause of death which resulted in change in ICD-10 chapter for 32%. The main indication for autopsy is "unclear cause of death", therefore these results are not suitable to apply on studies of death certificates from a general population. Yet, it is necessary to interpret data on cause of death with cautiousness due to these findings.

## 5. Conclusion

This study supports earlier findings in the majority of studies undertaken that CP and particular CWP are risk factors for increased mortality rate also in a general population of young-middle aged females. In contrast to earlier studies, no particular cause of death was found. However, more of the CP respondents died from other or unknown causes than the pain free respondents. This might be explained by both patients and doctors delay when individuals with CP get other severe, painful diseases. Moreover this study shows that feeling anxious, frightened or nervous is associated with an increased mortality even when the analyses were adjusted for CP. Explanations are still not clear.

New prospective studies with registration of possible confounding factors included depression, comorbidity, life style factors, social factors and knowledge about pain duration at baseline are needed to expand the knowledge of the assumed association between CP and death.

## Conflict of interest

The authors declare no financial or other relationships that might lead to a conflict of interest.

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## Appendix A. Questionnaire

1. Did you have pain and/or stiffness for at least three consecutive months during the last year at any of these sites?

	Yes	No
(a) Joints		
(b) Muscles		
(c) Back		
(d) Whole body		

2. General complaints

	Yes	No
(a)	Does the pain become worse after physical activity?	
(b)	Does the pain/stiffness change with the weather?	
(c)	Does the pain/stiffness increase if you become nervous, anxious, mentally stressed or depressed?	
(d)	Do you often have pain at night?	
(e)	Do you often wake up at night or have poor sleep?	
(f)	Do you often feel tired and listless?	
(g)	Do you feel refreshed in the morning?	
(h)	Do you feel anxious, frightened or nervous?	
(i)	Do you often have a headache?	
(j)	Does your stomach often rumble?	
(k)	Do you have alternately loose and hard stools?	
(l)	Do you feel numbness or tingling in skin or muscles?	
(m)	Do your joints and/or muscles feel swollen?	

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