

## SHORT COMMUNICATION

# NINE-YEAR TRAJECTORY OF PURCHASES OF PRESCRIBED PAIN MEDICATION BEFORE AND AFTER IN-PATIENT INTERDISCIPLINARY REHABILITATION FOR CHRONIC MUSCULOSKELETAL DISORDERS: A PROSPECTIVE, COHORT, REGISTER-BASED STUDY OF 4,365 SUBJECTS

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**Objective:** To investigate whether an interdisciplinary rehabilitation for chronic musculoskeletal disorders is associated with changes in the purchase of prescribed pain medication.

**Design:** Prospective register-based study.

**Subjects:** Employees in the public sector ( $n=4,365$ ) who participated in the rehabilitation programme between 1996 and 2009.

**Methods:** The changes in annual purchases of prescribed pain medication were measured for a 9-year exposure window, starting from 4 years before the start date of rehabilitation and ending 5 years after this date.

**Results:** Purchases of prescribed pain medication increased throughout the follow-up in all medication groups. The steepest increase was observed for analgesics, antidepressants, and hypnotics and sedatives. The growth rate of annual purchase, however, slowed significantly following the year of the start of rehabilitation for analgesics (annual growth rate (rate ratio) before and after rehabilitation 1.27 and 1.04, respectively, difference in trend  $p<0.001$ ); antidepressants (rate ratio 1.17 and 1.09,  $p=0.005$ ); and muscle relaxants (rate ratio 1.31 and 1.01,  $p<0.001$ ). For anxiolytics, and hypnotics and sedatives, no differences were observed in the trends of annual purchase before and after rehabilitation.

**Conclusion:** Rehabilitation was associated with a slowing increase in purchases of prescribed pain medication amongst rehabilitants. This may be a reflection of the positive effect that rehabilitation has on the need for pain medication.

**Key words:** chronic pain; medication; painkiller; antidepressants; anxiolytics; muscle relaxants; hypnotics; sedatives; trajectory.

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## INTRODUCTION

In Europe, two-thirds of people with chronic non-malignant pain use prescribed pain medication (PPM) (1). The use of PPM

is associated with a substantial risk of adverse effects, and it is expensive both for the individual and for society. For example, the total annual pharmacy costs of chronic non-malignant pain treatment are estimated to exceed \$60 billion in the USA (2). The mean annual pharmacy costs of chronic low-back pain alone in the USA is estimated to be almost \$9 billion (3).

One of the main objectives of rehabilitation for musculoskeletal disorders is to reduce the consumption of PPM. Although there is some evidence of reduction in PPM use after rehabilitation, further clarification of this effect is needed (2, 4, 5). Previous studies have focused mainly on widespread pain or pain intensity, with ambiguous results (2, 5). There is limited evidence of the effects of rehabilitation primarily focused on the treatment of pain due to chronic musculoskeletal disorders. For instance, Cochrane Reviews of the effects of multidisciplinary biopsychosocial rehabilitation on low-back, neck and shoulder pain, focused on change in rehabilitants' self-reported pain intensity, have mentioned PPM consumption only in passing (6, 7). In addition, change in PPM consumption is usually studied by comparing PPM usage shortly before and immediately, or only few months, after rehabilitation (2, 8). Although this approach is important, the need for rehabilitation, associated with extensive use of PPM, may develop several years before actual participation in rehabilitation. To our knowledge, no studies have examined long-term changes in PPM consumption after medical rehabilitation.

The objective of this study was to investigate changes in rehabilitants' PPM utilization over a 9-year exposure window, covering up to 4 years before and 4 years after the year of rehabilitation. The rehabilitation programme studied was general, in the sense that it was aimed at various chronic musculoskeletal problems rather than targeting specific musculoskeletal diseases (e.g. rheumatoid arthritis). We examined whether the rehabilitation was associated with a change in PPM utilization amongst rehabilitants by measuring trajectories 4 years before and 5 years after the start of rehabilitation. The study focused on the utilization of analgesics, antidepressants, anxiolytics, hypnotics and sedatives, and muscle relaxants.

## METHODS

This study was part of the Finnish Public Sector Study, an on-going prospective cohort study of employees working in 10 municipalities and 21 hospitals. The study cohort comprises all 151,618 employees with a  $\geq 6$  month job contract in any year between 1991 and 2005. The study was approved by the ethics committee of Helsinki and Uusimaa Hospital District. Data on rehabilitation, the start date of rehabilitation and the main diagnosis were acquired from the Rehabilitation Register kept by the Finnish Social Insurance Institution. A total of 4,365 individuals (86% women) participated in the in-patient, biopsychosocial, interdisciplinary rehabilitation due to chronic musculoskeletal disorders between 1996 and 2009. Using personal identification codes, the participants were linked with their pharmacy records. Demographic factors, including gender and age, were derived from the employers' registers.

### Rehabilitation

The Finnish Social Insurance Institution (SII) is one of the main providers of rehabilitation services in Finland for people of working age. It is a sponsor of several in-patient multidisciplinary rehabilitation programmes for people with musculoskeletal disorders. Subjects in the present study participated in rehabilitation programmes designed for people with chronic musculoskeletal disorders. The intervention represented an interdisciplinary, biopsychosocial rehabilitation targeted at improving or preserving health status and work ability of the working-age participants. The programmes were rehabilitation courses for musculoskeletal disorders and a so-called "workplace health promotion programme". These rehabilitation programmes have been described in detail elsewhere (9). The participants, selected from the workplace health promotion programme, had a confirmed diagnosis of musculoskeletal disorder (M-diagnosis according to International Classification of Diseases (ICD), version 10) as a main reason for rehabilitation. Although programmes were implemented in different independent rehabilitation facilities, SII strictly defined the inclusion criteria, the structure of the programmes, the multi-professional team composition, the modalities, and the assessment tests. The programmes studied were group-based (6–10 rehabilitants per group) comprising 2–4 in-patient periods with supervised activity 4–6 h per day (15–33 days in total), and a duration of 1–2 years. The modalities included physical training and psychological education. Participants were encouraged to adopt a healthier lifestyle, and were expected to achieve greater aerobic capacity, muscle strength, and endurance, as well as better self-management of stress. Between the inpatient periods, participants were expected to follow an individual exercise plan at home, which usually consisted of self-reliant physical activities and psychological exercises. The multi-professional team involved in the programme consisted of a physician, a physiotherapist, a psychologist, and a vocational rehabilitation specialist. In addition, a nurse, a social worker, an occupational therapist, an occupational physiotherapist, and a nutritionist were often involved.

Potential subjects for the rehabilitation programme were selected by their physicians. The subjects had a main diagnosis of a chronic musculoskeletal disorder that had already reduced their work ability, as measured by an increased rate of sickness absence. Applications for rehabilitation were approved by the local offices of SII, based on the physician's referral containing appropriate confirmed diagnoses.

### Annual purchase of prescribed pain medication

Data on purchase of PPM were obtained from the Drug Prescription Register kept by the Finnish Social Insurance Institution. This register includes all out-patient data on completed prescriptions classified according to the World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) classification code (10) from 1994 onwards. The Drug Prescription Register does not include diagnoses for prescriptions, but the data contain the exact dates of all purchases of prescribed medication and the corresponding number of defined daily doses (DDD). The dates and DDDs of all purchases of prescribed

analgesics (ATC code N02, M01A), antidepressants (N06A), anxiolytics (N05B), hypnotics and sedatives (N05C), and muscle relaxants (M03BX02, M03BC01, M03BC51) between 1 January 1994 and 31 December 2011 were linked to the rehabilitants. The purchase of antiepileptics (N03AX) was not included in the study as these medications have been used for the treatment of chronic pain for only a few recent years and there were no data available on their purchase before 2003. Data on annual mean PPM purchase (in DDDs) for each type of PPM was collected for the rehabilitants for the 9-year observation window, covering up to 4 years before the date of the start of the rehabilitation and 5 years after that date.

### Statistical analysis

The analyses were based on a 9-year observation window including 4 years before (years  $-4$  to  $-1$ ) and 5 years after (years  $0-5$ ) the date of the start of rehabilitation. Annual mean DDDs of PPM usage and their 95% confidence intervals (CI) were calculated using a repeated-measures negative binomial regression with the generalized estimating equations (GEE) method and autoregressive correlation structure. GEE takes into account the intra-individual correlation between measurements and is not sensitive to missing measurements. The models were adjusted for age at the start of rehabilitation, gender and, in order to eliminate period effects, for rehabilitation year. The mean of medication purchases in the years after rehabilitation compared with the years before rehabilitation were then modelled. These 2 mean estimates were compared by computing a rate ratio (RR) and its 95% CI for post-rehabilitation medication purchases compared with pre-rehabilitation medication. In order to examine the difference in the trends of PPM usage before and after rehabilitation, we calculated the mean estimate of the annual change in PPM purchases for 2 time-periods (the years before rehabilitation and those from the year of rehabilitation onwards), treating time as a continuous variable. The differences in these trends were tested by entering the interaction term "period\*year" into the model. All of the statistical analyses were performed using SAS<sup>®</sup> 9.2 software (SAS Institute, Inc., Cary, NC, USA).

## RESULTS

The mean age of the 4,365 participants was 50.8 years (standard deviation (SD) 6.5, range 23–71) at the start of the rehabilitation. Fig. 1 shows the annual mean purchases of PPM, expressed in DDDs by drug categories. During the mean follow-up of 8.3 years (range 5–9), PPM utilization increased in all medication groups, being higher in the last year of the 9-year trajectory compared with the first year. The magnitude and steepness of this increase, however, differed between studied medication groups.

Table I shows RRs of PPM purchases in the years after rehabilitation (years 0 to +4) compared with those prior to it (years  $-4$  to  $-1$ ). After rehabilitation, the mean rate was 1.6 times (95% CI 1.6–1.7) higher for analgesics, 2.2 times (95% CI 2.0–2.4) higher for antidepressants, and 1.8 times (95% CI 1.5–2.0) higher for hypnotics and sedatives compared with the mean rates before rehabilitation. The increase in purchases of anxiolytics and muscle relaxants after rehabilitation was clearly less significant: 1.2 (1.1–1.4) and 1.2 (1.0–1.3), respectively. Table I also shows the annual trend of PPM purchase within these 2 time-periods. Contrary to the clear increase in PPM purchase, the rate of growth of annual purchases of analgesics, antidepressants, and muscle relaxants flattened significantly after rehabilitation, the trends being 1.3 per year before and 1.0 after for analgesics (test of difference in the trend  $p < 0.001$ ), 1.2 and 1.1 per year for antidepressants ( $p = 0.005$ ) and 1.3 and 1.0

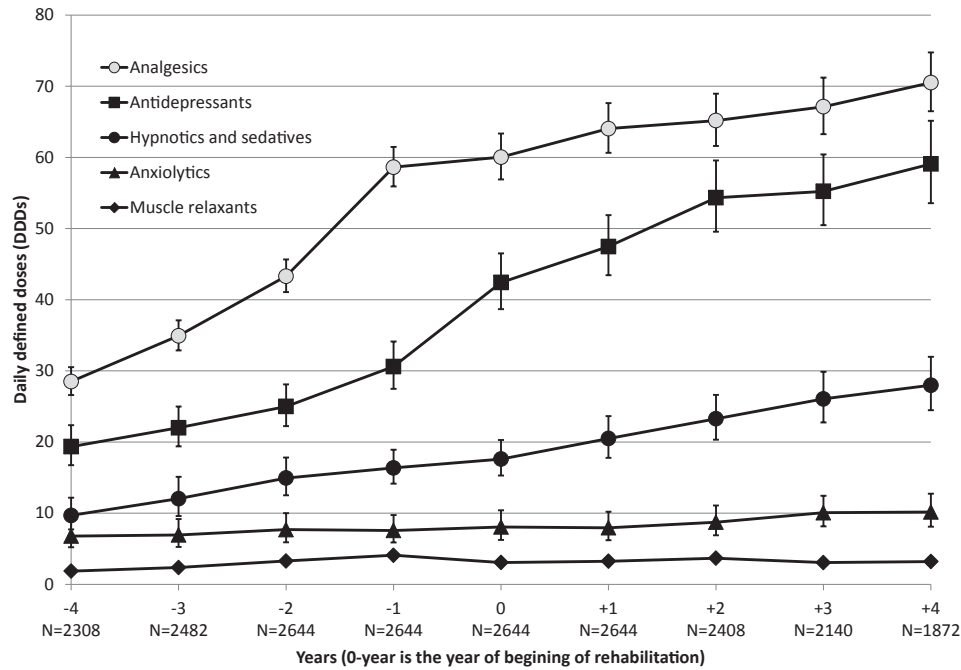


Fig. 1. Trajectories of annual mean purchase of prescribed pain medication before and after interdisciplinary rehabilitation for chronic musculoskeletal disorders.

per year for muscle relaxants ( $p < 0.001$ ). The trends in the use of anxiolytics and hypnotics and sedatives before rehabilitation did not deviate significantly from those after rehabilitation (test of interaction  $> 0.10$  for both medications).

### DISCUSSION

In this register-based study of 4,365 participants undergoing in-patient interdisciplinary musculoskeletal rehabilitation, annual purchases of PPM were followed before and after the start of rehabilitation. During the 9-year observation window, PPM purchases increased in all medication groups, more steeply in the period before rehabilitation and less steeply afterwards. The greatest increase was observed for analgesics, antidepressants, and hypnotics and sedatives. Interestingly, the increase in annual PPM purchases flattened off significantly in these medication groups in the years after rehabilitation compared with the years before the intervention.

The strengths of this study are the large study sample, the long period of follow-up before and after the intervention, and the use of data obtained from reliable national health registers. As the structure of the rehabilitation studied was strictly defined by the sponsor, we can assume that all participants were treated similarly.

The study had the following limitations. The sample was dominated by women, which might affect the results, as women are thought to use more pain medication than men (11). All participants were employed in the public sector, which may affect the generalization of the results. However, the occupational status of the participants varied widely, from managers to manual workers. Selection for the studied rehabilitation programme was based mainly on the physical health status of rehabilitants, and the rehabilitation methods used were mainly the methods of medical rehabilitation. Thus, the fact that the rehabilitants were employed by the Finnish public sector did not substantially reduce the representativeness of our results to an international setting. Antiepileptics, also used in the treatment of chronic pain,

Table I. Consumption of prescribed pain medication (PPM) before and after interdisciplinary rehabilitation for chronic musculoskeletal disorders

Period <sup>a</sup>	Analgesics RR (95% CI) <sup>b</sup>	Antidepressants RR (95% CI) <sup>b</sup>	Anxiolytics RR (95% CI) <sup>b</sup>	Hypnotics and sedatives RR (95% CI) <sup>b</sup>	Muscle relaxants RR (95% CI) <sup>b</sup>
After vs before <sup>c</sup>	1.64 (1.57–1.71)	2.15 (1.97–2.35)	1.24 (1.08–1.41)	1.75 (1.52–2.02)	1.17 (1.04–1.32)
Trend before <sup>d</sup>	1.27 (1.25–1.30)	1.17 (1.12–1.22)	1.04 (0.99–1.09)	1.19 (1.12–1.27)	1.31 (1.24–1.38)
Trend after <sup>d</sup>	1.04 (1.03–1.06)	1.09 (1.06–1.12)	1.06 (1.01–1.11)	1.12 (1.09–1.16)	1.01 (0.97–1.06)
Trend difference $p$ -value	$< 0.001$	0.005	0.590	0.119	$< 0.001$

<sup>a</sup>0-year is the year from the date of the start of rehabilitation.

<sup>b</sup>Rate ratios (95% confidence limits).

<sup>c</sup>Difference in the purchases of PPM after rehabilitation (years 0–4) compared with before rehabilitation (years –4 to –1).

<sup>d</sup>Trends are calculated based on the changes in annual purchases of PPM.

RR: rate ratio; 95% CI: 95% confidence interval.

were not included in this study. In addition, such medication as, for example, proton pump inhibitors, often prescribed to treat adverse effects of analgesics, were not included in this study.

Our findings are in line with previous studies suggesting that interdisciplinary rehabilitation programmes may reduce the utilization of PPM (2, 4, 12). It is possible however, that factors other than rehabilitation might cause the observed phenomenon. Such factors might be, for example, an increase in PPM use with ageing (even if our results were adjusted for age and the year of the start of rehabilitation), or the widely increasing usage of PPM in Western society observed in recent decades (4). Although confounding can never be ruled out in observational studies such as ours, the slowing increase in PPM purchase after rehabilitation may be due to the rehabilitation itself. If so, our findings support use of in-patient, interdisciplinary, biopsychosocial rehabilitation for chronic musculoskeletal disorders as a tool in pain management.

In conclusion, interdisciplinary rehabilitation was found to be associated with a slowing increase in PPM purchases amongst rehabilitants with chronic musculoskeletal disorders. This may reflect the positive effect of rehabilitation on the need for pain medication.

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