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Title: Longitudinal trajectories of neck–shoulder pain in workers: Influence on sick leave and work ability over 1 year

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DMH contributed to the statistical data analyses and drafting of the manuscript. AH and MBJ contributed to the conception, design, data collection and funding of the full DPHACTO study. All authors (DMH, AH, SDL, MBJ, and CDNR) contributed to the conception of this study, discussed the results and commented on the manuscript.

Data sharing statement:

Additional data can be accessed on request by email (aho@arbejdsmiljoforskning.dk).

The manuscript contains 3700 words, 3 tables, 2 figures, and 3 Supplemental figures (A-C).

Abstract

Objectives

The study aimed to determine the extent to which latent trajectories of neck-shoulder pain (NSP) are associated with self-reported sick leave and work ability based on frequent repeated measures over 1 year in an occupational population.

Methods

This longitudinal study included 748 Danish workers (blue-collar, n=620; white collar, n=128). A questionnaire was administered to collect data on personal and occupational factors at baseline. Text messages were used for repeated measurements of NSP intensity (numeric scale 0-10) over 1 year (14 waves in total). Simultaneously, self-reported sick leave (days/month) due to pain was assessed at four week intervals, while work ability was assessed using a single item (work ability index) at 12 week intervals over the year. Trajectories of NSP, distinguished by latent class growth analysis (LCGA), were used as predictors of sick leave and work ability in generalized estimation equations with multiple adjustments.

Results

Both sick leave and work ability were affected by NSP trajectory class. Referencing "low NSP", the relative risk (RR) from the fully adjusted model indicated a statistically significant ($p<0.001$) increase in sick leave for the NSP trajectories "moderate" (RR=3.1), "strong fluctuating" (RR=7.6) and "severe persistent" (RR 13.8). Similarly, the odds ratio (OR) for reduced work ability increased significantly ($p<0.001$) for the NSP trajectories "moderate" (OR=2.4), "strong" (OR=8.12) and "severe persistent" (OR=12.9).

Conclusion

Severe persistent NSP was strongly associated with sick leave and poor work ability over 1 year among workers. LCGA can be useful to distinguish important target groups in future observational/intervention studies on NSP.

Keywords: Chronic pain; LCGA; Neck pain; Occupational; Pain trajectories

Strengths and limitations of this study

- Some of the strengths of this study are:
  - Strength: identifying workers at high risk of sick leave and poor work ability due to pain is an important issue.
  - Strength: frequent repeated assessment of neck-shoulder pain, sick leave and work ability over 1 year.
  - Strength: high response rate during each month of follow-up.
- One of the limitations of this study was that sick leave was measured using self-report.

Introduction

Neck-shoulder pain (NSP) is a common musculoskeletal disorder in the working population.[1] Sick leave and reduced work ability due to NSP impose a considerable economic burden on organizations and society.[2-5]

NSP is considered a heterogeneous condition ranging from very mild symptoms to severe chronic pain [6] with a substantial individual variability in progression over time.[7-9] This heterogeneity may, however, comprise homogenous sub-populations with distinct patterns of pain, unique risk factors and different underlying pathophysiology.[10] Revealing such sub-populations is likely important for early identification, establishing risk factors, and improving prevention and treatment.[11] However, most existing studies have been conducted on patients with low back pain, e.g.,[11-13] while studies identifying and describing the patterns of NSP in working populations with a wide range of pain severities are sparse. Also, there is a lack of research on the predictive validity of NSP sub-populations. Thus, it is important to distinguish sub-populations of workers with different patterns of NSP (e.g. severity, temporal variability and time course) while assessing their predictive value against core prognostic outcomes, such as sick leave and work ability.[5 14 15]

Most previous studies on the prognosis of NSP have relied only on few measurements in time interspersed by long intervals, e.g. years.[7 16] Such studies are not designed to capture the detailed time course (trajectory) or temporal fluctuations in NSP (e.g. between weeks or months). In contrast, frequent repeated measurements of pain facilitate accurate and precise identification of individual pain trajectories [17] and minimize recall bias.[18]

Latent class growth analysis (LCGA) is a common statistical approach for identifying homogenous sub-populations (latent classes) based on individual growth parameters (i.e. intercept, slope and residual variance) in repeated measures data.[19] We have previously used LCGA to distinguish trajectory classes of NSP among workers based on frequent repeated measurements of NSP over 1 year[20] We identified six distinct trajectories of NSP ranging from “asymptomatic” (prevalence 11%) to “severe persistent NSP” (9%). However, understanding the occupational and clinical relevance of trajectories of NSP requires a determination of their predictive validity against core occupational and clinical outcomes.

The aim of this study is to determine the extent to which latent trajectories of NSP are associated with self-reported sick leave due to musculoskeletal pain and work ability based on frequent repeated measures over 1 year in an occupational population. A second aim is to investigate the temporal association (within person) between fluctuations in NSP and the outcomes sick leave and work ability.

Methods

Study design

This is a prospective study using data from the Danish Physical activity cohort with objective measurements (DPhacto). The study protocol for the cohort is reported in detail elsewhere.[21] Data collection took place from April 2012 to May 2014 at 15 Danish work places, including workers in four occupational sectors (cleaning, manufacturing, transportation and office work/administration).

Baseline data collection consisted of a brief web-based questionnaire, a standard health examination and objective diurnal measurements of physical activity and heart rate (presented elsewhere.[22 23] Prospective self-reported data on musculoskeletal pain, sick leave due to pain and work ability was collected repeatedly over 12 months using text messages.

Study population

The inclusion criterion for participation was current employment within any of the recruited work places. Exclusion criteria were holding a managing position or being pregnant or a student/trainee. In addition, workers not responding to the baseline questionnaire and/or the prospective measurements were excluded.

Among the 2107 invited workers, 1119 agreed to participate and 32 of them were excluded due to holding a managing position (n=17) or being pregnant (n=2) or a student/trainee (n=13). Of the remaining 1087 eligible workers, 782 responded to the questionnaire and 748 took part in the prospective measurements from baseline. Thus, the final study sample consisted of 748 workers (blue-collar, n=620; white collar, n=128). Descriptive characteristics of the study population are shown in Table 1.

All participants provided their written informed consent prior to participation. The present study was conducted according to the Declaration of Helsinki, approved by the Danish Data Protection Agency, and evaluated by the Regional Ethics Committee in Copenhagen, Denmark (H-2-2012-011).

Repeated assessment using text messages

Text messages (SMS) were used to assess self-reported pain intensity in the neck-shoulder region, days on sick leave and work ability using the commercial software "SMS-Track" (https://sms-track.com/). Starting at baseline, data on NSP and sick leave were collected at four week intervals (14 waves), while data on work ability were collected at 12 week intervals (4 waves in total) during the 1-year study. The SMS were sent on Sundays, with a reminder the following day.

Neck-shoulder pain

Pain intensity in the neck-shoulder region (NSP) the past month was assessed using an 11-point numeric rating scale (NRS), which ranges from 0 ("no pain") to 10 ("worst pain imaginable"). The worker responded to the question *"rate the worst pain you have experienced in your neck/shoulders within the past month?"* The NRS is a reliable and valid instrument for assessing pain intensity [24] and is recommended as an outcome in clinical trials.[25]

Sick leave

Sick-leave was assessed using a single-item from the validated Outcome Evaluation Questionnaire [26]: *"Within the past month, how many days have you been absent from work due to pain in muscles or joints?"* with response categories ranging from 0 to 31 days. Based on a recent meta-analysis, self-reported sick leave demonstrates good test-retest reliability and reasonably high convergent validity against records.[27]

Work ability

Work ability was assessed using a validated single item[28] from the work ability index.[29] The worker responded to the question "*Please rate your present work ability*?" with response categories ranging from 0 (unable to work) to 10 ("work ability as its best"). A score ≤ 7 denotes poor work ability.[30]

Assessment of possible confounders and effect modifiers

Theoretical assumptions and empirical evidence were used to select possible confounders and effect modifiers which were accounted for in the statistical analyses. The following variables were measured at baseline as previously described [20]: age (years,) and gender (male or female) based on civil registration number, body mass index (BMI) based on objectively measured height and weight, occupational sector (blue-collar or administration/office work), seniority in the current job (years), and physical work load (scale 1-10, with higher values indicating higher work load). Multisite pain was measured based on the Standardized Nordic questionnaire for the analysis of musculoskeletal symptoms [31] asking about pain intensity (NRS, scale 0-10) during the past three months in seven different anatomical areas (i.e. neck/shoulders, elbows, hands/wrists, lower back, hips, knees, and feet/ankles). A cut-point of >2 was used to indicate the occurrence of pain, whereby the number of pain sites was determined.[32] Since the relationship between NSP, sick leave and work ability may depend on the level of physical demands at work, physical work load was considered both a confounder and an effect modifier, while the other variables were solely included as possible confounders.

Statistical analyses

Growth trajectories (latent classes) of the intensity in NSP were identified using LCGA in Latent Gold version 5.1 (Statistical innovations Belmont, MA). The LCGA procedure and the resulting trajectory classes of NSP are described in detail elsewhere.[20] In brief, the LCGA assigns individuals to latent classes based on probabilities. That is, using growth parameters (i.e. intercept, slope and residual variance) reflecting change over time, LCGA assigns individuals to latent classes (categorical variable) assuming homogeneity within class and heterogeneity between classes.[19] In this study, LCGA models were performed using Time (14 waves over 1 year) as a continuous predictor and NSP intensity as a continuous dependent variable. Missing values were considered as missing at random and included in all models without imputations. The optimal number of classes was determined based on appropriate model fit indices, i.e. Bayesian information criterion (BIC), Entropy and Boot strap log likelihood ratio (BLRT), which were obtained in consecutive LCGA models with 1-10 a priori class solutions. Then, the models were evaluated based on the estimated growth parameters and clinical distinction between the identified classes. The identified trajectories of NSP were used as an independent variable in further statistical analyses.

The effect of NSP trajectories on sick leave (SMS at four week intervals over 1 year) and work ability (SMS each quarter) were determined using Generalized Estimation Equation (GEE) regression modeling with an auto regressive first order (AR1) covariance structure.

The effect of NSP trajectories on sick-leave (days/month) was tested using GEE with a Poisson distribution and a log link function. Fixed factors were NSP trajectory class (categories: low, moderate, strong fluctuating and severe persistent NSP) and time (continuous variable, 14 time points). The primary GEE models were constructed in three steps: (model 1) unadjusted, (model 2) adjusted for age, gender and BMI, and (model 3) additionally adjusted for occupational sector (four categories) and physical work load (continuous variable). To test the robustness of the primary models, secondary models were estimated with additional adjustment for the intensity of NSP (model 4) and the number of pain regions (model 5) at baseline (past three months). Finally, to test for potential effect modification by physical work load, model 3 was re-run with an interaction between NSP trajectory class and physical work load (model 6).

The effect of NSP trajectory class on work ability was tested using GEE regression modeling with a multinomial distribution and a cumulative logit link function. Fixed factors were NSP trajectory class and time (continuous variable, 4 time points). The models were constructed with and without adjustment for covariates, as explained above.

Additional GEE models were constructed to investigate the within person effect of temporal fluctuations in the intensity of NSP on fluctuations in sick leave and work ability. Due to the high work ability and low prevalence of sick leave in the classes with lower intensities of NSP, these analyses included only workers assigned to the trajectory classes "strong" and "severe persistent" NSP (n=248). To partition the within and between subjects variances in the predictor (intensity of NSP), the mean pain intensity score across all time points was determined for each individual. Then, the person mean pain score was subtracted from each repeated pain rating and used as an independent variable (within subject effect), while adjusting for the person mean pain as a covariate (between subjects effect).[33] The GEE model specifications for sick leave and work ability were the same as above. The models were estimated with and without adjustment for potential confounders as explained above.

The regression models were estimated using SPSS software version 22 (IBM, USA). For each model, we derived the exponential estimate, i.e. relative risk (RR) and odds ratio (OR) for sick leave and work ability, respectively, and 95% confidence intervals (CI). P-values <0.05 were considered significant.

Results

Characteristics of the study population

Characteristics of the study population are shown in Table 1. The study sample consisted of both males and females, and most were blue-collar workers. The workers were on average of middle age, slightly overweight, and had been in their current job for 14 years. The mean intensity of NSP across all time points was 2.6 (scale 0-10). Most of the workers rated high work ability (>7, scale 0-10) across the study period, while the average worker accumulated 6 days on sick leave due to pain over 1 year, although with a considerable dispersion between individuals. Compliance to the repeated measurements (SMS) in the study was high; the average worker responded to >90% of the SMS (Table 1).

[Insert Table 1 about here]

Identified latent trajectories of NSP

Based on model fit indices (BIC, Entropy and BLRT) and distinction between classes obtained from consecutive LCGA models, a six-class solution was chosen.[20] The growth pattern and prevalence (%) of the six identified trajectory classes of NSP were characterized as follows (see also Supplemental Figure A): class 1, *asymptomatic* (11%); class 2, *very low NSP* (10%); class 3, *low recovering NSP* (18%); class 4, *moderate fluctuating NSP* (28%); class 5, *strong fluctuating NSP* (24 %); and class 6, *severe persistent NSP* (9%). The trajectory classes with lower intensities of NSP (classes 1-3) did not differ in total days on sick leave (One-way ANOVA: p=0.32) or mean work ability (One way ANOVA: p=0.27) over 1 year; and the occurrence of sick leave was very low, while work ability was high across the three classes. Thus, classes 1-3 were merged into a single category (low NSP 39%), which was used as a reference in further analyses.

Descriptive data on sick leave and work ability over 1 year across the identified trajectories of NSP

The trajectory classes of NSP differed in both total days of sick leave and mean work ability over the 1 year study period (Supplemental Figures B and C). The total accumulated days on sick leave increased in the trajectory classes with moderate, strong and severe persistent NSP, while mean work ability decreased.

Effect of NSP trajectory classes on sick leave over 1 year

Poisson regression estimates of the effect of NSP trajectories on sick leave due to pain (days /month) are shown in Table 2. There was no significant time effect on sick leave (unadjusted RR=1.02, 95%CI 0.99-1.06). Thus, the interaction between NSP trajectory class and time was discarded from the models.

Days on sick leave due to pain were positively associated with the severity of NSP (Table 2, Figure 1). Referencing low NSP, the classes with moderate, strong fluctuating, and severe persistent NSP trajectories showed increasing positive RRs for days on sick leave each month. The estimated RR was only marginally reduced after adjustment for personal (age, gender and BMI) and occupational (sector and physical work load) factors (models 2 and 3).

Additional adjustment for multisite pain showed similar estimates for moderate NSP (RR=3.0, 95%CI 1.7–5.4), strong fluctuating NSP (RR=7.2, 95%CI 3.5–14.5) and severe persistent NSP (RR=13.1, 95%CI 6.1–28). Also, adjustment for baseline pain intensity revealed stronger estimates for moderate NSP (RR=3.7, 95%CI 2.1–6.8), strong fluctuating NSP (RR=10.9, 95%CI 5.1–23.7) and severe persistent NSP (RR=24.5, 95%CI 10.4–57.9), although with wider CIs.

There was no significant interaction between NSP trajectory class and physical work load on sick leave.

[Insert Figure 1 about here]

Effect of trajectories of NSP on work ability over 1 year

The ordinal regression estimates of the effect of trajectories of NSP on work ability (measured each quarter) are shown in Table 2.

There was a small time effect indicating reduced work ability over the year (unadjusted OR 1.05, 95%CI 0.99–1.11). There was no interaction between NSP trajectory class and time, whereby this interaction was discarded from the model.

NSP trajectory class was inversely associated with work ability (Table 2). The “strong fluctuating”, and “severe persistent” NSP trajectory classes showed increasing ORs for reduced work ability; particularly among those with severe persistent NSP. These significant associations persisted after adjustment for personal and occupational factors (model 2 and 3).

Additional adjustment for multisite pain showed slightly weaker estimates for moderate NSP (RR=2.2, 95%CI 1.7–2.9), strong fluctuating NSP (RR=6.4, 95%CI 4.6–9.0) and severe persistent NSP (RR=10.4, 95%CI 6.7–16.0). Further, adjustment for baseline pain intensity showed similar estimates for moderate NSP (RR=2.6, 95%CI 1.9–3.5), strong fluctuating NSP (RR=9.1, 95%CI 6.3–13.1) and severe persistent NSP (RR=15.4, 95%CI 9.3–25.5).

There was no significant interaction between NSP trajectory class and physical work load on work ability.

[Insert Table 2 about here]

Within-person effect of NSP on sick leave and workability

The within-person temporal effects of pain intensity on sick leave due to pain and work ability are shown in Table 3. Within person fluctuations in the intensity of NSP were positively associated with fluctuations in sick leave ($p<0.001$). That is, higher intensity of NSP was associated with more days of sick leave during a particular month at the individual level (Figure 2a). These results persisted in the adjusted models.

A similar within-person association was found between fluctuations in pain intensity and work ability, which did not change after adjustment for potential confounders (Table 3). For example, increasing intensity of NSP was associated with higher probabilities of poor work ability (Figure 2b).

[Insert Table 3 about here]

[Insert Figure 2]

Discussion

In summary, this prospective study investigated the relationship between LCGA-based trajectories of NSP and the outcomes sick leave and work ability. We found that the distinguished trajectory classes of NSP were strongly associated with sick leave due to pain and poor work ability over 1 year, and that the temporal fluctuations in pain intensity predicted fluctuations in sick leave and work ability at the individual level.

To our knowledge, this study is unique in assessing the predictive validity of LCGA-based trajectories of NSP against important prognostic outcomes among workers. A clear strength of the study is the use of frequent prospective measures of both exposure (intensity of NSP) and outcomes (work ability and sick leave) over 1 year. The high response rate to the SMS is also a strength supporting the feasibility of this method to obtain frequent repeated measurements of pain in future studies on the prognosis of NSP.

Trajectories of NSP, sick leave and work ability

The trajectory classes of NSP used in this study were distinguished using LCGA, resulting in six distinct trajectories of NSP.[20] This corroborates a study by Lövgren et al. (2014) which used Growth Mixture Modeling to identify six trajectory classes of NSP in nursing students entering working life. In contrast, the severity of NSP in the current sample of workers was much higher, perhaps due to the large proportion of blue-collar workers in this study.[1] The high prevalence of strong fluctuating (24%) and severe persistent NSP (9%), with mean pain intensities of 5 and 7 (scale 0-10), respectively, is noteworthy.

Trajectory class of NSP was strongly associated with the number of days on sick leave over the 1 year study period. Particularly, the fully adjusted model indicated a relative risk of sick leave 14 times higher in the trajectory class with severe persistent NSP, referencing the trajectory class with low NSP (Table 2, model 3). This result persisted even with adjustment for potential confounding by multisite pain, which was associated with NSP and sick leave in previous studies.[15 34 35] Thus, severe persistent NSP appears to be strongly associated with sick leave due to musculoskeletal pain, regardless of multisite pain and other personal and occupational factors.

The four trajectory classes of NSP were also associated with poor work ability over the year (Table 2). For instance, the probability of reporting reduced work ability was 13 times higher for the trajectory class with severe persistent NSP, referencing the trajectory class low NSP, regardless of inclusion of potential confounders in the model (Table 2, model 3). Interestingly, including baseline intensity of NSP (i.e. past 3 months) as an additional covariate in model 3 did not reduce the estimated association for sick leave or work ability. In fact, this adjustment resulted in even stronger estimates for work ability, which clearly indicates that the LCGA-based trajectory classes of NSP have a predictive value beyond that explained by past pain intensity assessed at a single time point.

The observed associations between the identified trajectories of NSP and the outcomes sick leave and work ability support the predictive validity of LCGA-based trajectories of NSP among workers. Thus, this study supports using LCGA to identify distinct sub-populations of workers with different patterns of NSP. Further, the predictive value for sick leave and work ability of the identified trajectory classes supports their usefulness as outcomes or target groups in future studies.

Effect modification by physical work load

High physical work load is a known risk factor for incident NSP and has been associated with a poor prognosis.[36] Thus, the association for NSP trajectories with sick leave and work ability was expected to be modified by the level of self-reported physical work load at baseline. However, we could not confirm any interaction between trajectory class of NSP and physical work load neither for sick leave nor work ability. Still, it is possible that more precise technical measurements of physical work exposure would have yielded different results.

Association between temporal fluctuations in NSP and fluctuations in sick leave and work ability

NSP is often referred to as a recurrent and fluctuating condition.[7] However, the temporal fluctuations in NSP have rarely been investigated in detail, and few, if any, studies have examined whether fluctuations in NSP are associated with concomitant changes in sick leave and work ability. The frequent repeated measures allowed us to assess the within-person temporal association between fluctuations in the intensity of NSP and changes in sick leave (every fourth week) and work ability (every twelfth week). We found that the within-person fluctuations in pain intensity were significantly associated with concomitant fluctuations in sick leave and work ability, which persisted in the fully adjusted model (Table 3). Thus, not only could we address the differences between workers in temporal patterns of NSP, but also whether the temporal fluctuations in NSP at the individual level are of predictive value.

Methodological discussion

As this study is limited to self-reported measures of pain and the outcomes sick leave and work ability, one cannot overlook the possibility of bias. Regarding self-reported sick leave, meta-analytic evidence indicates reasonably high convergent validity against organization and register-based records, although with a slight tendency for under-reporting.[27] Thus, there is a risk for underestimation of sick leave in this study.

Since this study was conducted in a non-random sample with a predominance of blue-collar workers, it is important to verify the study findings in other populations.

The general notion of NSP as a fluctuating and reoccurring condition is corroborated by our data, but this is rarely taken into account in observational studies on NSP. The inclusion of residual variance in the LCGA model allowed us to distinguish trajectory classes with more or less fluctuating patterns of NSP. Temporal fluctuations were more prominent in the NSP trajectories with moderate and strong pain, which may have contributed to the lower relative risk of sick leave and poor work ability compared to the trajectory class with severe persistent NSP.

Since the trajectories with lower intensities of NSP, i.e., including asymptomatic, very low NSP and low recovering NSP, did not differ regarding their low occurrence of sick leave and poor work ability, we decided to merge them into a single reference category in the prediction models. Still, it is possible that these three classes differ in other prognostic outcomes.

Conclusion

This study shows that severe persistent NSP is strongly associated with sick leave and poor work ability over 1 year among workers. The findings indicate that LCGA can be used to identify important sub-populations of workers with a poor prognosis of sick leave and work ability. Eventually, such sub-populations can be used as outcomes and target groups in future observational and/or intervention studies, which may improve prevention and treatment of NSP.

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Conflict of interest

The authors declare none.

Author contributions

DMH contributed to the statistical data analyses and drafting of the manuscript. AH and MBJ contributed to the conception, design, data collection and funding of the full DPHACTO study. All authors (DMH, AH, SDL, MBJ, and CDNR) contributed to the conception of this study, discussed the results and commented on the manuscript.

Data sharing statement

Additional data can be accessed on request by email (aho@arbejdsmiljoforskning.dk).

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Tables

Table 1 Descriptive characteristics of the study population (n=748)

	N	Range	Mean	SD
Age (years)	748	18–68	44.8	9.6
Men N (%)	411 (55)			
BMI (kg×m^{-2})	732	16–45	27.3	4.8
Seniority (years)	722	0–45	13.5	10.3
Administration workers N (%)	128 (17)			
Blue-collar workers N (%)	620 (83)			
Physical work load at baseline (scale 1-10)	723	1–10	5.3	2.4
Total days on sick leave (over all time points)	746	0–319	5.8	20.9
Mean work ability (over all time points) (scale 0-10)	748	0–10	8.3	1.7
Mean NSP intensity (over all time points) (scale 0-10)	748	0–9.6	2.6	2.3
NSP intensity at baseline (scale 0-10)	748	0–10	3.0	2.7
Number of pain regions (count)	745	0–6	1.7	1.5
Compliance to SMS (missing responses, count)				
NSP intensity	748	0–13	1.2	2.7
Sick leave	746	0–13	1.2	2.6
Work ability	748	0–3	0.4	0.7

Table 2. Effect of neck-shoulder pain (NSP) trajectory class on sick leave (days/month) and work ability (scale 0-10) over 1 year

	Sick leave				Work ability			
GEE models (classes)	p-value	RR	95%CI Lower	95%CI Upper	p-value	OR	95%CI Lower	95%CI Upper
Model 1								
Low NSP		1.00				1.00		
Moderate NSP	<0.001	3.28	1.89	5.68	<0.001	2.45	1.87	3.21
Strong NSP	<0.001	8.98	4.78	16.89	<0.001	8.64	6.38	11.69
Severe NSP	<0.001	17.64	9.36	33.23	<0.001	15.07	9.94	22.85
Model 2								
Low NSP		1.00				1.00		
Moderate NSP	<0.001	3.25	1.87	5.64	<0.001	2.40	1.83	3.16
Strong NSP	<0.001	8.61	4.54	16.33	<0.001	9.03	6.62	12.31
Severe NSP	<0.001	16.00	8.17	31.34	<0.001	14.77	9.63	22.66
Model 3								
Low NSP		1.00				1.00		
Moderate NSP	<0.001	3.11	1.75	5.52	<0.001	2.43	1.84	3.20
Strong NSP	<0.001	7.58	3.91	14.71	<0.001	8.12	5.91	11.16
Severe NSP	<0.001	13.83	6.72	28.49	<0.001	12.93	8.50	19.67

Relative risk (RR) estimates with 95% confidence intervals (CI) were obtained using Generalized Estimation Equation (GEE) with a Poisson distribution for days on sick-leave (measured at 4 week intervals). Odds ratios (OR) were obtained using GEE with a multinomial distribution for work ability (measured at 12 week intervals).
Model 1: Unadjusted.
Model 2: Adjusted for age, gender and body mass index.
Model 3: Additionally adjusted for occupational sector (four categories, referencing administration) and physical work load.

Table 3. Within-person effect of temporal fluctuations in neck-shoulder pain (NSP, scale 0-10) on fluctuations in sick leave (days/month) and work ability (scale 0-10) over 1 year

	Sick leave				**Work ability**			
			95% CI				95% CI	
GEE models	p-value	RR	Lower	Upper	p-value	OR	Lower	Upper
NSP intensity								
Model 1	0.008	1.12	1.03	1.21	0.005	1.11	1.03	1.19
Model 2	0.008	1.12	1.03	1.21	0.009	1.11	1.03	1.19
Model 3	0.011	1.11	1.02	1.21	0.002	1.13	1.04	1.21

Relative risk (RR) estimates with 95% confidence intervals (CI) were obtained using Generalized Estimation Equation (GEE) with a Poisson distribution for days on sick-leave (measured at 4 week intervals). Odds ratios (OR) were obtained using GEE with a multinomial distribution for work ability (measured at 12 week intervals). Estimates indicate the within-person effect of change in pain intensity on change in sick leave and work ability per month.

Model 1: adjusted for the person mean pain intensity across time points.

Model 2: additionally adjusted for age, gender and BMI.

Model 3: additionally adjusted for occupational sector and physical work load.

Figure legends

Figure 1. Mean 1-year trajectories of days on sick leave obtained in the fully adjusted model in each trajectory class of neck-shoulder pain (NSP). The x-axis represents the 14 pain ratings over 1 year. The y-axis represents the mean predicted number of days on sick leave per month.

Figure 2. Association between temporal fluctuations in neck-shoulder pain (NSP) and the outcomes sick leave and work ability. The x-axis represents the difference in pain intensity scores from the person mean pain intensity across time points. The y-axis represents the predicted number of days on sick leave per month (Fig. 2a) and the predicted cumulative probability of poor work ability (Fig. 2b), as defined by the cut-point ≤7 (scale 0-10) [30].

Supplemental Figures

Supplemental Figure A. Mean predicted intensity of neck-shoulder pain (NSP) over 1 year in the four trajectory classes of NSP obtained using Latent class growth analysis.

Supplemental Figure B. Mean and standard error bars of accumulated days on sick leave over 1 year in the four trajectory classes of neck-shoulder pain (NSP).

Supplemental Figure C. Mean and standard error for work ability averaged over 1 year in the four trajectory classes of neck-shoulder pain (NSP).

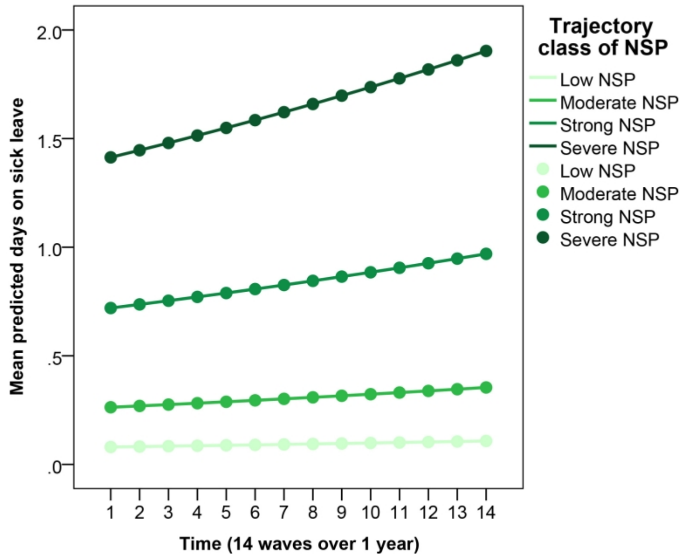


Figure 1.

Figure 1. Mean 1-year trajectories of days on sick leave obtained in the fully adjusted model in each trajectory class of neck-shoulder pain (NSP). The x-axis represents the 14 pain ratings over 1 year. The y-axis represents the mean predicted number of days on sick leave per month.

215x279mm (300 x 300 DPI)

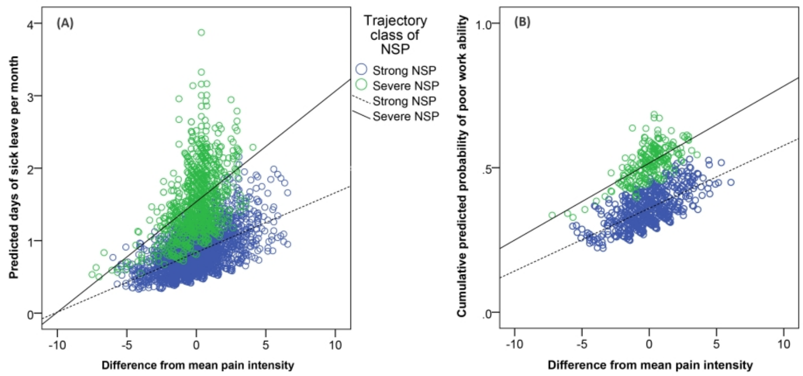
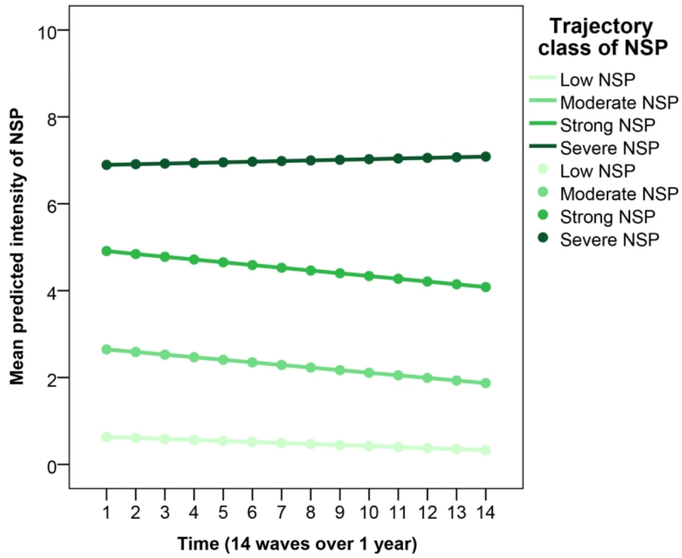


Figure 2

Figure 2. Association between temporal fluctuations in neck-shoulder pain (NSP) and the outcomes sick leave and work ability. The x-axis represents the difference in pain intensity scores from the person mean pain intensity across time points. The y-axis represents the predicted number of days on sick leave per month (Fig. 2a) and the predicted cumulative probability of poor work ability (Fig. 2b), as defined by the cut-point ≤7 (scale 0-10).

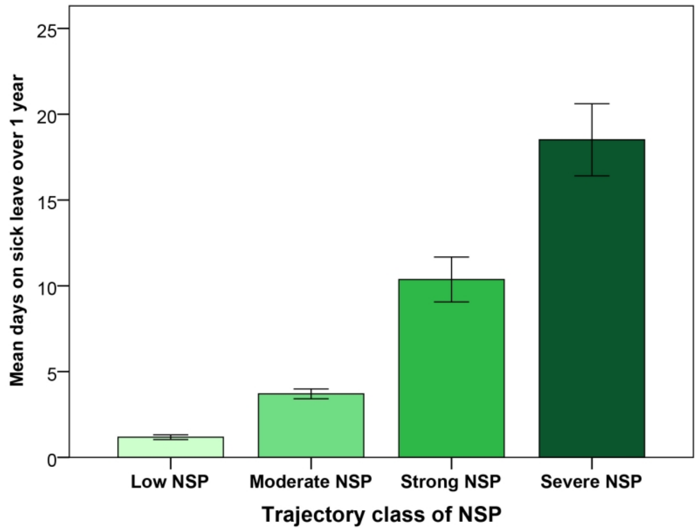
350x199mm (300 x 300 DPI)



Supplemental Figure A.

Supplemental Figure A. Mean predicted intensity of neck-shoulder pain (NSP) over 1 year in the four trajectory classes of NSP obtained using Latent class growth analysis.

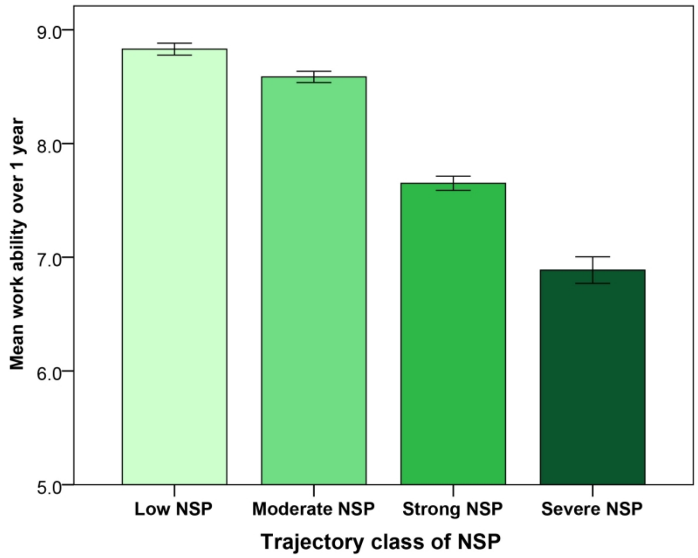
215x279mm (300 x 300 DPI)



Supplemental Figure B.

Supplemental Figure B. Mean and standard error bars of accumulated days on sick leave over 1 year in the four trajectory classes of neck-shoulder pain (NSP).

215x279mm (300 x 300 DPI)



Supplemental Figure C.

Supplemental Figure C. Mean and standard error for work ability averaged over 1 year in the four trajectory classes of neck-shoulder pain (NSP).

215x279mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Check yes/no
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	yes
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	yes, p4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	yes, p5
Methods			
Study design	4	Present key elements of study design early in the paper	yes, p5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	yes, p5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	a) yes, p5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	yes, p6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	yes, p6-7
Bias	9	Describe any efforts to address potential sources of bias	yes, p7-8 (confounders and statistical analyses)
Study size	10	Explain how the study size was arrived at	yes, p5 (flow)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	yes, p7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	yes p7-8

(*b*) Describe any methods used to examine subgroups and interactions	yes, p7-8
(*c*) Explain how missing data were addressed	yes, p7
(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	yes, p7
(*e*) Describe any sensitivity analyses	

Continued on next page

Results			Yes/no
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes, p7
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes, p9
		(b) Indicate number of participants with missing data for each variable of interest	Yes, p9
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	yes, Table 1
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Yes, tables 2-3
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	statistical methods and results
Discussion			
Key results	18	Summarise key results with reference to study objectives	yes, p15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	yes, p17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	yes, p18
Generalisability	21	Discuss the generalisability (external validity) of the study results	yes, p18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	yes, p18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Longitudinal trajectories of neck–shoulder pain in workers: Influence on sick leave and work ability over 1 year

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Title: Are trajectories of neck–shoulder pain associated with sick leave and work ability in workers? A one-year prospective study

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Conflict of interest: None to declare.

Author contributions:

DMH contributed to the statistical data analyses and drafting of the manuscript. AH and MBJ contributed to the conception, design, data collection and funding of the full DPHACTO study. All authors (DMH, AH, SDL, MBJ, and CDNR) contributed to the conception of this study, discussed the results and commented on the manuscript.

Data sharing statement:

Additional data can be accessed on request by email (aho@arbejdsmiljoforskning.dk).

The manuscript contains about 4300 words, 3 tables, 2 figures, and 1 Supplemental figure.

Abstract

Objectives

The study aimed to determine the extent to which latent trajectories of neck-shoulder pain (NSP) are associated with self-reported sick leave and work ability based on frequent repeated measures over 1 year in an occupational population.

Methods

This longitudinal study included 748 Danish workers (blue-collar, n=620; white collar, n=128). A questionnaire was administered to collect data on personal and occupational factors at baseline. Text messages were used for repeated measurements of NSP intensity (scale 0-10) over 1 year (14 waves in total). Simultaneously, self-reported sick leave (days/month) due to pain was assessed at four week intervals, while work ability (scale 0-10) was assessed using a single item (work ability index) at 12 week intervals over the year. Trajectories of NSP, distinguished by latent class growth analysis (LCGA), were used as predictors of sick leave and work ability in generalized estimation equations with multiple adjustments.

Results

Sick leave increased and work ability decreased across all NSP trajectory classes (low, moderate, strong fluctuating, and severe persistent pain intensity). In the adjusted model, the estimated number of days on sick leave was nearly 14 times larger for severe persistent NSP (RR=13.8, 95% CI 6.7–28.5; estimated mean 1.5 days/month) compared with low NSP (mean 0.1 days/month). Similarly, the likelihood of reduced work ability was nearly 13 times larger for severe persistent NSP (OR=12.9, CI 8.5–19.7: median 7.1) compared with low NSP (median 9.5).

Conclusion

Severe persistent NSP was strongly associated with sick leave and poor work ability over 1 year among workers. LCGA can be useful to distinguish important target groups in future observational/intervention studies on NSP.

Keywords: Chronic pain; LCGA; Neck pain; Occupational; Pain trajectories

Strengths and limitations of this study

- Some of the strengths of this study are:
  - Frequent repeated assessment of neck-shoulder pain, sick leave and work ability over 1 year.
  - High response rate during each month of follow-up.
- One of the limitations of this study was that sick leave was measured using self-report.

Introduction

Neck-shoulder pain (NSP) is a common condition, with annual prevalence rates between 27% and 48% in different working populations.[1] NSP is one of the leading causes of years lived with disability worldwide,[2] and is associated with reduced work ability[3] and high sick leave rates.[4 5] In workers with NSP, 20% had at least one spell of sick leave in one year.[4] Sick leave risks are higher in workers with more severe NSP intensity.[6] The economic burden of NSP on organizations and society is considerable.[7-9] The estimated total cost of neck pain in The Netherlands in 1996 was 686 million US dollars,[7] and the estimated total cost of both neck and back pain in Sweden in 2001was 1% of the gross national product (GNP).[9]

NSP is considered a heterogeneous condition ranging from very mild symptoms to severe chronic pain[10] with a substantial individual variability in progression over time.[11-13] This heterogeneity may, however, comprise homogenous sub-populations with distinct patterns of pain, unique risk factors and different underlying pathophysiology.[14] Revealing such sub-populations is likely important for early identification, establishing risk factors, and improving prevention and treatment.[15] However, most existing studies have been conducted on patients with low back pain, e.g.,[15-17] while studies identifying and describing the patterns of NSP in working populations with a wide range of pain severities are sparse. Also, there is a lack of research on the predictive value of NSP sub-populations; which is crucial for understanding the extent to which NSP sub-populations are of clinical and occupational relevance regarding intervention and treatment. Thus, it is important for research and occupational and clinical practice to distinguish sub-populations of workers with different trajectories of NSP (e.g. severity, temporal variability and time course) while assessing their predictive value against core prognostic outcomes, such as sick leave and work ability.[4 18 19]

Work ability, as defined as the balance between human resources and work demands,[20] is determined by multiple factors.[21] The perception of poor work ability is associated with sick leave and early retirement.[22] Sick leave due to pain is likely multifactorial, and several personal and work related (physical and psychosocial) factors have been identified as potential determinants of increased risks.[4 19 23 24] High physical workload is associated with poor workability and occurrence of sick leave due to pain,[4 25] and may hamper return to work.[23] Thus, the level of physical workload is a potential moderator of the relationship of NSP trajectories with work ability and sick leave.

Most previous studies on the prognosis of NSP have relied only on few measurements in time interspersed by long intervals, e.g. years.[11 26] Such studies are not designed to capture the detailed time course (trajectory) or temporal fluctuations in NSP (e.g. between weeks or months). In contrast, frequent repeated measurements of pain facilitate accurate and precise identification of individual pain trajectories [27] and minimize recall bias.[28]

Latent class growth analysis (LCGA) is a common statistical approach for identifying homogenous sub-populations (latent classes) based on individual growth parameters (i.e. intercept, slope and residual variance) in repeated measures data.[29] We have previously used LCGA to distinguish trajectory classes of NSP among workers based on frequent repeated measurements of NSP over 1 year[30] We identified six distinct trajectories of NSP ranging from "asymptomatic" (prevalence 11%) to "severe persistent NSP" (9%). Several personal and occupational factors, as well as symptom characteristics at baseline predicted trajectory class membership. However, understanding the occupational and clinical relevance of trajectories of NSP requires a determination of their predictive value against core occupational and clinical outcomes. Particularly, identifying NSP trajectories associated with unfavorable outcomes would likely aid targeted prevention and treatment.

The aim of this study is to determine the extent to which latent trajectories of NSP are associated with self-reported sick leave due to musculoskeletal pain and work ability based on frequent repeated measures over 1 year in an occupational population. A second aim is to investigate the temporal association (within person) between fluctuations in NSP and the outcomes sick leave and work ability.

Methods

Study design

This is a prospective study using data from the Danish Physical activity cohort with objective measurements (DPhacto). The study protocol for the cohort is reported in detail elsewhere.[31] Data collection took place from April 2012 to May 2014 at 15 Danish companies, including workers in four occupational sectors (cleaning, manufacturing, transportation and office work/administration). The initial contact and recruitment of companies were performed in

collaboration with a large Danish union. The companies were selected to represent blue-collar occupations with different levels of physical demands at work.

Baseline data collection consisted of a brief web-based questionnaire, a standard health examination and objective diurnal measurements of physical activity and heart rate (presented elsewhere.[32 33] Prospective self-reported data on musculoskeletal pain, sick leave due to pain and work ability was collected repeatedly over 12 months using text messages.

Study population

The inclusion criterion for participation was current employment within any of the recruited work places. Exclusion criteria were holding a managing position or being pregnant or a student/trainee. In addition, workers not responding to the baseline questionnaire and/or the prospective measurements were excluded.

Among the 2107 invited workers, 1119 agreed to participate and 32 of them were excluded due to holding a managing position (n=17) or being pregnant (n=2) or a student/trainee (n=13). Of the remaining 1087 eligible workers, 782 responded to the questionnaire and 748 took part in the prospective measurements from baseline. Thus, the final study sample consisted of 748 workers (blue-collar, n=620; white collar, n=128). Descriptive characteristics of the study population are shown in Table 1.

All participants provided their written informed consent prior to participation. The present study was conducted according to the Declaration of Helsinki, approved by the Danish Data Protection Agency, and evaluated by the Regional Ethics Committee in Copenhagen, Denmark (H-2-2012-011).

Repeated assessment using text messages

Text messages (SMS) were used to assess self-reported pain intensity in the neck-shoulder region, days on sick leave and work ability using the commercial software “SMS-Track” (https://sms-track.com/). Starting at baseline, data on NSP and sick leave were collected at four week intervals (14 waves), while data on work ability were collected at 12 week intervals (4 waves in total) during the 1-year study. The SMS were sent on Sundays, with a reminder the following day.

Neck-shoulder pain

Pain intensity in the neck-shoulder region (NSP) the past month was assessed using an 11-point numeric rating scale (NRS), which ranges from 0 ("no pain") to 10 ("worst pain imaginable"). The worker responded to the question *"rate the worst pain you have experienced in your neck/shoulders within the past month?"* The NRS is a reliable and valid instrument for assessing pain intensity [34] and is recommended as an outcome in clinical trials.[35]

Sick leave

Sick-leave due to pain was assessed using a single-item from the validated Outcome Evaluation Questionnaire [36]: *"Within the past month, how many days have you been absent from work due to pain in muscles or joints?"* with response categories ranging from 0 to 31 days. Based on a recent meta-analysis, self-reported sick leave demonstrates good test-retest reliability and reasonably high convergent validity against records.[37]

Work ability

Work ability was assessed using a validated single item[22] from the work ability index.[38] The worker responded to the question "*Please rate your present work ability*?" with response categories ranging from 0 (unable to work) to 10 ("work ability as its best"). A score ≤ 7 denotes poor work ability.[39]

Assessment of possible confounders and effect modifiers

Theoretical assumptions and empirical evidence were used to select possible confounders and effect modifiers which were accounted for in the statistical analyses. The following variables were measured at baseline as previously described [30]: age (years,) and gender (male or female) based on civil registration number, body mass index (BMI) based on objectively measured height and weight, occupational sector (manufacturing, cleaning, transportation, and administration/office work within the same workplaces), and seniority in the current job (years). Physical work load was measured by the question *"How physically demanding do you normally consider your present work?"* using a ten-point (1-10) response scale modified from Borg,[40] with higher values indicating higher physical demands. Multisite pain was measured based on the Standardized Nordic questionnaire for the analysis of musculoskeletal symptoms [41] asking about pain intensity (NRS, scale 0-10) during the past three months in

seven different anatomical areas (i.e. neck/shoulders, elbows, hands/wrists, lower back, hips, knees, and feet/ankles). A cut-point of >2 was used to indicate the occurrence of pain, whereby the number of pain sites was determined.[42] Since the relationship between NSP, sick leave and work ability may depend on the level of physical demands at work, physical work load was considered both a confounder and an effect modifier, while the other variables were solely included as possible confounders.

Statistical analyses

Growth trajectories (latent classes) of the intensity in NSP were identified using LCGA in Latent Gold version 5.1 (Statistical innovations Belmont, MA). The LCGA procedure and the resulting trajectory classes of NSP are described in detail elsewhere.[30] In brief, the LCGA assigns individuals to latent classes based on probabilities. That is, using growth parameters (i.e. intercept, slope and residual variance) reflecting change over time, LCGA assigns individuals to latent classes (categorical variable) assuming homogeneity within class and heterogeneity between classes.[29]

The LCGA models were performed using Time (14 waves over 1 year) as a continuous predictor and NSP intensity as a continuous dependent variable. Missing values were considered as missing at random and included in all models without imputations. The optimal number of classes was determined based on appropriate model fit indices, i.e. Bayesian information criterion (BIC), Entropy and Boot strap log likelihood ratio (BLRT), which were obtained in consecutive LCGA models with 1-10 a priori class solutions. Then, the models were evaluated based on the estimated growth parameters and clinical distinction between the identified classes. The identified trajectories of NSP were used as an independent variable in further statistical analyses of associations with sick leave and work ability over the same year.

The effect of NSP trajectories on sick leave (SMS at four week intervals over 1 year) and work ability (SMS each quarter) during the same year were determined using Generalized Estimation Equation (GEE) regression modeling with an auto regressive first order (AR1) covariance structure.

The effect of NSP trajectories on sick-leave (days/month) was tested using GEE with a Poisson distribution and a log link function. Fixed factors were NSP trajectory class (categorical variable) and time (continuous variable, 14 time points). The primary GEE models were constructed in three steps: (model 1) unadjusted, (model 2) adjusted for age, gender and BMI, and (model 3) additionally adjusted for occupational sector (four categories) and physical work load (continuous variable). To test the robustness of the primary models, secondary models were estimated with additional adjustment for the intensity of NSP (model 4) and the number of pain regions (model 5) at baseline (past three months). Finally, to test for potential effect modification by physical work load, model 3 was re-run with an interaction between NSP trajectory class and physical work load (model 6).

The effect of NSP trajectory class on work ability (dependent variable, ordinal scale) was tested using GEE regression modeling with a multinomial distribution and a cumulative logit link function. Fixed factors were NSP trajectory class (categorical variable) and time (continuous variable, 4 time points). The models were constructed with and without adjustment for covariates, as explained above.

Additional GEE models were constructed to investigate the within person effect of temporal fluctuations in the intensity of NSP on fluctuations in sick leave and work ability. To partition the within and between subjects variances in the predictor (intensity of NSP), the mean pain intensity score across all time points was determined for each individual. Then, the person mean pain score was subtracted from each repeated pain rating and used as an independent variable (within subject effect), while adjusting for the person mean pain as a covariate (between subjects effect).[43] Thus, these GEE models were constructed with three fixed factors: (i) time (14 waves), (ii) the person mean pain intensity across waves, and (iii) the difference from the mean pain intensity (within subject effect). Model specifications for sick leave and work ability were the same as above. The models were estimated with and without adjustment for potential confounders as explained above.

The regression models were estimated using SPSS software version 22 (IBM, USA). For each model, we derived the exponential estimate, i.e. relative risk (RR) and odds ratio (OR) for sick leave and work ability, respectively, and 95% confidence intervals (CI). P-values <0.05 were considered significant.

Patient and public involvement

No patients or public were directly involved in setting the research questions and outcomes, design and conduct of this study, or interpretation of the results. Results will be disseminated to the participants at http://www.nfa.dk/.

Results

Characteristics of the study population

Characteristics of the study population are shown in Table 1. The study sample consisted of both males and females, and most were blue-collar workers. The workers were on average of middle age, slightly overweight, and had been in their current job for 14 years. The mean intensity of NSP across all time points was 2.6 (scale 0-10). Most of the workers rated high work ability (>7, scale 0-10) across the study period, while the average worker accumulated 6 days on sick leave due to pain over 1 year, although with a considerable dispersion between individuals. Compliance to the repeated measurements (SMS) in the study was high; on average, the workers had 1.2 missing responses to pain and sick leave (14 waves) and 0.4 missing responses to work ability (4 waves) (Table 1).

[Insert Table 1 about here]

Identified latent trajectories of NSP

Based on model fit indices (BIC, Entropy and BLRT) and distinction between classes obtained from consecutive LCGA models, a six-class solution was chosen.[30] The growth pattern and prevalence (%) of the six identified trajectory classes of NSP were characterized as follows (see also Supplemental Figure A): class 1, *asymptomatic* (11%); class 2, *very low NSP* (10%); class 3, *low recovering NSP* (18%); class 4, *moderate fluctuating NSP* (28%); class 5, *strong fluctuating NSP* (24 %); and class 6, *severe persistent NSP* (9%). The trajectory classes with lower intensities of NSP (classes 1-3) did not differ in total days on sick leave (One-way ANOVA: p=0.32) or mean work ability (One way ANOVA: p=0.27) over 1 year; and the occurrence of sick leave was very low, while work ability was high across the three classes. Thus, classes 1-3 were merged into a single category (low NSP 39%), which was used as a reference in further analyses.

Effect of NSP trajectory classes on sick leave over 1 year

Poisson regression estimates of the effect of NSP trajectories on sick leave due to pain (days /month) are shown in Table 2. There was no significant time effect on sick leave (unadjusted RR=1.02, 95%CI 0.99-1.06). Thus, the interaction between NSP trajectory class and time was discarded from the models.

Based on the fully adjusted model (Table 2, model 3) referencing low NSP, the relative risk of sick leave increased for moderate (RR=3.1, 95%CI 1.8–5.5), strong fluctuating (RR=7.6, 95%CI 3.9–14.7), and severe persistent NSP (RR=13.8, 95%CI 6.7–28.5). The estimated number of days on sick leave per month was nearly 14 times higher in those with severe persistent NSP compared with low NSP. On average, the mean predicted estimates across 14 waves were 0.0 days/month (low NSP), 0.3 days/month (moderate NSP), 0.8 days/month (strong NSP), and 1.5 days/month (severe persistent NSP). Predicted values of sick leave for each wave over 1 year are shown in Figure 1.

Additional adjustment for multisite pain showed similar estimates for moderate NSP (RR=3.0, 95%CI 1.7–5.4), strong fluctuating NSP (RR=7.2, 95%CI 3.5–14.5) and severe persistent NSP (RR=13.1, 95%CI 6.1–28). Also, adjustment for baseline pain intensity revealed stronger estimates for moderate NSP (RR=3.7, 95%CI 2.1–6.8), strong fluctuating NSP (RR=10.9, 95%CI 5.1–23.7) and severe persistent NSP (RR=24.5, 95%CI 10.4–57.9), although with wider CIs.

There was no significant interaction between NSP trajectory class and physical work load on sick leave.

[Insert Figure 1 about here]

Effect of trajectories of NSP on work ability over 1 year

The ordinal regression estimates of the effect of trajectories of NSP on work ability (measured each quarter) are shown in Table 2.

There was a small time effect indicating reduced work ability over the year (unadjusted OR 1.05, 95%CI 0.99–1.11). There was no interaction between NSP trajectory class and time, whereby this interaction was discarded from the model.

NSP trajectory class was inversely associated with work ability (Table 2). Based on the fully adjusted model referencing low NSP (Table 2, model 3), the likelihood of a 1-unit reduction in work ability increased for moderate (OR=2.4, 95%CI 1.8–3.2), strong fluctuating (OR=8.1, 95%CI 5.9–11.2), and severe persistent NSP (OR=12.9, 95%CI 8.5–19.7). The median scores (IQR) of work ability during the year were 9.5(1.7) for low NSP, 9.0(2.0) for moderate NSP, 7.8(2.0) for strong NSP, and 7.1(2.5) for severe persistent NSP.

Additional adjustment for multisite pain showed slightly weaker estimates for moderate NSP (OR=2.2, 95%CI 1.7–2.9), strong fluctuating NSP (OR=6.4, 95%CI 4.6–9.0) and severe persistent NSP (OR=10.4, 95%CI 6.7–16.0). Further, adjustment for baseline pain intensity showed similar estimates for moderate NSP (OR=2.6, 95%CI 1.9–3.5), strong fluctuating NSP (OR=9.1, 95%CI 6.3–13.1) and severe persistent NSP (OR=15.4, 95%CI 9.3–25.5).

There was no significant interaction between NSP trajectory class and physical work load on work ability.

[Insert Table 2 about here]

Within-person effect of NSP on sick leave and workability

The within-person temporal effects of pain intensity on sick leave due to pain and work ability are shown in Table 3. Due to the high work ability scores and low prevalence of sick leave in the classes with lower intensities of NSP, these analyses included only workers assigned to the trajectory classes strong fluctuating and severe persistent NSP (n=248).

Within person fluctuations in the intensity of NSP were positively associated with fluctuations in sick leave (adjusted RR=1.11, 95%CI 1.02–1.21). That is, higher intensity of NSP was associated with more days of sick leave during a particular month at the individual level (Table 3 and Figure 2a).

A similar within-person association was found between fluctuations in pain intensity and work ability (adjusted OR 1.13, 95%CI 1.04–1.21). For example, increasing intensity of NSP was associated with higher probabilities of reduced work ability (Table 3). This association is illustrated in Figure 2b as the estimated probability of reporting poor work ability (≤7 on the 0-10 scale).[39]

[Insert Table 3 about here]

[Insert Figure 2]

Discussion

In summary, this prospective study investigated the relationship between LCGA-based trajectories of NSP and the outcomes sick leave and work ability. We found that the distinguished trajectory classes of NSP were strongly associated with sick leave due to pain and poor work ability over 1 year, and that the temporal fluctuations in pain intensity predicted fluctuations in sick leave and work ability at the individual level.

To our knowledge, this study is unique in assessing the association between LCGA-based trajectories of NSP and important prognostic outcomes among workers. A clear strength of the study is the use of frequent prospective measures of both exposure (intensity of NSP) and outcomes (work ability and sick leave) over 1 year. The high response rate to the SMS is also a strength supporting the feasibility of this method to obtain frequent repeated measurements of pain in future studies on the prognosis of NSP.

Trajectories of NSP, sick leave and work ability

The trajectory classes of NSP used in this study were distinguished using LCGA, resulting in six distinct trajectories of NSP.[30] This corroborates a study by Lövgren et al. (2014) which used Growth Mixture Modeling to identify six trajectory classes of NSP in nursing students entering working life. In contrast, the severity of NSP in the current sample of workers was much higher, perhaps due to the large proportion of blue-collar workers in this study.[1] The high prevalence of strong fluctuating (24%) and severe persistent NSP (9%), with mean pain intensities of 5 and 7 (scale 0-10), respectively, is noteworthy.

Trajectory class of NSP was strongly associated with the number of days on sick leave over the 1 year study period. Particularly, the fully adjusted model indicated a relative risk of sick leave 14 times higher in the trajectory class with severe persistent NSP (mean 1.5 days/month), compared with low NSP (mean 0.0 days/month). This result is in line with previous prospective studies showing a positive association between NSP intensity and sick leave.[4 6] This result persisted with adjustment for potential confounding by multisite pain, which was associated with NSP and sick leave in previous studies.[19 44 45] Thus, severe persistent NSP appears to be strongly associated with sick leave due to musculoskeletal pain, regardless of multisite pain and other personal and occupational factors.

The four trajectory classes of NSP were also associated with poor work ability over the year (Table 2). For instance, the probability of reporting reduced work ability was 13 times higher for the trajectory class with severe persistent NSP (median work ability 7.1 on the 0-10 scale), compared with low NSP (median work ability 9.5), regardless of inclusion of potential confounders in the model (Table 2, model 3). In agreement, previous studies have found that intense NSP is associated with reduced work ability in workers,[3 46] although none of these examined pain trajectories. Interestingly, including baseline intensity of NSP (i.e. past 3 months) as an additional covariate in model 3 did not reduce the estimated association for sick leave or work ability. In fact, this adjustment resulted in even stronger estimates for work ability, which clearly indicates that the LCGA-based trajectory classes of NSP have a predictive value beyond that explained by past pain intensity assessed at a single time point.

The observed consistent associations between the identified trajectories of NSP and the outcomes sick leave and work ability support the prognostic value of LCGA-based trajectories of NSP among workers, and suggests that such sub-populations can be of clinical and occupational relevance. Thus, this study supports using LCGA to identify distinct sub-populations of workers with different patterns of NSP. Further, the increase in sick leave and reduction in work ability across the four identified trajectory classes supports their usefulness as outcomes or target groups in future studies.

Effect modification by physical work load

High physical work load is a known risk factor for incident NSP and has been associated with a poor prognosis.[47] Thus, the association for NSP trajectories with sick leave and work ability was expected to be modified by the level of self-reported physical work load at baseline. However, we could not confirm any interaction between trajectory class of NSP and physical work load neither for sick leave nor work ability. Still, it is possible that more precise technical measurements of physical work exposure would have yielded different results.

Association between temporal fluctuations in NSP and fluctuations in sick leave and work ability

NSP is often referred to as a recurrent and fluctuating condition.[11] However, the temporal fluctuations in NSP have rarely been investigated in detail, and few, if any, studies have examined whether fluctuations in NSP are associated with concomitant changes in sick leave and work ability. The frequent repeated measures allowed us to assess the within-person temporal association between fluctuations in the intensity of NSP and changes in sick leave (every fourth week) and work ability (every twelfth week). We found that the within-person fluctuations in pain intensity were significantly associated with concomitant fluctuations in sick leave and work ability, which persisted in the fully adjusted model (Table 3). Thus, not only could we address the differences between workers in temporal patterns of NSP, but also whether the temporal fluctuations in NSP at the individual level are of predictive value.

Methodological discussion

As this study is limited to self-reported measures of pain and the outcomes sick leave and work ability, one cannot overlook the possibility of bias. Regarding self-reported sick leave, meta-analytic evidence indicates reasonably high convergent validity against organization and register-based records, although with a slight tendency for under-reporting.[37] Thus, there is a risk for underestimation of sick leave in this study. The question about days on sick leave the past month did not distinguish between work days and non-work days, which may have resulted in less precise estimates. Also, although both outcomes sick leave and work ability were assessed prospectively over 1 year, the NSP trajectories were determined during the same time period and thus causal inferences should be made with caution. Still, it seems most likely that pain preceded the occurrence of sick leave, rather than the reverse relationship.

We addressed several relevant factors as confounders or effect modifiers (physical work load) of the association of pain trajectories with sick leave and work ability. However, as the causes of sick leave and poor work ability are likely multifactorial,[4 19 21] the focus on pain trajectories as predictors is a potential limitation. Also, the possibility of residual confounding by non-measured factors cannot be ruled out.

Since this study was conducted in a non-random sample with a predominance of blue-collar workers, it is important to verify the study findings in other working populations. The general notion of NSP as a fluctuating and reoccurring condition[11] is corroborated by our data, but this is rarely taken into account in observational studies on NSP. The inclusion of residual variance in the LCGA model allowed us to distinguish trajectory classes with more or less fluctuating patterns of NSP. Temporal fluctuations were more prominent in the NSP trajectories with moderate and strong pain, which may have contributed to the lower relative risk of sick leave and poor work ability compared to the trajectory class with severe persistent NSP.

Since the trajectories with lower intensities of NSP, i.e., including asymptomatic, very low NSP and low recovering NSP, did not differ regarding their low occurrence of sick leave and poor work ability, we decided to merge them into a single reference category in the prediction models. Still, it is possible that these three classes differ in other prognostic outcomes.

Conclusion

This study shows that severe persistent NSP is strongly associated with sick leave and reduced work ability over 1 year among workers. The findings indicate that LCGA can be used to identify important sub-populations of workers with a poor prognosis of sick leave and work ability. Eventually, such sub-populations can be used as outcomes and target groups in future observational and/or intervention studies, which may improve prevention and treatment of NSP.

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Conflict of interest

The authors declare none.

Author contributions

DMH contributed to the statistical data analyses and drafting of the manuscript. AH and MBJ contributed to the conception, design, data collection and funding of the full DPhacto study. All authors (DMH, AH, SDL, MBJ, and CDNR) contributed to the conception of this study, discussed the results and commented on the manuscript.

Data sharing statement

Additional data can be accessed on request by email (aho@arbejdsmiljoforskning.dk).

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Tables

Table 1 Descriptive characteristics of the study population (n=748)

	N	Median	IQR	Mean	SD
Age (years)	748			44.8	9.6
Men N (%)	411 (55)				
BMI (kg×m^{-2})	732			27.3	4.8
Seniority (years)	722			13.5	10.3
Administration workers N (%)	128 (17)				
Blue-collar workers N (%)	620 (83)				
Cleaning	115 (15)				
Manufacturing	448 (60)				
Transportation	57 (8)				
Physical work load at baseline (scale 1-10)	723			5.3	2.4
Total days on sick leave (over all time points)	746	0.0	3.0	5.8	20.9
Mean work ability (over all time points) (scale 0-10)	732	8.8	2.5	8.3	1.7
Mean NSP intensity (over all time points) (scale 0-10)	748	2.0	3.6	2.6	2.3
NSP intensity at baseline (scale 0-10)	748	3.0	5.0	3.3	2.9
Number of pain regions at baseline (count)	745	1.0	3.0	1.7	1.5
Compliance to SMS (missing responses, count)					
NSP intensity	748	0.0	1.0	1.2	2.7
Sick leave	746	0.0	1.0	1.2	2.6
Work ability	732	0.0	1.0	0.4	0.7

Note: median values with inter quartile range (IQR) are shown for skewed data. Abbreviations: BMI, body mass index; NSP, neck-shoulder pain.

Table 2. Effect of neck-shoulder pain (NSP) trajectory class on sick leave (days/month) and work ability (ordinal scale 0-10) over 1 year, referencing low NSP.

		Sick leave				**Work ability**			
GEE models (classes)	N	p-value	RR	95%CI Lower	95%CI Upper	p-value	OR	95%CI Lower	95%CI Upper
Model 1									
Low NSP	292		1.00				1.00		
Moderate NSP	208	<0.001	3.28	1.89	5.68	<0.001	2.45	1.87	3.21
Strong NSP	178	<0.001	8.98	4.78	16.89	<0.001	8.64	6.38	11.69
Severe NSP	70	<0.001	17.64	9.36	33.23	<0.001	15.07	9.94	22.85
Model 2									
Low NSP	286		1.00				1.00		
Moderate NSP	204	<0.001	3.25	1.87	5.64	<0.001	2.40	1.83	3.16
Strong NSP	174	<0.001	8.61	4.54	16.33	<0.001	9.03	6.62	12.31
Severe NSP	68	<0.001	16.00	8.17	31.34	<0.001	14.77	9.63	22.66
Model 3									
Low NSP	277		1.00				1.00		
Moderate NSP	199	<0.001	3.11	1.75	5.52	<0.001	2.43	1.84	3.20
Strong NSP	165	<0.001	7.58	3.91	14.71	<0.001	8.12	5.91	11.16
Severe NSP	66	<0.001	13.83	6.72	28.49	<0.001	12.93	8.50	19.67

Relative risk (RR) estimates, indicating the relative increase in the number of days on sick leave per month, were obtained using Generalized Estimation Equation (GEE) with a Poisson distribution for days on sick-leave (measured at 4 week intervals). Odds ratios (OR), indicating the likelihood of a 1-unit reduction in work ability, were obtained using GEE with a multinomial distribution for work ability (measured at 12 week intervals).
Model 1: Unadjusted.
Model 2: Adjusted for age, gender and body mass index.
Model 3: Additionally adjusted for occupational sector (four categories, referencing administration) and physical work load.

Table 3. Within-person effect of temporal fluctuations in neck-shoulder pain (NSP, scale 0-10) on fluctuations in sick leave (days/month) and work ability (scale 0-10) over 1 year

		Sick leave				**Work ability**			
				95% CI				95% CI	
GEE models	N	p-value	RR	Lower	Upper	p-value	OR	Lower	Upper
NSP intensity									
Model 1	248	0.008	1.12	1.03	1.21	0.005	1.11	1.03	1.19
Model 2	242	0.008	1.12	1.03	1.21	0.009	1.11	1.03	1.19
Model 3	231	0.011	1.11	1.02	1.21	0.002	1.13	1.04	1.21

Relative risk (RR) estimates, indicating the relative increase in the number of days on sick leave per month, were obtained using Generalized Estimation Equation (GEE) with a Poisson distribution for days on sick-leave (measured at 4 week intervals). Odds ratios (OR), indicating the likelihood of a 1-unit reduction in work ability, were obtained using GEE with a multinomial distribution for work ability (measured at 12 week intervals). Estimates indicate the within-person effect of change in pain intensity on change in sick leave and work ability per month.

Model 1: adjusted for the person mean pain intensity across time points.

Model 2: additionally adjusted for age, gender and BMI.

Model 3: additionally adjusted for occupational sector and physical work load.

Figure legends

Figure 1. Mean 1-year trajectories of days on sick leave obtained in the fully adjusted model in each trajectory class of neck-shoulder pain (NSP). The x-axis represents the 14 pain ratings over 1 year. The y-axis represents the mean predicted number of days on sick leave per month.

Figure 2. Association between temporal fluctuations in neck-shoulder pain (NSP) and the outcomes sick leave and work ability. The x-axis represents the difference in pain intensity scores from the person mean pain intensity across time points. The y-axis represents the predicted number of days on sick leave per month (Fig. 2a) and the predicted cumulative probability of poor work ability (Fig. 2b), as defined by the cut-point ≤7 (scale 0-10).[39]

Supplemental Figures

Supplemental Figure A. Mean predicted intensity of neck-shoulder pain (NSP) over 1 year in the four trajectory classes of NSP obtained using Latent class growth analysis.

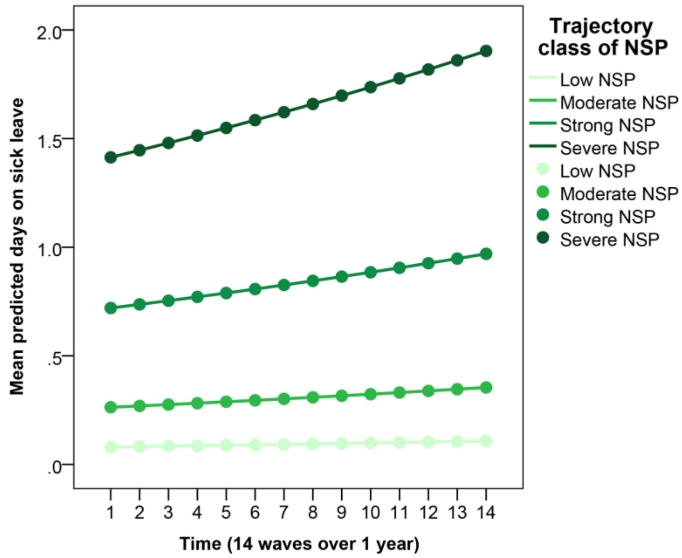


Figure 1.

Figure 1. Mean 1-year trajectories of days on sick leave obtained in the fully adjusted model in each trajectory class of neck-shoulder pain (NSP). The x-axis represents the 14 pain ratings over 1 year. The y-axis represents the mean predicted number of days on sick leave per month.

215x279mm (300 x 300 DPI)

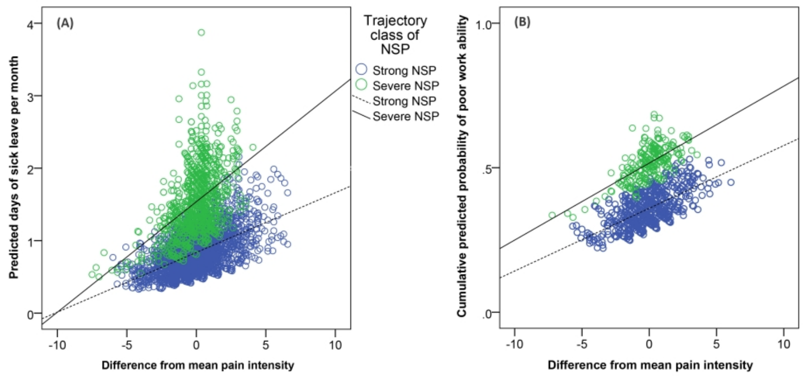
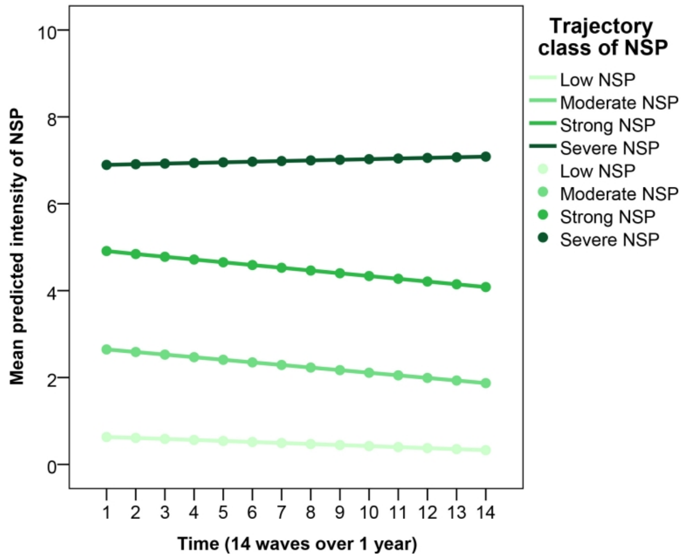


Figure 2

Figure 2. Association between temporal fluctuations in neck-shoulder pain (NSP) and the outcomes sick leave and work ability. The x-axis represents the difference in pain intensity scores from the person mean pain intensity across time points. The y-axis represents the predicted number of days on sick leave per month (Fig. 2a) and the predicted cumulative probability of poor work ability (Fig. 2b), as defined by the cut-point ≤7 (scale 0-10).

350x199mm (300 x 300 DPI)



Supplemental Figure A.

Supplemental Figure A. Mean predicted intensity of neck-shoulder pain (NSP) over 1 year in the four trajectory classes of NSP obtained using Latent class growth analysis.

215x279mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Check yes/no
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	yes
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	yes, p4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	yes, p5
Methods			
Study design	4	Present key elements of study design early in the paper	yes, p5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	yes, p5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	a) yes, p5-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	yes, p6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	yes, p6-8
Bias	9	Describe any efforts to address potential sources of bias	yes, p7-8 and 9 (confounders and statistical analyses)
Study size	10	Explain how the study size was arrived at	yes, p6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	yes, p8-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	yes p8-9

	(*b*) Describe any methods used to examine subgroups and interactions	yes, p8-9
	(*c*) Explain how missing data were addressed	yes, p8
	(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	yes, p8; page 11
	(*e*) Describe any sensitivity analyses	

Continued on next page

Results			Yes/no
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes, p6 (flow) p 11 (compliance), and results tables 1-3.
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes, p11
		(b) Indicate number of participants with missing data for each variable of interest	Yes, p11 (table 1)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	yes, p 11 (table 1)
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Yes, tables 2-3
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	statistical methods and results
Discussion			
Key results	18	Summarise key results with reference to study objectives	yes, p15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	yes, p17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	yes, p18
Generalisability	21	Discuss the generalisability (external validity) of the study results	yes, p17 (last paragraph)
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	yes, p18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Are trajectories of neck–shoulder pain associated with sick leave and work ability in workers? A one-year prospective study

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Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Public health
Keywords:	Chronic pain, LCGA, Neck pain, Occupational, Pain trajectories

Title: Are trajectories of neck–shoulder pain associated with sick leave and work ability in workers? A one-year prospective study

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Conflict of interest: None to declare.

Author contributions:

DMH contributed to the statistical data analyses and drafting of the manuscript. AH and MBJ contributed to the conception, design, data collection and funding of the full DPHACTO study. All authors (DMH, AH, SDL, MBJ, and CDNR) contributed to the conception of this study, discussed the results and commented on the manuscript.

Data sharing statement:

Additional data can be accessed on request by email (aho@arbejdsmiljoforskning.dk).

The manuscript contains about 4300 words, 3 tables, 2 figures, and 1 Supplemental figure.

Abstract

Objectives

The study aimed to determine the extent to which latent trajectories of neck-shoulder pain (NSP) are associated with self-reported sick leave and work ability based on frequent repeated measures over 1 year in an occupational population.

Methods

This longitudinal study included 748 Danish workers (blue-collar, n=620; white collar, n=128). A questionnaire was administered to collect data on personal and occupational factors at baseline. Text messages were used for repeated measurements of NSP intensity (scale 0-10) over 1 year (14 waves in total). Simultaneously, self-reported sick leave (days/month) due to pain was assessed at four week intervals, while work ability (scale 0-10) was assessed using a single item (work ability index) at 12 week intervals over the year. Trajectories of NSP, distinguished by latent class growth analysis (LCGA), were used as predictors of sick leave and work ability in generalized estimation equations with multiple adjustments.

Results

Sick leave increased and work ability decreased across all NSP trajectory classes (low, moderate, strong fluctuating, and severe persistent pain intensity). In the adjusted model, the estimated number of days on sick leave was 1.5 days/month for severe persistent NSP compared with 0.1 days/month for low NSP (RR=13.8, 95%CI 6.7–28.5). Similarly, work ability decreased markedly for severe persistent NSP (OR=12.9, 95%CI 8.5–19.7; median 7.1) compared with low NSP (median 9.5).

Conclusion

Severe persistent NSP was associated with sick leave and poor work ability over 1 year among workers. Preventive strategies aiming at reducing severe persistent NSP among working populations are needed.

Keywords: Chronic pain; LCGA; Neck pain; Occupational; Pain trajectories

Strengths and limitations of this study

- Some of the strengths of this study are:
  - Frequent repeated assessment of neck-shoulder pain, sick leave and work ability over 1 year.
  - High response rate during each month of follow-up.
- One of the limitations of this study was that sick leave was measured using self-report.

Introduction

Neck-shoulder pain (NSP) is a common condition, with annual prevalence rates between 27% and 48% in different working populations.[1] NSP is one of the leading causes of years lived with disability worldwide,[2] and is associated with reduced work ability[3] and high sick leave rates.[4 5] In workers with NSP, 20% had at least one spell of sick leave in one year.[4] Sick leave risks are higher in workers with more severe NSP intensity.[6] The economic burden of NSP on organizations and society is considerable.[7-9] The estimated total cost of neck pain in The Netherlands in 1996 was 686 million US dollars,[7] and the estimated total cost of both neck and back pain in Sweden in 2001was 1% of the gross national product (GNP).[9]

NSP is considered a heterogeneous condition ranging from very mild symptoms to severe chronic pain[10] with a substantial individual variability in progression over time.[11-13] This heterogeneity may, however, comprise homogenous sub-populations with distinct patterns of pain, unique risk factors and different underlying pathophysiology.[14] Revealing such sub-populations is likely important for early identification, establishing risk factors, and improving prevention and treatment.[15] However, most existing studies have been conducted on patients with low back pain, e.g.,[15-17] while studies identifying and describing the patterns of NSP in working populations with a wide range of pain severities are sparse. Also, there is a lack of research on the predictive value of NSP sub-populations; which is crucial for understanding the extent to which NSP sub-populations are of clinical and occupational relevance regarding intervention and treatment. Thus, it is important for research and occupational and clinical practice to distinguish sub-populations of workers with different trajectories of NSP (e.g. severity, temporal variability and time course) while assessing their predictive value against core prognostic outcomes, such as sick leave and work ability.[4 18 19]

Work ability, as defined as the balance between human resources and work demands,[20] is determined by multiple factors.[21] The perception of poor work ability is associated with sick leave and early retirement.[22] Sick leave due to pain is likely multifactorial, and several personal and work related (physical and psychosocial) factors have been identified as potential determinants of increased risks.[4 19 23 24] High physical workload is associated with poor work ability and occurrence of sick leave due to pain,[4 25] and may hamper return to work.[23] Thus, the level of physical workload is a potential moderator of the relationship of NSP trajectories with work ability and sick leave.

Most previous studies on the prognosis of NSP have relied only on few measurements in time interspersed by long intervals, e.g. years.[11 26] Such studies are not designed to capture the detailed time course (trajectory) or temporal fluctuations in NSP (e.g. between weeks or months). In contrast, frequent repeated measurements of pain facilitate accurate and precise identification of individual pain trajectories [27] and minimize recall bias.[28]

Latent class growth analysis (LCGA) is a common statistical approach for identifying homogenous sub-populations (latent classes) based on individual growth parameters (i.e. intercept, slope and residual variance) in repeated measures data.[29] We have previously used LCGA to distinguish trajectory classes of NSP among the current population of workers based on frequent repeated measurements of NSP over 1 year.[30] We identified six distinct trajectories of NSP ranging from "asymptomatic" (prevalence 11%) to "severe persistent NSP" (9%). Several personal and occupational factors, as well as symptom characteristics at baseline predicted trajectory class membership. However, understanding the occupational and clinical relevance of trajectories of NSP requires a determination of their predictive value against core occupational and clinical outcomes. Particularly, identifying NSP trajectories associated with unfavorable outcomes would likely aid targeted prevention and treatment.

The aim of this study is to determine the extent to which latent trajectories of NSP are associated with self-reported sick leave due to musculoskeletal pain and with work ability based on frequent repeated measures over 1 year in an occupational population. A second aim is to investigate the temporal association (within person) between fluctuations in NSP and the outcomes sick leave and work ability.

Methods

Study design

This is a prospective study using data from the Danish Physical activity cohort with objective measurements (DPhacto). The study protocol for the cohort is reported in detail elsewhere.[31] Data collection took place from April 2012 to May 2014 at 15 Danish companies, including workers in four occupational sectors (cleaning, manufacturing, transportation and office work/administration). The initial contact and recruitment of companies were performed in

collaboration with a large Danish union. The companies were selected to represent blue-collar occupations with different levels of physical demands at work.

Baseline data collection consisted of a brief web-based questionnaire, a standard health examination and objective diurnal measurements of physical activity and heart rate (presented elsewhere.[32 33] Prospective self-reported data on musculoskeletal pain, sick leave due to pain and work ability was collected repeatedly over 12 months using text messages.

Study population

The inclusion criterion for participation was current employment within any of the recruited work places. Exclusion criteria were holding a managing position or being pregnant or a student/trainee. In addition, workers not responding to the baseline questionnaire and/or the prospective measurements were excluded.

Among the 2107 invited workers, 1119 agreed to participate and 32 of them were excluded due to holding a managing position (n=17) or being pregnant (n=2) or a student/trainee (n=13). Of the remaining 1087 eligible workers, 782 responded to the questionnaire and 748 took part in the prospective measurements from baseline. Thus, the final study sample consisted of 748 workers (blue-collar, n=620; white collar, n=128). Descriptive characteristics of the study population are shown in Table 1.

All participants provided their written informed consent prior to participation. The present study was conducted according to the Declaration of Helsinki, approved by the Danish Data Protection Agency, and evaluated by the Regional Ethics Committee in Copenhagen, Denmark (H-2-2012-011).

Repeated assessment using text messages

Text messages (SMS) were used to assess self-reported pain intensity in the neck-shoulder region, days on sick leave and work ability using the commercial software "SMS-Track" (https://sms-track.com/). Starting at baseline, data on NSP and sick leave were collected at four week intervals (14 waves), while data on work ability were collected at 12 week intervals (4 waves in total) during the 1-year study. The SMS were sent on Sundays, with a reminder the following day.

Neck-shoulder pain

Pain intensity in the neck-shoulder region (NSP) the past month was assessed using an 11-point numeric rating scale (NRS), which ranges from 0 ("no pain") to 10 ("worst pain imaginable"). The worker responded to the question *"rate the worst pain you have experienced in your neck/shoulders within the past month?"* The NRS is a reliable and valid instrument for assessing pain intensity [34] and is recommended as an outcome in clinical trials.[35]

Sick leave

Sick-leave due to pain was assessed using a single-item from the validated Outcome Evaluation Questionnaire [36]: *"Within the past month, how many days have you been absent from work due to pain in muscles or joints?"* with response categories ranging from 0 to 31 days. Based on a recent meta-analysis, self-reported sick leave demonstrates good test-retest reliability and reasonably high convergent validity against records.[37]

Work ability

Work ability was assessed using a validated single item[22] from the work ability index.[38] The worker responded to the question "*Please rate your present work ability*?" with response categories ranging from 0 (unable to work) to 10 ("work ability as its best"). A score ≤ 7 denotes poor work ability.[39]

Assessment of possible confounders and effect modifiers

Theoretical assumptions and empirical evidence were used to select possible confounders and effect modifiers which were accounted for in the statistical analyses. The following variables were measured at baseline as previously described [30]: age (years,) and gender (male or female) based on civil registration number, body mass index (BMI) based on objectively measured height and weight, occupational sector (manufacturing, cleaning, transportation, and administration/office work within the same workplaces), and seniority in the current job (years). Physical work load was measured by the question *"How physically demanding do you normally consider your present work?"* using a ten-point (1-10) response scale modified from Borg,[40] with higher values indicating higher physical demands. Multisite pain was measured based on the Standardized Nordic questionnaire for the analysis of musculoskeletal symptoms [41] asking about pain intensity (NRS, scale 0-10) during the past three months in

seven different anatomical areas (i.e. neck/shoulders, elbows, hands/wrists, lower back, hips, knees, and feet/ankles). A cut-point of >2 was used to indicate the occurrence of pain, whereby the number of pain sites was determined.[42] Since the relationship between NSP, sick leave and work ability may depend on the level of physical demands at work, physical work load was considered both a confounder and an effect modifier, while the other variables were solely included as possible confounders.

Statistical analyses

Growth trajectories (latent classes) of the intensity in NSP were identified using LCGA in Latent Gold version 5.1 (Statistical innovations Belmont, MA, USA). The LCGA procedure and the resulting trajectory classes of NSP are described in a previous study on the same population.[30] In brief, the LCGA assigns individuals to latent classes based on maximum posterior probabilities. That is, using growth parameters (i.e. intercept, slope and residual variance) reflecting change in an observed variable (i.e. pain intensity) over time, LCGA assigns individuals to latent classes (categorical variable) assuming homogeneity within class and heterogeneity between classes.[29 43]

The LCGA models were performed using Time (14 waves over 1 year) as a continuous linear predictor and NSP intensity as a continuous dependent variable. Missing values were considered as missing at random and included in all models without imputations. The optimal number of classes was determined based on appropriate model fit indices, i.e. Bayesian information criterion (BIC), Entropy and Bootstrap log likelihood ratio (BLRT), which were obtained in consecutive LCGA models with 1-10 a priori class solutions. Then, the models were evaluated based on the estimated growth parameters and clinical distinction between the identified classes. The identified trajectories of NSP were used as an independent variable in further statistical analyses of associations with sick leave and work ability over the same year.

The association of NSP trajectories with sick leave (SMS at four week intervals over 1 year) and work ability (SMS each quarter) during the same year was determined using Generalized Estimation Equation (GEE) regression modeling with an auto regressive first order (AR1) covariance structure to account for weaker correlations with increasing distance between time points.

The association of NSP trajectories with sick-leave (days/month) was tested using GEE with a Poisson distribution and a log link function. Fixed factors were NSP trajectory class (categorical variable), time (continuous variable, 14 time points) and the interaction between trajectory class and time. The interaction term was kept in the model if it was significant ($p<0.05$). We tested both linear and quadratic time trends, but decided on a linear model since the quadratic model did not improve model fit. The primary GEE models were constructed in three steps: (model 1) unadjusted, (model 2) adjusted for age, gender and BMI, and (model 3) additionally adjusted for occupational sector (four categories) and physical work load (continuous variable). Then, we tested if the results of the primary models were consistent when accounting for baseline pain intensity and comorbidity of multisite pain, as they may be associated with both NSP trajectories and the outcomes. Thus, secondary models were estimated with additional adjustment for the intensity of NSP (model 4) and the number of pain regions (model 5) at baseline (past three months). Finally, to test for potential effect modification by physical work load, model 3 was re-run with an interaction between NSP trajectory class and physical work load (model 6).

The association of NSP trajectory class with work ability (dependent variable, ordinal scale) was tested using GEE regression modeling with a multinomial distribution and a cumulative logit link function. Fixed factors were NSP trajectory class (categorical variable), time (linear continuous variable, 4 time points), and the interaction between trajectory class and time, which was kept only if reaching significance ($p<0.05$). The models were constructed with and without adjustment for covariates, as explained above.

Additional GEE models were constructed to investigate the within person association of temporal fluctuations in the intensity of NSP with sick leave and work ability (outcomes). To partition the within and between subjects variances in the predictor (intensity of NSP), the mean pain intensity score across all time points was determined for each individual. Then, the person mean pain score was subtracted from each repeated pain rating and used as an independent variable (within subject effect), while adjusting for the person mean pain as a covariate (between-subjects effect).[43] Thus, these GEE models were constructed with three fixed factors: (i) time (14 waves), (ii) the person mean pain intensity across waves, and (iii) the difference from the mean pain intensity during each wave for the individual (within subject effect). The within-subject effect would then reflect the population averaged association with the outcome for each unit change in pain intensity per month for the individual. Model specifications for sick leave and work ability were the same as above. The models were estimated with and without adjustment for potential confounders as explained above.

The regression models were estimated using SPSS software version 22 (IBM, USA). For each model, we derived the exponential estimate, i.e. relative risk (RR) and odds ratio (OR) for sick leave and work ability, respectively, and 95% confidence intervals (CI). P-values <0.05 were considered significant.

Patient and public involvement

No patients or public were directly involved in setting the research questions and outcomes, design and conduct of this study, or interpretation of the results. Results will be disseminated to the participants at http://www.nfa.dk/.

Results

Characteristics of the study population

Characteristics of the study population are shown in Table 1. The study sample consisted of both males and females, and most were blue-collar workers. The workers were on average of middle age, slightly overweight, and had been in their current job for 14 years. The mean intensity of NSP across all time points was 2.6 (scale 0-10). Most of the workers rated high work ability (>7, scale 0-10) across the study period, while the average worker accumulated 6 days on sick leave due to pain over 1 year, although with a considerable dispersion between individuals. Compliance to the repeated measurements (SMS) in the study was high; on average, the workers had 1.2 missing responses to pain and sick leave (14 waves) and 0.4 missing responses to work ability (4 waves) (Table 1). The amount of missing data increased over time. During the second wave, the response rates were 96%, 96% and 93% for pain, sick leave and work ability, respectively, while the response rates dropped to 87%, 88% and 90% during the last wave.

[Insert Table 1 about here]

Identified latent trajectories of NSP

Based on model fit indices (BIC, Entropy and BLRT) and distinction between classes obtained from consecutive LCGA models, a six-class solution was chosen.[30] The growth pattern and prevalence (%) of the six identified trajectory classes of NSP were characterized as follows (see also Supplemental Figure A): class 1, *asymptomatic* (11%); class 2, *very low NSP* (10%); class 3, *low recovering NSP* (18%); class 4, *moderate fluctuating NSP* (28%); class 5, *strong fluctuating NSP* (24 %); and class 6, *severe persistent NSP* (9%). The trajectory classes with lower intensities of NSP (classes 1-3) did not differ in total days on sick leave or mean work ability over 1 year; and the occurrence of sick leave was very low, while work ability was high across the three classes. Thus, classes 1-3 were merged into a single category (low NSP 39%), which was used as a reference in further analyses.

Association between NSP trajectory classes and sick leave over 1 year

Poisson regression estimates of the association of NSP trajectories with sick leave due to pain (days /month) are shown in Table 2. There was no significant time effect on sick leave (unadjusted RR=1.02, 95%CI 0.99-1.06). Thus, the interaction between NSP trajectory class and time was discarded from the models.

Based on the fully adjusted model (Table 2, model 3) referencing low NSP, the relative risk of sick leave increased for moderate (RR=3.1, 95%CI 1.8–5.5), strong fluctuating (RR=7.6, 95%CI 3.9–14.7), and severe persistent NSP (RR=13.8, 95%CI 6.7–28.5). On average, the estimated number of days on sick leave per month was 0.1 (95%CI 0.1–0.15) for low NSP, 0.3 (95%CI 0.2–0.4) for moderate NSP, 0.8 (95%CI 0.5–1.2) for strong NSP, and 1.5 (95%CI 1.0–2.4) for severe persistent NSP. Predicted values of sick leave for each wave over 1 year are shown in Figure 1.

Additional adjustment for multisite pain showed similar estimates for moderate NSP (RR=3.0, 95%CI 1.7–5.4), strong fluctuating NSP (RR=7.2, 95%CI 3.5–14.5) and severe persistent NSP (RR=13.1, 95%CI 6.1–28). Also, adjustment for baseline pain intensity revealed stronger estimates for moderate NSP (RR=3.7, 95%CI 2.1–6.8), strong fluctuating NSP (RR=10.9, 95%CI 5.1–23.7) and severe persistent NSP (RR=24.5, 95%CI 10.4–57.9), although with wider CIs.

There was no significant interaction between NSP trajectory class and physical work load on sick leave.

[Insert Figure 1 about here]

Association between NSP trajectory classes and work ability over 1 year

The ordinal regression estimates of the association between trajectories of NSP and work ability (measured each quarter) are shown in Table 2.

There was a small time effect indicating reduced work ability over the year (unadjusted OR 1.05, 95%CI 0.99–1.11). There was no interaction between NSP trajectory class and time, whereby this interaction was discarded from the model.

NSP trajectory class was inversely associated with work ability (Table 2). Based on the fully adjusted model referencing low NSP (Table 2, model 3), the likelihood of a 1-unit reduction in work ability increased for moderate (OR=2.4, 95%CI 1.8–3.2), strong fluctuating (OR=8.1, 95%CI 5.9–11.2), and severe persistent NSP (OR=12.9, 95%CI 8.5–19.7). The median scores (IQR) of work ability during the year were 9.5(1.7) for low NSP, 9.0(2.0) for moderate NSP, 7.8(2.0) for strong NSP, and 7.1(2.5) for severe persistent NSP.

Additional adjustment for multisite pain showed slightly weaker estimates for moderate NSP (OR=2.2, 95%CI 1.7–2.9), strong fluctuating NSP (OR=6.4, 95%CI 4.6–9.0) and severe persistent NSP (OR=10.4, 95%CI 6.7–16.0). Further, adjustment for baseline pain intensity showed similar estimates for moderate NSP (OR=2.6, 95%CI 1.9–3.5), strong fluctuating NSP (OR=9.1, 95%CI 6.3–13.1) and severe persistent NSP (OR=15.4, 95%CI 9.3–25.5).

There was no significant interaction between NSP trajectory class and physical work load on work ability.

[Insert Table 2 about here]

Within-person association of NSP with sick leave and workability

Due to the high work ability scores and low prevalence of sick leave in the classes with lower intensities of NSP, these analyses included only workers assigned to the trajectory classes strong fluctuating and severe persistent NSP (n=248).

The within-person associations of pain intensity with sick leave due to pain and work ability are shown in Table 3.

Within person fluctuations in the intensity of NSP were positively associated with sick leave (adjusted RR=1.11, 95%CI 1.02–1.21). That is, higher intensity of NSP was associated with more days of sick leave during a particular month at the individual level (Table 3 and Figure 2a).

A similar within-person association was found between fluctuations in pain intensity and work ability (adjusted OR 1.13, 95%CI 1.04–1.21). For example, increasing intensity of NSP was associated with higher probabilities of reduced work ability (Table 3). This association is illustrated in Figure 2b as the estimated probability of reporting poor work ability (≤7 on the 0-10 scale).[39]

[Insert Table 3 about here]

[Insert Figure 2]

Discussion

In summary, this prospective study investigated the relationship between LCGA-based trajectories of NSP and the outcomes sick leave and work ability. We found that the distinguished trajectory classes of NSP were strongly associated with sick leave due to pain and poor work ability over 1 year, and that the temporal fluctuations in pain intensity predicted sick leave and work ability at the individual level.

To our knowledge, this study is unique in assessing the association between LCGA-based trajectories of NSP and important prognostic outcomes among workers. A clear strength of the study is the use of frequent prospective measures of both exposure (intensity of NSP) and outcomes (work ability and sick leave) over 1 year. The high response rate to the SMS is also a strength supporting the feasibility of this method to obtain frequent repeated measurements of pain in future studies on the prognosis of NSP.

Trajectories of NSP, sick leave and work ability

The trajectory classes of NSP used in this study were distinguished using LCGA, resulting in six distinct trajectories of NSP.[30] This corroborates a study by Lövgren et al. (2014) which used Growth Mixture Modeling to identify six trajectory classes of NSP in nursing students entering working life. In contrast, the severity of NSP in the current sample of workers was much higher, perhaps due to the large proportion of blue-collar workers in this study.[1] The high prevalence of strong fluctuating (24%) and severe persistent NSP (9%), with mean pain intensities of 5 and 7 (scale 0-10), respectively, is noteworthy.

Trajectory class of NSP was strongly associated with the number of days on sick leave over the 1-year study period. Particularly, the fully adjusted model indicated an increased relative risk of sick leave in the trajectory class with severe persistent NSP (mean 1.5 days/month), compared with low NSP (mean 0.1 days/month). This result is in line with previous prospective studies showing a positive association between NSP intensity and sick leave.[4 6] This result persisted with adjustment for potential confounding by multisite pain, which was associated with NSP and sick leave in previous studies.[19 44 45] Thus, severe persistent NSP appears to be strongly associated with sick leave due to musculoskeletal pain, regardless of multisite pain and other personal and occupational factors.

The four trajectory classes of NSP were also associated with poor work ability over the year (Table 2). For instance, the probability of reporting reduced work ability was 13 times higher for the trajectory class with severe persistent NSP (median work ability 7.1 on the 0-10 scale), compared with low NSP (median work ability 9.5), regardless of inclusion of potential confounders in the model (Table 2, model 3). In agreement, previous studies have found that intense NSP is associated with reduced work ability in workers,[3 46] although none of these examined pain trajectories. Interestingly, including baseline intensity of NSP (i.e. past 3 months) as an additional covariate in model 3 did not reduce the estimated association for sick leave or work ability. In fact, this adjustment resulted in even stronger estimates for work ability, which clearly indicates that the LCGA-based trajectory classes of NSP have a predictive value beyond that explained by past pain intensity assessed at a single time point.

The observed consistent associations between the identified trajectories of NSP and the outcomes sick leave and work ability support the prognostic value of LCGA-based trajectories of NSP among workers, and suggests that such sub-populations can be of clinical and occupational relevance. Thus, this study supports using LCGA to identify distinct sub-populations of workers with different patterns of NSP. Further, the increase in relative risk of sick leave and poor work ability for severe persistent NSP points to the need for interventions and preventive strategies aiming at reducing severe persistent NSP in working populations.

Effect modification by physical work load

High physical work load is a known risk factor for incident NSP and has been associated with a poor prognosis.[47] Thus, the association for NSP trajectories with sick leave and work ability was expected to be modified by the level of self-reported physical work load at baseline. However, we could not confirm any interaction between trajectory class of NSP and physical work load neither for sick leave nor work ability. Still, it is possible that more precise technical measurements of physical work exposure would have yielded different results.

Association of temporal fluctuations in NSP with sick leave and work ability

NSP is often referred to as a recurrent and fluctuating condition.[11] However, the temporal fluctuations in NSP have rarely been investigated in detail, and few, if any, studies have

examined whether fluctuations in NSP are associated with sick leave and work ability. The frequent repeated measures allowed us to assess the within-person temporal association between fluctuations in the intensity of NSP and sick leave (every fourth week) and work ability (every twelfth week). We found that the within-person fluctuations in pain intensity were significantly associated with both sick leave and work ability, which persisted in the fully adjusted model (Table 3). That is, when the individual pain score increased, the likelihood of sick leave and poor work ability also increased. Thus, not only could we address the differences between workers in temporal patterns of NSP, but also whether the temporal fluctuations in NSP at the individual level are of predictive value.

Methodological discussion

As this study is limited to self-reported measures of pain and the outcomes sick leave and work ability, one cannot overlook the possibility of bias. Regarding self-reported sick leave, meta-analytic evidence indicates reasonably high convergent validity against organization and register-based records, although with a slight tendency for under-reporting.[37] Thus, there is a risk for underestimation of sick leave in this study. The question about days on sick leave the past month did not distinguish between work days and non-work days, which may have resulted in less precise estimates. Also, although both outcomes sick leave and work ability were assessed prospectively over 1 year, the NSP trajectories were determined during the same time period and thus causal inferences should be made with caution. Still, it seems most likely that pain preceded the occurrence of sick leave, rather than the reverse relationship. The compliance to text messages was very high on average (Table 1). Still, missing data increased slightly over time, which might have introduced some uncertainties in the models.

We addressed several relevant factors as confounders or effect modifiers (physical work load) of the association of pain trajectories with sick leave and work ability. However, as the causes of sick leave and poor work ability are likely multifactorial,[4 19 21] the focus on pain trajectories as predictors is a potential limitation because it does not inform about other potentially important prognostic factors. Also, the possibility of residual confounding by non-measured factors cannot be ruled out. For instance, we did not measure comorbidity of chronic conditions that might be associated with both NSP trajectories and the outcomes.

Since this study was conducted in a non-random sample with a predominance of blue-collar workers, it is important to verify the study findings in other working populations. The general notion of NSP as a fluctuating and reoccurring condition[11] is corroborated by our data, but this is rarely taken into account in observational studies on NSP. The inclusion of residual variance in the LCGA model allowed us to distinguish trajectory classes with more or less fluctuating patterns of NSP. Temporal fluctuations were more prominent in the NSP trajectories with moderate and strong pain, which may have contributed to the lower relative risk of sick leave and poor work ability compared to the trajectory class with severe persistent NSP.

Since the trajectories with lower intensities of NSP, i.e., including asymptomatic, very low NSP and low recovering NSP, did not differ regarding their low occurrence of sick leave and poor work ability, we decided to merge them into a single reference category in the prediction models. Still, it is possible that these three classes differ in other prognostic outcomes.

Conclusion

This longitudinal study shows that severe persistent NSP is associated with sick leave due to pain and reduced work ability over 1 year among workers. The high prevalence of severe persistent NSP and the increase in relative risk of sick leave and poor work ability point to the need for preventive strategies aiming at reducing severe persistent NSP among workers. Overall, our findings contribute with further understanding of the possible consequences of different time patterns and levels of NSP, which can be of general importance for researchers, practitioners and clinicians.

Acknowledgements

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Conflict of interest

The authors declare none.

Author contributions

DMH contributed to the statistical data analyses and drafting of the manuscript. AH and MBJ contributed to the conception, design, data collection and funding of the full DPhacto study. All authors (DMH, AH, SDL, MBJ, and CDNR) contributed to the conception of this study, discussed the results and commented on the manuscript.

Data sharing statement

Additional data can be accessed on request by email (aho@arbejdsmiljoforskning.dk).

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Tables

Table 1 Descriptive characteristics of the study population (n=748)

	N	Median	IQR	Mean	SD
Age (years)	748			44.8	9.6
Men N (%)	411 (55)				
BMI (kg×m^{-2})	732			27.3	4.8
Seniority (years)	722			13.5	10.3
Administration workers N (%)	128 (17)				
Blue-collar workers N (%)	620 (83)				
Cleaning	115 (15)				
Manufacturing	448 (60)				
Transportation	57 (8)				
Physical work load at baseline (scale 1-10)	723			5.3	2.4
Sick leave days					
Baseline (days/month)	741	0.0	0.0	0.3	1.9
Last follow-up (days/month)	655	0.0	0.0	0.4	2.5
Total days (over all time points)	746	0.0	3.0	5.8	20.9
Work ability (scale 0-10)					
Baseline	646	9.0	2.0	8.5	2.0
Last follow-up	671	9.0	2.0	8.2	2.4
Mean work ability (over all time points)	732	8.8	2.5	8.3	1.7
NSP intensity (scale 0-10)					
Baseline	748	2.0	5.0	3.0	2.7
Last follow-up	652	2.0	4.0	2.4	2.7
Mean NSP intensity (over all time points)	748	2.0	3.6	2.6	2.3
Number of pain regions at baseline (count)	745	1.0	3.0	1.7	1.5
Compliance to SMS (missing responses, count)					
NSP intensity	748	0.0	1.0	1.2	2.7
Sick leave	746	0.0	1.0	1.2	2.6
Work ability	732	0.0	1.0	0.4	0.7

Abbreviations: BMI, body mass index; NSP, neck-shoulder pain; IQR, inter quartile range.

Table 2. Association of neck-shoulder pain (NSP) trajectory class with sick leave (days/month) and work ability (ordinal scale 0-10) over 1 year, referencing low NSP.

		Sick leave				Work ability			
GEE models (classes)	N	p-value	RR	95%CI Lower	95%CI Upper	p-value	OR	95%CI Lower	95%CI Upper
Model 1									
Low NSP	292		1.00				1.00		
Moderate NSP	208	<0.001	3.28	1.89	5.68	<0.001	2.45	1.87	3.21
Strong NSP	178	<0.001	8.98	4.78	16.89	<0.001	8.64	6.38	11.69
Severe NSP	70	<0.001	17.64	9.36	33.23	<0.001	15.07	9.94	22.85
Model 2									
Low NSP	286		1.00				1.00		
Moderate NSP	204	<0.001	3.25	1.87	5.64	<0.001	2.40	1.83	3.16
Strong NSP	174	<0.001	8.61	4.54	16.33	<0.001	9.03	6.62	12.31
Severe NSP	68	<0.001	16.00	8.17	31.34	<0.001	14.77	9.63	22.66
Model 3									
Low NSP	277		1.00				1.00		
Moderate NSP	199	<0.001	3.11	1.75	5.52	<0.001	2.43	1.84	3.20
Strong NSP	165	<0.001	7.58	3.91	14.71	<0.001	8.12	5.91	11.16
Severe NSP	66	<0.001	13.83	6.72	28.49	<0.001	12.93	8.50	19.67

Relative risk (RR) estimates, indicating the relative increase in the number of days on sick leave per month, were obtained using Generalized Estimation Equation (GEE) with a Poisson distribution for days on sick-leave (measured at 4 week intervals). Odds ratios (OR), indicating the likelihood of a 1-unit reduction in work ability, were obtained using GEE with a multinomial distribution for work ability (measured at 12 week intervals).
Model 1: Unadjusted.
Model 2: Adjusted for age, gender and body mass index.
Model 3: Additionally adjusted for occupational sector (four categories, referencing administration) and physical work load.

Table 3. Within-person effect of temporal fluctuations in neck-shoulder pain (NSP, scale 0-10) on sick leave (days/month) and work ability (scale 0-10) over 1 year

		Sick leave				**Work ability**			
				95% CI				95% CI	
GEE models	N	p-value	RR	Lower	Upper	p-value	OR	Lower	Upper
NSP intensity									
Model 1	248	0.008	1.12	1.03	1.21	0.005	1.11	1.03	1.19
Model 2	242	0.008	1.12	1.03	1.21	0.009	1.11	1.03	1.19
Model 3	231	0.011	1.11	1.02	1.21	0.002	1.13	1.04	1.21

Relative risk (RR) estimates, indicating the relative increase in the number of days on sick leave per month, were obtained using Generalized Estimation Equation (GEE) with a Poisson distribution for days on sick-leave (measured at 4 week intervals). Odds ratios (OR), indicating the likelihood of a 1-unit reduction in work ability, were obtained using GEE with a multinomial distribution for work ability (measured at 12 week intervals). Estimates indicate the within-person effect of change in pain intensity on change in sick leave and work ability per month.

Model 1: adjusted for the person mean pain intensity across time points.

Model 2: additionally adjusted for age, gender and BMI.

Model 3: additionally adjusted for occupational sector and physical work load.

Figure legends

Figure 1. Mean 1-year trajectories of days on sick leave obtained in the fully adjusted model in each trajectory class of neck-shoulder pain (NSP). The x-axis represents the 14 pain ratings over 1 year. The y-axis represents the mean predicted number of days on sick leave per month.

Figure 2. Association between temporal fluctuations in neck-shoulder pain (NSP) and the outcomes sick leave and work ability. The x-axis represents the difference in pain intensity scores from the person mean pain intensity across time points. The y-axis represents the predicted number of days on sick leave per month (Fig. 2a) and the predicted cumulative probability of poor work ability (Fig. 2b), as defined by the cut-point ≤7 (scale 0-10).[39]

Supplemental Figures

Supplemental Figure A. Mean predicted intensity of neck-shoulder pain (NSP) over 1 year in the four trajectory classes of NSP obtained using Latent class growth analysis.

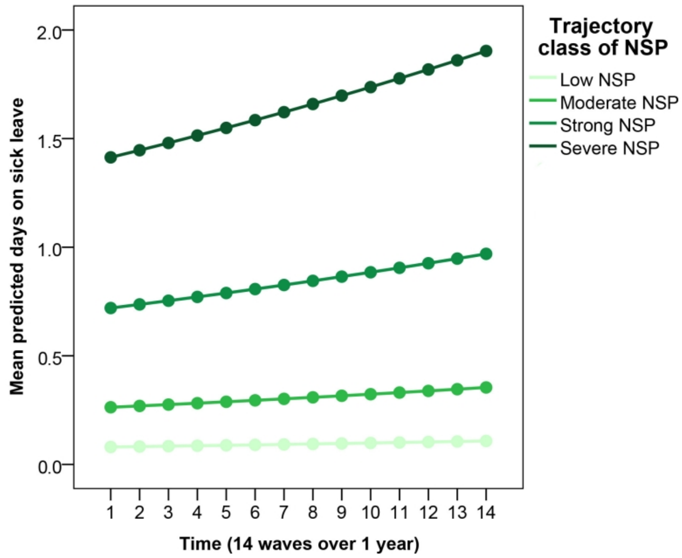


Figure 1.

Figure 1. Mean 1-year trajectories of days on sick leave obtained in the fully adjusted model in each trajectory class of neck-shoulder pain (NSP). The x-axis represents the 14 pain ratings over 1 year. The y-axis represents the mean predicted number of days on sick leave per month.

215x279mm (300 x 300 DPI)

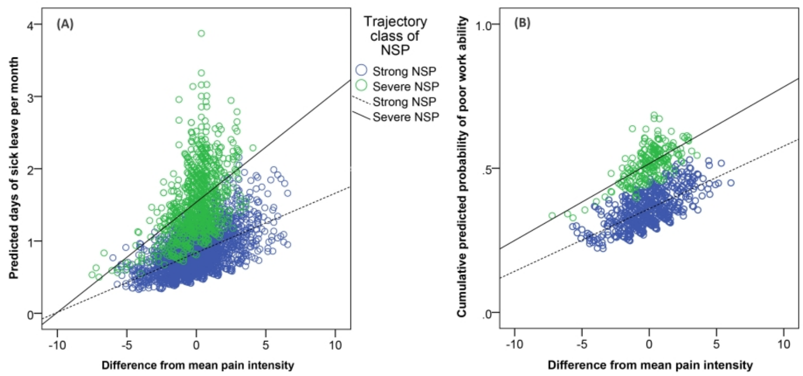
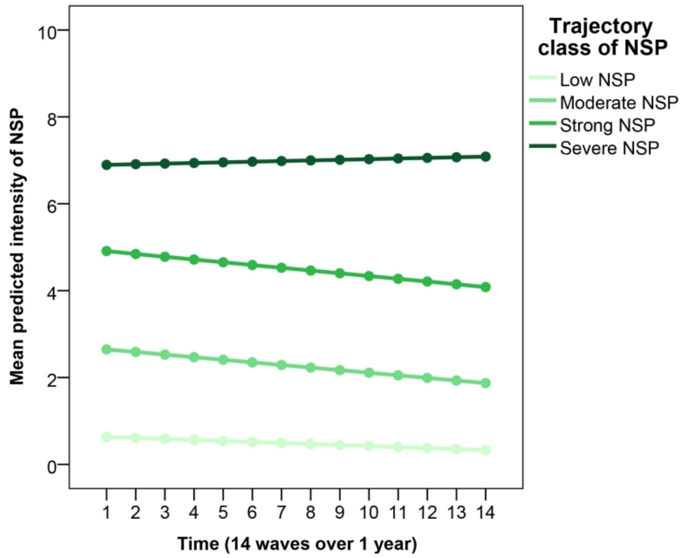


Figure 2

Figure 2. Association between temporal fluctuations in neck-shoulder pain (NSP) and the outcomes sick leave and work ability. The x-axis represents the difference in pain intensity scores from the person mean pain intensity across time points. The y-axis represents the predicted number of days on sick leave per month (Fig. 2a) and the predicted cumulative probability of poor work ability (Fig. 2b), as defined by the cut-point ≤7 (scale 0-10).

350x199mm (300 x 300 DPI)



Supplemental Figure A.

Supplemental Figure A. Mean predicted intensity of neck-shoulder pain (NSP) over 1 year in the four trajectory classes of NSP obtained using Latent class growth analysis.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Check yes/no
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	yes
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	yes, p4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	yes, p5
Methods			
Study design	4	Present key elements of study design early in the paper	yes, p5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	yes, p5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	a) yes, p5-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	yes, p6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	yes, p6-8
Bias	9	Describe any efforts to address potential sources of bias	yes, p7-8 and 9 (confounders and statistical analyses)
Study size	10	Explain how the study size was arrived at	yes, p6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	yes, p8-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	yes p8-9

	(*b*) Describe any methods used to examine subgroups and interactions	yes, p8-9
	(*c*) Explain how missing data were addressed	yes, p8
	(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	yes, p8; page 11
	(*e*) Describe any sensitivity analyses	

Continued on next page

Results			**Yes/no**
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes, p6 (flow) p 11 (compliance), and results tables 1-3.
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes, p11
		(b) Indicate number of participants with missing data for each variable of interest	Yes, p11 (table 1)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	yes, p 11 (table 1)
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Yes, tables 2-3
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	statistical methods and results
Discussion			
Key results	18	Summarise key results with reference to study objectives	yes, p15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	yes, p17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	yes, p18
Generalisability	21	Discuss the generalisability (external validity) of the study results	yes, p17 (last paragraph)
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	yes, p18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Are trajectories of neck–shoulder pain associated with sick leave and work ability in workers? A one-year prospective study

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Primary Subject Heading:	Occupational and environmental medicine
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Keywords:	Chronic pain, LCGA, Neck pain, Occupational, Pain trajectories

Title: Are trajectories of neck–shoulder pain associated with sick leave and work ability in workers? A one-year prospective study

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Author contributions:

DMH contributed to the statistical data analyses and drafting of the manuscript. AH and MBJ contributed to the conception, design, data collection and funding of the full DPHACTO study. All authors (DMH, AH, SDL, MBJ, and CDNR) contributed to the conception of this study, discussed the results and commented on the manuscript.

Data sharing statement:

Additional data can be accessed on request by email (aho@arbejdsmiljoforskning.dk).

The manuscript contains about 4300 words, 3 tables, 2 figures, and 1 Supplemental figure.

Abstract

Objectives

The study aimed to determine the extent to which latent trajectories of neck-shoulder pain (NSP) are associated with self-reported sick leave and work ability based on frequent repeated measures over 1 year in an occupational population.

Methods

This longitudinal study included 748 Danish workers (blue-collar, n=620; white collar, n=128). A questionnaire was administered to collect data on personal and occupational factors at baseline. Text messages were used for repeated measurements of NSP intensity (scale 0-10) over 1 year (14 waves in total). Simultaneously, self-reported sick leave (days/month) due to pain was assessed at four week intervals, while work ability (scale 0-10) was assessed using a single item (work ability index) at 12 week intervals over the year. Trajectories of NSP, distinguished by latent class growth analysis (LCGA), were used as predictors of sick leave and work ability in generalized estimation equations with multiple adjustments.

Results

Sick leave increased and work ability decreased across all NSP trajectory classes (low, moderate, strong fluctuating, and severe persistent pain intensity). In the adjusted model, the estimated number of days on sick leave was 1.5 days/month for severe persistent NSP compared with 0.1 days/month for low NSP (RR=13.8, 95%CI 6.7–28.5). Similarly, work ability decreased markedly for severe persistent NSP (OR=12.9, 95%CI 8.5–19.7; median 7.1) compared with low NSP (median 9.5).

Conclusion

Severe persistent NSP was associated with sick leave and poor work ability over 1 year among workers. Preventive strategies aiming at reducing severe persistent NSP among working populations are needed.

Keywords: Chronic pain; LCGA; Neck pain; Occupational; Pain trajectories

Strengths and limitations of this study

- Some of the strengths of this study are:
  - Frequent repeated assessment of neck-shoulder pain, sick leave and work ability over 1 year.
  - High response rate during each month of follow-up.
- One of the limitations of this study was that sick leave was measured using self-report.

Introduction

Neck-shoulder pain (NSP) is a common condition, with annual prevalence rates between 27% and 48% in different working populations.[1] NSP is one of the leading causes of years lived with disability worldwide,[2] and is associated with reduced work ability[3] and high sick leave rates.[4 5] In workers with NSP, 20% had at least one spell of sick leave in one year.[4] Sick leave risks are higher in workers with more severe NSP intensity.[6] The economic burden of NSP on organizations and society is considerable.[7-9] The estimated total cost of neck pain in The Netherlands in 1996 was 686 million US dollars,[7] and the estimated total cost of both neck and back pain in Sweden in 2001was 1% of the gross national product (GNP).[9]

NSP is considered a heterogeneous condition ranging from very mild symptoms to severe chronic pain[10] with a substantial individual variability in progression over time.[11-13] This heterogeneity may, however, comprise homogenous sub-populations with distinct patterns of pain, unique risk factors and different underlying pathophysiology.[14] Revealing such sub-populations is likely important for early identification, establishing risk factors, and improving prevention and treatment.[15] However, most existing studies have been conducted on patients with low back pain, e.g.,[15-17] while studies identifying and describing the patterns of NSP in working populations with a wide range of pain severities are sparse. Also, there is a lack of research on the predictive value of NSP sub-populations; which is crucial for understanding the extent to which NSP sub-populations are of clinical and occupational relevance regarding intervention and treatment. Thus, it is important for research and occupational and clinical practice to distinguish sub-populations of workers with different trajectories of NSP (e.g. severity, temporal variability and time course) while assessing their predictive value against core prognostic outcomes, such as sick leave and work ability.[4 18 19]

Work ability, as defined as the balance between human resources and work demands,[20] is determined by multiple factors.[21] The perception of poor work ability is associated with sick leave and early retirement.[22] Sick leave due to pain is likely multifactorial, and several personal and work related (physical and psychosocial) factors have been identified as potential determinants of increased risks.[4 19 23 24] High physical workload is associated with poor work ability and occurrence of sick leave due to pain,[4 25] and may hamper return to work.[23] Thus, the level of physical workload is a potential moderator of the relationship of NSP trajectories with work ability and sick leave.

Most previous studies on the prognosis of NSP have relied only on few measurements in time interspersed by long intervals, e.g. years.[11 26] Such studies are not designed to capture the detailed time course (trajectory) or temporal fluctuations in NSP (e.g. between weeks or months). In contrast, frequent repeated measurements of pain facilitate accurate and precise identification of individual pain trajectories [27] and minimize recall bias.[28]

Latent class growth analysis (LCGA) is a common statistical approach for identifying homogenous sub-populations (latent classes) based on individual growth parameters (i.e. intercept, slope and residual variance) in repeated measures data.[29] We have previously used LCGA to distinguish trajectory classes of NSP among the current population of workers based on frequent repeated measurements of NSP over 1 year.[30] We identified six distinct trajectories of NSP ranging from "asymptomatic" (prevalence 11%) to "severe persistent NSP" (9%). Several personal and occupational factors, as well as symptom characteristics at baseline predicted trajectory class membership. However, understanding the occupational and clinical relevance of trajectories of NSP requires a determination of their predictive value against core occupational and clinical outcomes. Particularly, identifying NSP trajectories associated with unfavorable outcomes would likely aid targeted prevention and treatment.

The aim of this study is to determine the extent to which latent trajectories of NSP are associated with self-reported sick leave due to musculoskeletal pain and with work ability based on frequent repeated measures over 1 year in an occupational population. A second aim is to investigate the temporal association (within person) between fluctuations in NSP and the outcomes sick leave and work ability.

Methods

Study design

This is a prospective study using data from the Danish Physical activity cohort with objective measurements (DPhacto). The study protocol for the cohort is reported in detail elsewhere.[31] Data collection took place from April 2012 to May 2014 at 15 Danish companies, including workers in four occupational sectors (cleaning, manufacturing, transportation and office work/administration). The initial contact and recruitment of companies were performed in

collaboration with a large Danish union. The companies were selected to represent blue-collar occupations with different levels of physical demands at work.

Baseline data collection consisted of a brief web-based questionnaire, a standard health examination and objective diurnal measurements of physical activity and heart rate (presented elsewhere.[32 33] Prospective self-reported data on musculoskeletal pain, sick leave due to pain and work ability was collected repeatedly over 12 months using text messages.

Study population

The inclusion criterion for participation was current employment within any of the recruited work places. Exclusion criteria were holding a managing position or being pregnant or a student/trainee. In addition, workers not responding to the baseline questionnaire and/or the prospective measurements were excluded.

Among the 2107 invited workers, 1119 agreed to participate and 32 of them were excluded due to holding a managing position (n=17) or being pregnant (n=2) or a student/trainee (n=13). Of the remaining 1087 eligible workers, 782 responded to the questionnaire and 748 took part in the prospective measurements from baseline. Thus, the final study sample consisted of 748 workers (blue-collar, n=620; white collar, n=128). Descriptive characteristics of the study population are shown in Table 1.

All participants provided their written informed consent prior to participation. The present study was conducted according to the Declaration of Helsinki, approved by the Danish Data Protection Agency, and evaluated by the Regional Ethics Committee in Copenhagen, Denmark (H-2-2012-011).

Repeated assessment using text messages

Text messages (SMS) were used to assess self-reported pain intensity in the neck-shoulder region, days on sick leave and work ability using the commercial software "SMS-Track" (https://sms-track.com/). Starting at baseline, data on NSP and sick leave were collected at four week intervals (14 waves), while data on work ability were collected at 12 week intervals (4 waves in total) during the 1-year study. The SMS were sent on Sundays, with a reminder the following day.

Neck-shoulder pain

Pain intensity in the neck-shoulder region (NSP) the past month was assessed using an 11-point numeric rating scale (NRS), which ranges from 0 ("no pain") to 10 ("worst pain imaginable"). The worker responded to the question *"rate the worst pain you have experienced in your neck/shoulders within the past month?"* The NRS is a reliable and valid instrument for assessing pain intensity [34] and is recommended as an outcome in clinical trials.[35]

Sick leave

Sick-leave due to pain was assessed using a single-item from the validated Outcome Evaluation Questionnaire [36]: *"Within the past month, how many days have you been absent from work due to pain in muscles or joints?"* with response categories ranging from 0 to 31 days. Based on a recent meta-analysis, self-reported sick leave demonstrates good test-retest reliability and reasonably high convergent validity against records.[37]

Work ability

Work ability was assessed using a validated single item[22] from the work ability index.[38] The worker responded to the question "*Please rate your present work ability*?" with response categories ranging from 0 (unable to work) to 10 ("work ability as its best"). A score ≤ 7 denotes poor work ability.[39]

Assessment of possible confounders and effect modifiers

Theoretical assumptions and empirical evidence were used to select possible confounders and effect modifiers which were accounted for in the statistical analyses. The following variables were measured at baseline as previously described [30]: age (years,) and gender (male or female) based on civil registration number, body mass index (BMI) based on objectively measured height and weight, occupational sector (manufacturing, cleaning, transportation, and administration/office work within the same workplaces), and seniority in the current job (years). Physical work load was measured by the question *"How physically demanding do you normally consider your present work?"* using a ten-point (1-10) response scale modified from Borg,[40] with higher values indicating higher physical demands. Multisite pain was measured based on the Standardized Nordic questionnaire for the analysis of musculoskeletal symptoms [41] asking about pain intensity (NRS, scale 0-10) during the past three months in

seven different anatomical areas (i.e. neck/shoulders, elbows, hands/wrists, lower back, hips, knees, and feet/ankles). A cut-point of >2 was used to indicate the occurrence of pain, whereby the number of pain sites was determined.[42] Since the relationship between NSP, sick leave and work ability may depend on the level of physical demands at work, physical work load was considered both a confounder and an effect modifier, while the other variables were solely included as possible confounders.

Statistical analyses

Growth trajectories (latent classes) of the intensity in NSP were identified using LCGA in Latent Gold version 5.1 (Statistical innovations Belmont, MA, USA). The LCGA procedure and the resulting trajectory classes of NSP are described in a previous study on the same population.[30] In brief, the LCGA assigns individuals to latent classes based on maximum posterior probabilities. That is, using growth parameters (i.e. intercept, slope and residual variance) reflecting change in an observed variable (i.e. pain intensity) over time, LCGA assigns individuals to latent classes (categorical variable) assuming homogeneity within class and heterogeneity between classes.[29 43]

The LCGA models were performed using Time (14 waves over 1 year) as a continuous linear predictor and NSP intensity as a continuous dependent variable. Missing values were considered as missing at random and included in all models without imputations. The optimal number of classes was determined based on appropriate model fit indices, i.e. Bayesian information criterion (BIC), Entropy and Bootstrap log likelihood ratio (BLRT), which were obtained in consecutive LCGA models with 1-10 a priori class solutions. Then, the models were evaluated based on the estimated growth parameters and clinical distinction between the identified classes. The identified trajectories of NSP were used as an independent variable in further statistical analyses of associations with sick leave and work ability over the same year.

The association of NSP trajectories with sick leave (SMS at four week intervals over 1 year) and work ability (SMS each quarter) during the same year was determined using Generalized Estimation Equation (GEE) models with an auto regressive first order (AR1) covariance structure to account for weaker correlations with increasing distance between time points.

The association of NSP trajectories with sick-leave (days/month) was tested using GEE models with a Poisson distribution and a log link function. Fixed factors were NSP trajectory class (categorical variable), time (continuous variable, 14 time points) and the interaction between trajectory class and time. The interaction term was kept in the model if it was significant ($p<0.05$). We tested both linear and quadratic time trends, but decided on a linear model since the quadratic model did not improve model fit. The primary GEE models were constructed in three steps: (model 1) unadjusted, (model 2) adjusted for age, gender and BMI, and (model 3) additionally adjusted for occupational sector (four categories) and physical work load (continuous variable). Then, we tested if the results of the primary models were consistent when accounting for baseline pain intensity and comorbidity of multisite pain, as they may be associated with both NSP trajectories and the outcomes. Thus, secondary models were estimated with additional adjustment for the intensity of NSP (model 4) and the number of pain regions (model 5) at baseline (past three months). Finally, to test for potential effect modification by physical work load, model 3 was re-run with an interaction between NSP trajectory class and physical work load (model 6).

The association of NSP trajectory class with work ability (dependent variable, ordinal scale) was tested using GEE models with a multinomial distribution and a cumulative logit link function. Fixed factors were NSP trajectory class (categorical variable), time (linear continuous variable, 4 time points), and the interaction between trajectory class and time, which was kept only if reaching significance ($p<0.05$). The models were constructed with and without adjustment for covariates, as explained above.

Additional GEE models were constructed to investigate the within person association of temporal fluctuations in the intensity of NSP with sick leave and work ability (outcomes). To partition the within and between subjects variances in the predictor (intensity of NSP), the mean pain intensity score across all time points was determined for each individual. Then, the person mean pain score was subtracted from each repeated pain rating and used as an independent variable (within subject effect), while adjusting for the person mean pain as a covariate (between-subjects effect).[43] Thus, these GEE models were constructed with three fixed factors: (i) time (14 waves), (ii) the person mean pain intensity across waves, and (iii) the difference from the mean pain intensity during each wave for the individual (within subject effect). The within-subject effect would then reflect the population averaged association with the outcome for each unit change in pain intensity per month for the individual. Model specifications for sick leave and work ability were the same as above. The models were estimated with and without adjustment for potential confounders as explained above.

The GEE models were estimated using SPSS software version 22 (IBM, USA). For each model, we derived the exponential estimate, i.e. relative risk (RR) and odds ratio (OR) for sick leave and work ability, respectively, and 95% confidence intervals (CI). P-values <0.05 were considered significant.

Patient and public involvement

No patients or public were directly involved in setting the research questions and outcomes, design and conduct of this study, or interpretation of the results. Results will be disseminated to the participants at http://www.nfa.dk/.

Results

Characteristics of the study population

Characteristics of the study population are shown in Table 1. The study sample consisted of both males and females, and most were blue-collar workers. The workers were on average of middle age, slightly overweight, and had been in their current job for 14 years. The mean intensity of NSP across all time points was 2.6 (scale 0-10). Most of the workers rated high work ability (>7, scale 0-10) across the study period, while the average worker accumulated 6 days on sick leave due to pain over 1 year, although with a considerable dispersion between individuals. Compliance to the repeated measurements (text messages) in the study was high; on average, the workers had 1.2 missing responses to pain and sick leave (14 waves) and 0.4 missing responses to work ability (4 waves) (Table 1). The amount of missing data increased over time. During the second wave, the response rates were 96%, 96% and 93% for pain, sick leave and work ability, respectively, while the response rates dropped to 87%, 88% and 90% during the last wave.

[Insert Table 1 about here]

Identified latent trajectories of NSP

Based on model fit indices (BIC, Entropy and BLRT) and distinction between classes obtained from consecutive LCGA models, a six-class solution was chosen.[30] The growth pattern and prevalence (%) of the six identified trajectory classes of NSP were characterized as follows (see also Supplemental Figure A): class 1, *asymptomatic* (11%); class 2, *very low NSP* (10%); class 3, *low recovering NSP* (18%); class 4, *moderate fluctuating NSP* (28%); class 5, *strong fluctuating NSP* (24 %); and class 6, *severe persistent NSP* (9%). The trajectory classes with lower intensities of NSP (classes 1-3) did not differ in total days on sick leave or mean work ability over 1 year; and the occurrence of sick leave was very low, while work ability was high across the three classes. Thus, classes 1-3 were merged into a single category (low NSP 39%), which was used as a reference in further analyses.

Association between NSP trajectory classes and sick leave over 1 year

Estimates of the association of NSP trajectories with sick leave due to pain (days /month) are shown in Table 2. There was no significant time effect on sick leave (unadjusted RR=1.02, 95%CI 0.99-1.06). Thus, the interaction between NSP trajectory class and time was discarded from the models.

Based on the fully adjusted model (Table 2, model 3) referencing low NSP, the relative risk of sick leave increased for moderate (RR=3.1, 95%CI 1.8–5.5), strong fluctuating (RR=7.6, 95%CI 3.9–14.7), and severe persistent NSP (RR=13.8, 95%CI 6.7–28.5). On average, the estimated number of days on sick leave per month was 0.1 (95%CI 0.1–0.15) for low NSP, 0.3 (95%CI 0.2–0.4) for moderate NSP, 0.8 (95%CI 0.5–1.2) for strong NSP, and 1.5 (95%CI 1.0–2.4) for severe persistent NSP. Predicted values of sick leave for each wave over 1 year are shown in Figure 1.

Additional adjustment for multisite pain showed similar estimates for moderate NSP (RR=3.0, 95%CI 1.7–5.4), strong fluctuating NSP (RR=7.2, 95%CI 3.5–14.5) and severe persistent NSP (RR=13.1, 95%CI 6.1–28). Also, adjustment for baseline pain intensity revealed stronger estimates for moderate NSP (RR=3.7, 95%CI 2.1–6.8), strong fluctuating NSP (RR=10.9, 95%CI 5.1–23.7) and severe persistent NSP (RR=24.5, 95%CI 10.4–57.9), although with wider CIs.

There was no significant interaction between NSP trajectory class and physical work load on sick leave.

[Insert Figure 1 about here]

Association between NSP trajectory classes and work ability over 1 year

Estimates of the association between trajectories of NSP and work ability (measured each quarter) are shown in Table 2.

There was a small time effect indicating reduced work ability over the year (unadjusted OR 1.05, 95%CI 0.99–1.11). There was no interaction between NSP trajectory class and time, whereby this interaction was discarded from the model.

NSP trajectory class was inversely associated with work ability (Table 2). Based on the fully adjusted model referencing low NSP (Table 2, model 3), the likelihood of a 1-unit reduction in work ability increased for moderate (OR=2.4, 95%CI 1.8–3.2), strong fluctuating (OR=8.1, 95%CI 5.9–11.2), and severe persistent NSP (OR=12.9, 95%CI 8.5–19.7). The median scores (IQR) of work ability during the year were 9.5(1.7) for low NSP, 9.0(2.0) for moderate NSP, 7.8(2.0) for strong NSP, and 7.1(2.5) for severe persistent NSP.

Additional adjustment for multisite pain showed slightly weaker estimates for moderate NSP (OR=2.2, 95%CI 1.7–2.9), strong fluctuating NSP (OR=6.4, 95%CI 4.6–9.0) and severe persistent NSP (OR=10.4, 95%CI 6.7–16.0). Further, adjustment for baseline pain intensity showed similar estimates for moderate NSP (OR=2.6, 95%CI 1.9–3.5), strong fluctuating NSP (OR=9.1, 95%CI 6.3–13.1) and severe persistent NSP (OR=15.4, 95%CI 9.3–25.5).

There was no significant interaction between NSP trajectory class and physical work load on work ability.

[Insert Table 2 about here]

Within-person association of NSP with sick leave and workability

Due to the high work ability scores and low prevalence of sick leave in the classes with lower intensities of NSP, these analyses included only workers assigned to the trajectory classes strong fluctuating and severe persistent NSP (n=248).

The within-person associations of pain intensity with sick leave due to pain and work ability are shown in Table 3.

Within person fluctuations in the intensity of NSP were positively associated with sick leave (adjusted RR=1.11, 95%CI 1.02–1.21). That is, higher intensity of NSP was associated with more days of sick leave during a particular month at the individual level (Table 3 and Figure 2a).

A similar within-person association was found between fluctuations in pain intensity and work ability (adjusted OR 1.13, 95%CI 1.04–1.21). For example, increasing intensity of NSP was associated with higher probabilities of reduced work ability (Table 3). This association is illustrated in Figure 2b as the estimated probability of reporting poor work ability (≤7 on the 0-10 scale).[39]

[Insert Table 3 about here]

[Insert Figure 2]

Discussion

In summary, this prospective study investigated the relationship between LCGA-based trajectories of NSP and the outcomes sick leave and work ability. We found that the distinguished trajectory classes of NSP were strongly associated with sick leave due to pain and poor work ability over 1 year, and that the temporal fluctuations in pain intensity predicted sick leave and work ability at the individual level.

To our knowledge, this study is unique in assessing the association between LCGA-based trajectories of NSP and important prognostic outcomes among workers. A clear strength of the study is the use of frequent prospective measures of both exposure (intensity of NSP) and outcomes (work ability and sick leave) over 1 year. The high response rate to the SMS is also a strength supporting the feasibility of this method to obtain frequent repeated measurements of pain in future studies on the prognosis of NSP.

Trajectories of NSP, sick leave and work ability

The trajectory classes of NSP used in this study were distinguished using LCGA, resulting in six distinct trajectories of NSP.[30] This corroborates a study by Lövgren et al. (2014) which used Growth Mixture Modeling to identify six trajectory classes of NSP in nursing students entering working life. In contrast, the severity of NSP in the current sample of workers was much higher, perhaps due to the large proportion of blue-collar workers in this study.[1] The high prevalence of strong fluctuating (24%) and severe persistent NSP (9%), with mean pain intensities of 5 and 7 (scale 0-10), respectively, is noteworthy.

Trajectory class of NSP was strongly associated with the number of days on sick leave over the 1-year study period. Particularly, the fully adjusted model indicated an increased relative risk of sick leave in the trajectory class with severe persistent NSP (mean 1.5 days/month), compared with low NSP (mean 0.1 days/month). This result is in line with previous prospective studies showing a positive association between NSP intensity and sick leave.[4 6] This result persisted with adjustment for potential confounding by multisite pain, which was associated with NSP and sick leave in previous studies.[19 44 45] Thus, severe persistent NSP appears to be strongly associated with sick leave due to musculoskeletal pain, regardless of multisite pain and other personal and occupational factors.

The four trajectory classes of NSP were also associated with poor work ability over the year (Table 2). For instance, the probability of reporting reduced work ability was 13 times higher for the trajectory class with severe persistent NSP (median work ability 7.1 on the 0-10 scale), compared with low NSP (median work ability 9.5), regardless of inclusion of potential confounders in the model (Table 2, model 3). In agreement, previous studies have found that intense NSP is associated with reduced work ability in workers,[3 46] although none of these examined pain trajectories. Interestingly, including baseline intensity of NSP (i.e. past 3 months) as an additional covariate in model 3 did not reduce the estimated association for sick leave or work ability. In fact, this adjustment resulted in even stronger estimates for work ability, which clearly indicates that the LCGA-based trajectory classes of NSP have a predictive value beyond that explained by past pain intensity assessed at a single time point.

The observed consistent associations between the identified trajectories of NSP and the outcomes sick leave and work ability support the prognostic value of LCGA-based trajectories of NSP among workers, and suggests that such sub-populations can be of clinical and occupational relevance. Thus, this study supports using LCGA to identify distinct sub-populations of workers with different patterns of NSP. Further, the increase in relative risk of sick leave and poor work ability for severe persistent NSP points to the need for interventions and preventive strategies aiming at reducing severe persistent NSP in working populations.

Effect modification by physical work load

High physical work load is a known risk factor for incident NSP and has been associated with a poor prognosis.[47] Thus, the association for NSP trajectories with sick leave and work ability was expected to be modified by the level of self-reported physical work load at baseline. However, we could not confirm any interaction between trajectory class of NSP and physical work load neither for sick leave nor work ability. Still, it is possible that more precise technical measurements of physical work exposure would have yielded different results.

Association of temporal fluctuations in NSP with sick leave and work ability

NSP is often referred to as a recurrent and fluctuating condition.[11] However, the temporal fluctuations in NSP have rarely been investigated in detail, and few, if any, studies have

examined whether fluctuations in NSP are associated with sick leave and work ability. The frequent repeated measures allowed us to assess the within-person temporal association between fluctuations in the intensity of NSP and sick leave (every fourth week) and work ability (every twelfth week). We found that the within-person fluctuations in pain intensity were significantly associated with both sick leave and work ability, which persisted in the fully adjusted model (Table 3). That is, when the individual pain score increased, the likelihood of sick leave and poor work ability also increased. Thus, not only could we address the differences between workers in temporal patterns of NSP, but also whether the temporal fluctuations in NSP at the individual level are of predictive value.

Methodological discussion

As this study is limited to self-reported measures of pain and the outcomes sick leave and work ability, one cannot overlook the possibility of bias. Regarding self-reported sick leave, meta-analytic evidence indicates reasonably high convergent validity against organization and register-based records, although with a slight tendency for under-reporting.[37] Thus, there is a risk for underestimation of sick leave in this study. The question about days on sick leave the past month did not distinguish between work days and non-work days, which may have resulted in less precise estimates. Also, although both outcomes sick leave and work ability were assessed prospectively over 1 year, the NSP trajectories were determined during the same time period and thus causal inferences should be made with caution. Still, it seems most likely that pain preceded the occurrence of sick leave, rather than the reverse relationship. The compliance to text messages was very high on average (Table 1). Still, missing data increased slightly over time, which might have introduced some uncertainties in the models.

We addressed several relevant factors as confounders or effect modifiers (physical work load) of the association of pain trajectories with sick leave and work ability. However, as the causes of sick leave and poor work ability are likely multifactorial,[4 19 21] the focus on pain trajectories as predictors is a potential limitation because it does not inform about other potentially important prognostic factors. Also, the possibility of residual confounding by non-measured factors cannot be ruled out. For instance, we did not measure comorbidity of chronic conditions that might be associated with both NSP trajectories and the outcomes.

Since this study was conducted in a non-random sample with a predominance of blue-collar workers, it is important to verify the study findings in other working populations. The general notion of NSP as a fluctuating and reoccurring condition[11] is corroborated by our data, but this is rarely taken into account in observational studies on NSP. The inclusion of residual variance in the LCGA model allowed us to distinguish trajectory classes with more or less fluctuating patterns of NSP. Temporal fluctuations were more prominent in the NSP trajectories with moderate and strong pain, which may have contributed to the lower relative risk of sick leave and poor work ability compared to the trajectory class with severe persistent NSP.

Since the trajectories with lower intensities of NSP, i.e., including asymptomatic, very low NSP and low recovering NSP, did not differ regarding their low occurrence of sick leave and poor work ability, we decided to merge them into a single reference category in the prediction models. Still, it is possible that these three classes differ in other prognostic outcomes.

Conclusion

This longitudinal study shows that severe persistent NSP is associated with sick leave due to pain and reduced work ability over 1 year among workers. The high prevalence of severe persistent NSP and the increase in relative risk of sick leave and poor work ability point to the need for preventive strategies aiming at reducing severe persistent NSP among workers. Overall, our findings contribute with further understanding of the possible consequences of different time patterns and levels of NSP, which can be of general importance for researchers, practitioners and clinicians.

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Conflict of interest

The authors declare none.

Author contributions

DMH contributed to the statistical data analyses and drafting of the manuscript. AH and MBJ contributed to the conception, design, data collection and funding of the full DPhacto study. All authors (DMH, AH, SDL, MBJ, and CDNR) contributed to the conception of this study, discussed the results and commented on the manuscript.

Data sharing statement

Additional data can be accessed on request by email (aho@arbejdsmiljoforskning.dk).

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Tables

Table 1 Descriptive characteristics of the study population (n=748)

	N	Median	IQR	Mean	SD
Age (years)	748			44.8	9.6
Men N (%)	411 (55)				
BMI ($kg \times m^{-2}$)	732			27.3	4.8
Seniority (years)	722			13.5	10.3
Administration workers N (%)	128 (17)				
Blue-collar workers N (%)	620 (83)				
Cleaning	115 (15)				
Manufacturing	448 (60)				
Transportation	57 (8)				
Physical work load at baseline (scale 1-10)	723			5.3	2.4
Sick leave days					
Baseline (days/month)	741	0.0	0.0	0.3	1.9
Last follow-up (days/month)	655	0.0	0.0	0.4	2.5
Total days (over all time points)	746	0.0	3.0	5.8	20.9
Work ability (scale 0-10)					
Baseline	646	9.0	2.0	8.5	2.0
Last follow-up	671	9.0	2.0	8.2	2.4
Mean work ability (over all time points)	732	8.8	2.5	8.3	1.7
NSP intensity (scale 0-10)					
Baseline	748	2.0	5.0	3.0	2.7
Last follow-up	652	2.0	4.0	2.4	2.7
Mean NSP intensity (over all time points)	748	2.0	3.6	2.6	2.3
Number of pain regions at baseline (count)	745	1.0	3.0	1.7	1.5
Compliance to text messages (missing responses, count)					
NSP intensity	748	0.0	1.0	1.2	2.7
Sick leave	746	0.0	1.0	1.2	2.6
Work ability	732	0.0	1.0	0.4	0.7

Abbreviations: BMI, body mass index; NSP, neck-shoulder pain; IQR, inter quartile range.

Table 2. Association of neck-shoulder pain (NSP) trajectory class with sick leave (days/month) and work ability (ordinal scale 0-10) over 1 year, referencing low NSP.

		Sick leave				Work ability			
GEE models (classes)	N	p-value	RR	95%CI Lower	95%CI Upper	p-value	OR	95%CI Lower	95%CI Upper
Model 1									
Low NSP	292		1.00				1.00		
Moderate NSP	208	<0.001	3.28	1.89	5.68	<0.001	2.45	1.87	3.21
Strong NSP	178	<0.001	8.98	4.78	16.89	<0.001	8.64	6.38	11.69
Severe NSP	70	<0.001	17.64	9.36	33.23	<0.001	15.07	9.94	22.85
Model 2									
Low NSP	286		1.00				1.00		
Moderate NSP	204	<0.001	3.25	1.87	5.64	<0.001	2.40	1.83	3.16
Strong NSP	174	<0.001	8.61	4.54	16.33	<0.001	9.03	6.62	12.31
Severe NSP	68	<0.001	16.00	8.17	31.34	<0.001	14.77	9.63	22.66
Model 3									
Low NSP	277		1.00				1.00		
Moderate NSP	199	<0.001	3.11	1.75	5.52	<0.001	2.43	1.84	3.20
Strong NSP	165	<0.001	7.58	3.91	14.71	<0.001	8.12	5.91	11.16
Severe NSP	66	<0.001	13.83	6.72	28.49	<0.001	12.93	8.50	19.67

Relative risk (RR) estimates, indicating the relative increase in the number of days on sick leave per month, were obtained using Generalized Estimation Equation (GEE) with a Poisson distribution for days on sick-leave (measured at 4 week intervals). Odds ratios (OR), indicating the likelihood of a 1-unit reduction in work ability, were obtained using GEE with a multinomial distribution for work ability (measured at 12 week intervals).
Model 1: Unadjusted.
Model 2: Adjusted for age, gender and body mass index.
Model 3: Additionally adjusted for occupational sector (four categories, referencing administration) and physical work load.

Table 3. Within-person effect of temporal fluctuations in neck-shoulder pain intensity (scale 0-10) on sick leave (days/month) and work ability (scale 0-10) over 1 year

		Sick leave				**Work ability**			
				95% CI				95% CI	
GEE models	N	p-value	RR	Lower	Upper	p-value	OR	Lower	Upper
Model 1	248	0.008	1.12	1.03	1.21	0.005	1.11	1.03	1.19
Model 2	242	0.008	1.12	1.03	1.21	0.009	1.11	1.03	1.19
Model 3	231	0.011	1.11	1.02	1.21	0.002	1.13	1.04	1.21

Relative risk (RR) estimates, indicating the relative increase in the number of days on sick leave per month, were obtained using Generalized Estimation Equation (GEE) with a Poisson distribution for days on sick-leave (measured at 4 week intervals). Odds ratios (OR), indicating the likelihood of a 1-unit reduction in work ability, were obtained using GEE with a multinomial distribution for work ability (measured at 12 week intervals). Estimates indicate the within-person effect of change in pain intensity on change in sick leave and work ability per month.
Model 1: adjusted for the person mean pain intensity across time points.
Model 2: additionally adjusted for age, gender and BMI.
Model 3: additionally adjusted for occupational sector and physical work load.

Figure legends

Figure 1. Mean 1-year trajectories of days on sick leave obtained in the fully adjusted model in each trajectory class of neck-shoulder pain (NSP). The x-axis represents the 14 pain ratings over 1 year. The y-axis represents the mean predicted number of days on sick leave per month.

Figure 2. Association between temporal fluctuations in neck-shoulder pain intensity (NSP) and the outcomes sick leave and work ability. The x-axis represents the difference in pain intensity scores from the person mean pain intensity across time points. The y-axis represents the predicted number of days on sick leave per month (Fig. 2a) and the predicted cumulative probability of poor work ability (Fig. 2b), as defined by the cut-point ≤7 (scale 0-10).[39]

Supplemental Figures

Supplemental Figure A. Mean predicted intensity of neck-shoulder pain (NSP) over 1 year in the four trajectory classes of NSP obtained using Latent class growth analysis.

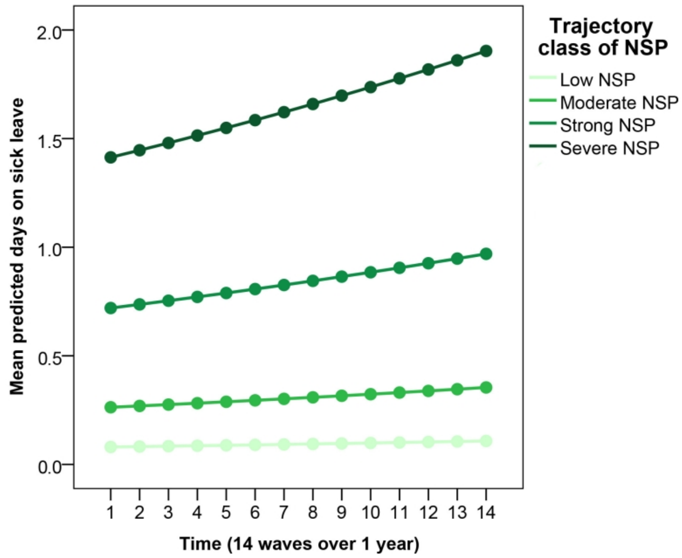


Figure 1.

Figure 1. Mean 1-year trajectories of days on sick leave obtained in the fully adjusted model in each trajectory class of neck-shoulder pain (NSP). The x-axis represents the 14 pain ratings over 1 year. The y-axis represents the mean predicted number of days on sick leave per month.

215x279mm (300 x 300 DPI)

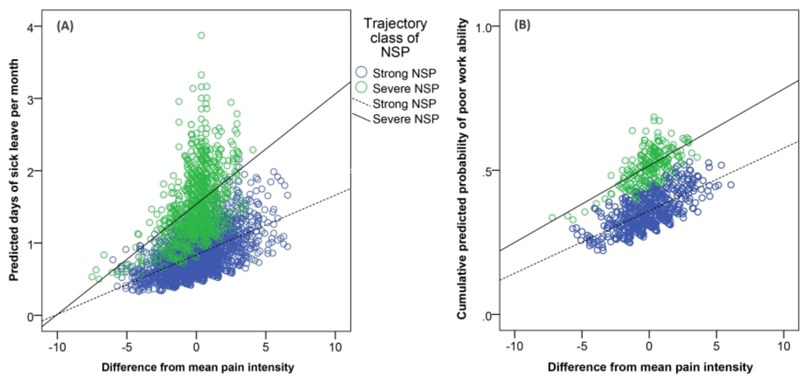
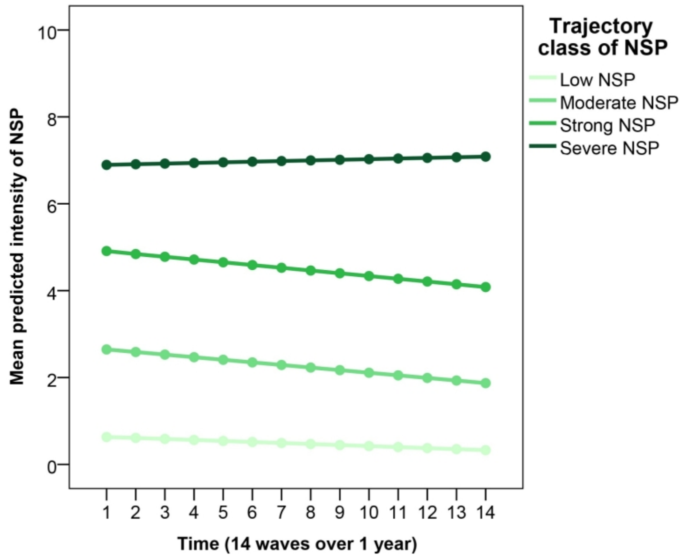


Figure 2

Figure 2. Association between temporal fluctuations in neck-shoulder pain (NSP) and the outcomes sick leave and work ability. The x-axis represents the difference in pain intensity scores from the person mean pain intensity across time points. The y-axis represents the predicted number of days on sick leave per month (Fig. 2a) and the predicted cumulative probability of poor work ability (Fig. 2b), as defined by the cut-point ≤7 (scale 0-10).

350x199mm (300 x 300 DPI)



Supplemental Figure A.

Supplemental Figure A. Mean predicted intensity of neck-shoulder pain (NSP) over 1 year in the four trajectory classes of NSP obtained using Latent class growth analysis.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Check yes/no
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	yes
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	yes, p4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	yes, p5
Methods			
Study design	4	Present key elements of study design early in the paper	yes, p5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	yes, p5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	a) yes, p5-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	yes, p6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	yes, p6-8
Bias	9	Describe any efforts to address potential sources of bias	yes, p7-8 and 9 (confounders and statistical analyses)
Study size	10	Explain how the study size was arrived at	yes, p6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	yes, p8-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	yes p8-9

	(*b*) Describe any methods used to examine subgroups and interactions	yes, p8-9
	(*c*) Explain how missing data were addressed	yes, p8
	(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	yes, p8; page 11
	(*e*) Describe any sensitivity analyses	

Continued on next page

Results			Yes/no
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes, p6 (flow) p 11 (compliance), and results tables 1-3.
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes, p11
		(b) Indicate number of participants with missing data for each variable of interest	Yes, p11 (table 1)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	yes, p 11 (table 1)
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Yes, tables 2-3
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	statistical methods and results
Discussion			
Key results	18	Summarise key results with reference to study objectives	yes, p15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	yes, p17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	yes, p18
Generalisability	21	Discuss the generalisability (external validity) of the study results	yes, p17 (last paragraph)
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	yes, p18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Are trajectories of neck–shoulder pain associated with sick leave and work ability in workers? A one-year prospective study

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Secondary Subject Heading:	Public health
Keywords:	Chronic pain, LCGA, Neck pain, Occupational, Pain trajectories

Title: Are trajectories of neck–shoulder pain associated with sick leave and work ability in workers? A one-year prospective study

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Author contributions:

DMH contributed to the statistical data analyses and drafting of the manuscript. AH and MBJ contributed to the conception, design, data collection and funding of the full DPHACTO study. All authors (DMH, AH, SDL, MBJ, and CDNR) contributed to the conception of this study, discussed the results and commented on the manuscript.

Data sharing statement:

Additional data can be accessed on request by email (aho@arbejdsmiljoforskning.dk).

The manuscript contains about 4300 words, 3 tables, 2 figures, and 1 Supplemental figure.

Abstract

Objectives

The study aimed to determine the extent to which latent trajectories of neck-shoulder pain (NSP) are associated with self-reported sick leave and work ability based on frequent repeated measures over 1 year in an occupational population.

Methods

This longitudinal study included 748 Danish workers (blue-collar, n=620; white collar, n=128). A questionnaire was administered to collect data on personal and occupational factors at baseline. Text messages were used for repeated measurements of NSP intensity (scale 0-10) over 1 year (14 waves in total). Simultaneously, self-reported sick leave (days/month) due to pain was assessed at four week intervals, while work ability (scale 0-10) was assessed using a single item (work ability index) at 12 week intervals over the year. Trajectories of NSP, distinguished by latent class growth analysis (LCGA), were used as predictors of sick leave and work ability in generalized estimation equations with multiple adjustments.

Results

Sick leave increased and work ability decreased across all NSP trajectory classes (low, moderate, strong fluctuating, and severe persistent pain intensity). In the adjusted model, the estimated number of days on sick leave was 1.5 days/month for severe persistent NSP compared with 0.1 days/month for low NSP (RR=13.8, 95%CI 6.7–28.5). Similarly, work ability decreased markedly for severe persistent NSP (OR=12.9, 95%CI 8.5–19.7; median 7.1) compared with low NSP (median 9.5).

Conclusion

Severe persistent NSP was associated with sick leave and poor work ability over 1 year among workers. Preventive strategies aiming at reducing severe persistent NSP among working populations are needed.

Keywords: Chronic pain; LCGA; Neck pain; Occupational; Pain trajectories

Strengths and limitations of this study

- This is the first study investigating the association of longitudinal trajectories of neck-shoulder pain with sick leave and work ability.
- Repeated monthly assessments over 1 year allowed detailed analyses of the time course of pain intensity, sick leave and work ability.
- High response rates were obtained during each month of follow-up.
- Self-reported measurements of exposure and outcome during the same time-period are potential limitations.

Introduction

Neck-shoulder pain (NSP) is a common condition, with annual prevalence rates between 27% and 48% in different working populations.[1] NSP is one of the leading causes of years lived with disability worldwide,[2] and is associated with reduced work ability[3] and high sick leave rates.[4 5] In workers with NSP, 20% had at least one spell of sick leave in one year.[4] Sick leave risks are higher in workers with more severe NSP intensity.[6] The economic burden of NSP on organizations and society is considerable.[7-9] The estimated total cost of neck pain in The Netherlands in 1996 was 686 million US dollars,[7] and the estimated total cost of both neck and back pain in Sweden in 2001was 1% of the gross national product (GNP).[9]

NSP is considered a heterogeneous condition ranging from very mild symptoms to severe chronic pain[10] with a substantial individual variability in progression over time.[11-13] This heterogeneity may, however, comprise homogenous sub-populations with distinct patterns of pain, unique risk factors and different underlying pathophysiology.[14] Revealing such sub-populations is likely important for early identification, establishing risk factors, and improving prevention and treatment.[15] However, most existing studies have been conducted on patients with low back pain, e.g.,[15-17] while studies identifying and describing the patterns of NSP in working populations with a wide range of pain severities are sparse. Also, there is a lack of research on the predictive value of NSP sub-populations; which is crucial for understanding the extent to which NSP sub-populations are of clinical and occupational relevance regarding intervention and treatment. Thus, it is important for research and occupational and clinical practice to distinguish sub-populations of workers with different trajectories of NSP (e.g. severity, temporal variability and time course) while assessing their predictive value against core prognostic outcomes, such as sick leave and work ability.[4 18 19]

Work ability, as defined as the balance between human resources and work demands,[20] is determined by multiple factors.[21] The perception of poor work ability is associated with sick leave and early retirement.[22] Sick leave due to pain is likely multifactorial, and several personal and work related (physical and psychosocial) factors have been identified as potential determinants of increased risks.[4 19 23 24] High physical workload is associated with poor work ability and occurrence of sick leave due to pain,[4 25] and may hamper return to work.[23] Thus, the level of physical workload is a potential moderator of the relationship of NSP trajectories with work ability and sick leave.

Most previous studies on the prognosis of NSP have relied only on few measurements in time interspersed by long intervals, e.g. years.[11 26] Such studies are not designed to capture the detailed time course (trajectory) or temporal fluctuations in NSP (e.g. between weeks or months). In contrast, frequent repeated measurements of pain facilitate accurate and precise identification of individual pain trajectories [27] and minimize recall bias.[28]

Latent class growth analysis (LCGA) is a common statistical approach for identifying homogenous sub-populations (latent classes) based on individual growth parameters (i.e. intercept, slope and residual variance) in repeated measures data.[29] We have previously used LCGA to distinguish trajectory classes of NSP among the current population of workers based on frequent repeated measurements of NSP over 1 year.[30] We identified six distinct trajectories of NSP ranging from "asymptomatic" (prevalence 11%) to "severe persistent NSP" (9%). Several personal and occupational factors, as well as symptom characteristics at baseline predicted trajectory class membership. However, understanding the occupational and clinical relevance of trajectories of NSP requires a determination of their predictive value against core occupational and clinical outcomes. Particularly, identifying NSP trajectories associated with unfavorable outcomes would likely aid targeted prevention and treatment.

The aim of this study is to determine the extent to which latent trajectories of NSP are associated with self-reported sick leave due to musculoskeletal pain and with work ability based on frequent repeated measures over 1 year in an occupational population. A second aim is to investigate the temporal association (within person) between fluctuations in NSP and the outcomes sick leave and work ability.

Methods

Study design

This is a prospective study using data from the Danish Physical activity cohort with objective measurements (DPhacto). The study protocol for the cohort is reported in detail elsewhere.[31] Data collection took place from April 2012 to May 2014 at 15 Danish companies, including workers in four occupational sectors (cleaning, manufacturing, transportation and office work/administration). The initial contact and recruitment of companies were performed in

collaboration with a large Danish union. The companies were selected to represent blue-collar occupations with different levels of physical demands at work.

Baseline data collection consisted of a brief web-based questionnaire, a standard health examination and objective diurnal measurements of physical activity and heart rate (presented elsewhere.[32 33] Prospective self-reported data on musculoskeletal pain, sick leave due to pain and work ability was collected repeatedly over 12 months using text messages.

Study population

The inclusion criterion for participation was current employment within any of the recruited work places. Exclusion criteria were holding a managing position or being pregnant or a student/trainee. In addition, workers not responding to the baseline questionnaire and/or the prospective measurements were excluded.

Among the 2107 invited workers, 1119 agreed to participate and 32 of them were excluded due to holding a managing position (n=17) or being pregnant (n=2) or a student/trainee (n=13). Of the remaining 1087 eligible workers, 782 responded to the questionnaire and 748 took part in the prospective measurements from baseline. Thus, the final study sample consisted of 748 workers (blue-collar, n=620; white collar, n=128). Descriptive characteristics of the study population are shown in Table 1.

All participants provided their written informed consent prior to participation. The present study was conducted according to the Declaration of Helsinki, approved by the Danish Data Protection Agency, and evaluated by the Regional Ethics Committee in Copenhagen, Denmark (H-2-2012-011).

Repeated assessment using text messages

Text messages (SMS) were used to assess self-reported pain intensity in the neck-shoulder region, days on sick leave and work ability using the commercial software “SMS-Track” (https://sms-track.com/). Starting at baseline, data on NSP and sick leave were collected at four week intervals (14 waves), while data on work ability were collected at 12 week intervals (4 waves in total) during the 1-year study. The SMS were sent on Sundays, with a reminder the following day.

Neck-shoulder pain

Pain intensity in the neck-shoulder region (NSP) the past month was assessed using an 11-point numeric rating scale (NRS), which ranges from 0 (“no pain”) to 10 (“worst pain imaginable”). The worker responded to the question *“rate the worst pain you have experienced in your neck/shoulders within the past month?”* The NRS is a reliable and valid instrument for assessing pain intensity [34] and is recommended as an outcome in clinical trials.[35]

Sick leave

Sick-leave due to pain was assessed using a single-item from the validated Outcome Evaluation Questionnaire [36]: *“Within the past month, how many days have you been absent from work due to pain in muscles or joints?”* with response categories ranging from 0 to 31 days. Based on a recent meta-analysis, self-reported sick leave demonstrates good test-retest reliability and reasonably high convergent validity against records.[37]

Work ability

Work ability was assessed using a validated single item[22] from the work ability index.[38] The worker responded to the question “*Please rate your present work ability*?” with response categories ranging from 0 (unable to work) to 10 (“work ability as its best”). A score ≤ 7 denotes poor work ability.[39]

Assessment of possible confounders and effect modifiers

Theoretical assumptions and empirical evidence were used to select possible confounders and effect modifiers which were accounted for in the statistical analyses. The following variables were measured at baseline as previously described [30]: age (years,) and gender (male or female) based on civil registration number, body mass index (BMI) based on objectively measured height and weight, occupational sector (manufacturing, cleaning, transportation, and administration/office work within the same workplaces), and seniority in the current job (years). Physical work load was measured by the question *“How physically demanding do you normally consider your present work?”* using a ten-point (1-10) response scale modified from Borg,[40] with higher values indicating higher physical demands. Multisite pain was measured based on the Standardized Nordic questionnaire for the analysis of musculoskeletal symptoms [41] asking about pain intensity (NRS, scale 0-10) during the past three months in

seven different anatomical areas (i.e. neck/shoulders, elbows, hands/wrists, lower back, hips, knees, and feet/ankles). A cut-point of >2 was used to indicate the occurrence of pain, whereby the number of pain sites was determined.[42] Since the relationship between NSP, sick leave and work ability may depend on the level of physical demands at work, physical work load was considered both a confounder and an effect modifier, while the other variables were solely included as possible confounders.

Statistical analyses

Growth trajectories (latent classes) of the intensity in NSP were identified using LCGA in Latent Gold version 5.1 (Statistical innovations Belmont, MA, USA). The LCGA procedure and the resulting trajectory classes of NSP are described in a previous study on the same population.[30] In brief, the LCGA assigns individuals to latent classes based on maximum posterior probabilities. That is, using growth parameters (i.e. intercept, slope and residual variance) reflecting change in an observed variable (i.e. pain intensity) over time, LCGA assigns individuals to latent classes (categorical variable) assuming homogeneity within class and heterogeneity between classes.[29 43]

The LCGA models were performed using Time (14 waves over 1 year) as a continuous linear predictor and NSP intensity as a continuous dependent variable. Missing values were considered as missing at random and included in all models without imputations. The optimal number of classes was determined based on appropriate model fit indices, i.e. Bayesian information criterion (BIC), Entropy and Bootstrap log likelihood ratio (BLRT), which were obtained in consecutive LCGA models with 1-10 a priori class solutions. Then, the models were evaluated based on the estimated growth parameters and clinical distinction between the identified classes. The identified trajectories of NSP were used as an independent variable in further statistical analyses of associations with sick leave and work ability over the same year.

The association of NSP trajectories with sick leave (SMS at four week intervals over 1 year) and work ability (SMS each quarter) during the same year was determined using Generalized Estimation Equation (GEE) models with an auto regressive first order (AR1) covariance structure to account for weaker correlations with increasing distance between time points.

The association of NSP trajectories with sick-leave (days/month) was tested using GEE models with a Poisson distribution and a log link function. Fixed factors were NSP trajectory class (categorical variable), time (continuous variable, 14 time points) and the interaction between trajectory class and time. The interaction term was kept in the model if it was significant ($p<0.05$). We tested both linear and quadratic time trends, but decided on a linear model since the quadratic model did not improve model fit. The primary GEE models were constructed in three steps: (model 1) unadjusted, (model 2) adjusted for age, gender and BMI, and (model 3) additionally adjusted for occupational sector (four categories) and physical work load (continuous variable). Then, we tested if the results of the primary models were consistent when accounting for baseline pain intensity and comorbidity of multisite pain, as they may be associated with both NSP trajectories and the outcomes. Thus, secondary models were estimated with additional adjustment for the intensity of NSP (model 4) and the number of pain regions (model 5) at baseline (past three months). Finally, to test for potential effect modification by physical work load, model 3 was re-run with an interaction between NSP trajectory class and physical work load (model 6).

The association of NSP trajectory class with work ability (dependent variable, ordinal scale) was tested using GEE models with a multinomial distribution and a cumulative logit link function. Fixed factors were NSP trajectory class (categorical variable), time (linear continuous variable, 4 time points), and the interaction between trajectory class and time, which was kept only if reaching significance ($p<0.05$). The models were constructed with and without adjustment for covariates, as explained above.

Additional GEE models were constructed to investigate the within person association of temporal fluctuations in the intensity of NSP with sick leave and work ability (outcomes). To partition the within and between subjects variances in the predictor (intensity of NSP), the mean pain intensity score across all time points was determined for each individual. Then, the person mean pain score was subtracted from each repeated pain rating and used as an independent variable (within subject effect), while adjusting for the person mean pain as a covariate (between-subjects effect).[43] Thus, these GEE models were constructed with three fixed factors: (i) time (14 waves), (ii) the person mean pain intensity across waves, and (iii) the difference from the mean pain intensity during each wave for the individual (within subject effect). The within-subject effect would then reflect the population averaged association with the outcome for each unit change in pain intensity per month for the individual. Model specifications for sick leave and work ability were the same as above. The models were estimated with and without adjustment for potential confounders as explained above.

The GEE models were estimated using SPSS software version 22 (IBM, USA). For each model, we derived the exponential estimate, i.e. relative risk (RR) and odds ratio (OR) for sick leave and work ability, respectively, and 95% confidence intervals (CI). P-values <0.05 were considered significant.

Patient and public involvement

No patients or public were directly involved in setting the research questions and outcomes, design and conduct of this study, or interpretation of the results. Results will be disseminated to the participants at http://www.nfa.dk/.

Results

Characteristics of the study population

Characteristics of the study population are shown in Table 1. The study sample consisted of both males and females, and most were blue-collar workers. The workers were on average of middle age, slightly overweight, and had been in their current job for 14 years. The mean intensity of NSP across all time points was 2.6 (scale 0-10). Most of the workers rated high work ability (>7, scale 0-10) across the study period, while the average worker accumulated 6 days on sick leave due to pain over 1 year, although with a considerable dispersion between individuals. Compliance to the repeated measurements (text messages) in the study was high; on average, the workers had 1.2 missing responses to pain and sick leave (14 waves) and 0.4 missing responses to work ability (4 waves) (Table 1). The amount of missing data increased over time. During the second wave, the response rates were 96%, 96% and 93% for pain, sick leave and work ability, respectively, while the response rates dropped to 87%, 88% and 90% during the last wave.

[Insert Table 1 about here]

Identified latent trajectories of NSP

Based on model fit indices (BIC, Entropy and BLRT) and distinction between classes obtained from consecutive LCGA models, a six-class solution was chosen.[30] The growth pattern and prevalence (%) of the six identified trajectory classes of NSP were characterized as follows (see also Supplemental Figure A): class 1, *asymptomatic* (11%); class 2, *very low NSP* (10%); class 3, *low recovering NSP* (18%); class 4, *moderate fluctuating NSP* (28%); class 5, *strong fluctuating NSP* (24 %); and class 6, *severe persistent NSP* (9%). The trajectory classes with lower intensities of NSP (classes 1-3) did not differ in total days on sick leave or mean work ability over 1 year; and the occurrence of sick leave was very low, while work ability was high across the three classes. Thus, classes 1-3 were merged into a single category (low NSP 39%), which was used as a reference in further analyses.

Association between NSP trajectory classes and sick leave over 1 year

Estimates of the association of NSP trajectories with sick leave due to pain (days /month) are shown in Table 2. There was no significant time effect on sick leave (unadjusted RR=1.02, 95%CI 0.99-1.06). Thus, the interaction between NSP trajectory class and time was discarded from the models.

Based on the fully adjusted model (Table 2, model 3) referencing low NSP, the relative risk of sick leave increased for moderate (RR=3.1, 95%CI 1.8–5.5), strong fluctuating (RR=7.6, 95%CI 3.9–14.7), and severe persistent NSP (RR=13.8, 95%CI 6.7–28.5). On average, the estimated number of days on sick leave per month was 0.1 (95%CI 0.1–0.15) for low NSP, 0.3 (95%CI 0.2–0.4) for moderate NSP, 0.8 (95%CI 0.5–1.2) for strong NSP, and 1.5 (95%CI 1.0–2.4) for severe persistent NSP. Predicted values of sick leave for each wave over 1 year are shown in Figure 1.

Additional adjustment for multisite pain showed similar estimates for moderate NSP (RR=3.0, 95%CI 1.7–5.4), strong fluctuating NSP (RR=7.2, 95%CI 3.5–14.5) and severe persistent NSP (RR=13.1, 95%CI 6.1–28). Also, adjustment for baseline pain intensity revealed stronger estimates for moderate NSP (RR=3.7, 95%CI 2.1–6.8), strong fluctuating NSP (RR=10.9, 95%CI 5.1–23.7) and severe persistent NSP (RR=24.5, 95%CI 10.4–57.9), although with wider CIs.

There was no significant interaction between NSP trajectory class and physical work load on sick leave.

[Insert Figure 1 about here]

Association between NSP trajectory classes and work ability over 1 year

Estimates of the association between trajectories of NSP and work ability (measured each quarter) are shown in Table 2.

There was a small time effect indicating reduced work ability over the year (unadjusted OR 1.05, 95%CI 0.99–1.11). There was no interaction between NSP trajectory class and time, whereby this interaction was discarded from the model.

NSP trajectory class was inversely associated with work ability (Table 2). Based on the fully adjusted model referencing low NSP (Table 2, model 3), the likelihood of a 1-unit reduction in work ability increased for moderate (OR=2.4, 95%CI 1.8–3.2), strong fluctuating (OR=8.1, 95%CI 5.9–11.2), and severe persistent NSP (OR=12.9, 95%CI 8.5–19.7). The median scores (IQR) of work ability during the year were 9.5(1.7) for low NSP, 9.0(2.0) for moderate NSP, 7.8(2.0) for strong NSP, and 7.1(2.5) for severe persistent NSP.

Additional adjustment for multisite pain showed slightly weaker estimates for moderate NSP (OR=2.2, 95%CI 1.7–2.9), strong fluctuating NSP (OR=6.4, 95%CI 4.6–9.0) and severe persistent NSP (OR=10.4, 95%CI 6.7–16.0). Further, adjustment for baseline pain intensity showed similar estimates for moderate NSP (OR=2.6, 95%CI 1.9–3.5), strong fluctuating NSP (OR=9.1, 95%CI 6.3–13.1) and severe persistent NSP (OR=15.4, 95%CI 9.3–25.5).

There was no significant interaction between NSP trajectory class and physical work load on work ability.

[Insert Table 2 about here]

Within-person association of NSP with sick leave and workability

Due to the high work ability scores and low prevalence of sick leave in the classes with lower intensities of NSP, these analyses included only workers assigned to the trajectory classes strong fluctuating and severe persistent NSP (n=248).

The within-person associations of pain intensity with sick leave due to pain and work ability are shown in Table 3.

Within person fluctuations in the intensity of NSP were positively associated with sick leave (adjusted RR=1.11, 95%CI 1.02–1.21). That is, higher intensity of NSP was associated with more days of sick leave during a particular month at the individual level (Table 3 and Figure 2a).

A similar within-person association was found between fluctuations in pain intensity and work ability (adjusted OR 1.13, 95%CI 1.04–1.21). For example, increasing intensity of NSP was associated with higher probabilities of reduced work ability (Table 3). This association is illustrated in Figure 2b as the estimated probability of reporting poor work ability (≤7 on the 0-10 scale).[39]

[Insert Table 3 about here]

[Insert Figure 2]

Discussion

In summary, this prospective study investigated the relationship between LCGA-based trajectories of NSP and the outcomes sick leave and work ability. We found that the distinguished trajectory classes of NSP were strongly associated with sick leave due to pain and poor work ability over 1 year, and that the temporal fluctuations in pain intensity predicted sick leave and work ability at the individual level.

To our knowledge, this study is unique in assessing the association between LCGA-based trajectories of NSP and important prognostic outcomes among workers. A clear strength of the study is the use of frequent prospective measures of both exposure (intensity of NSP) and outcomes (work ability and sick leave) over 1 year. The high response rate to the SMS is also a strength supporting the feasibility of this method to obtain frequent repeated measurements of pain in future studies on the prognosis of NSP.

Trajectories of NSP, sick leave and work ability

The trajectory classes of NSP used in this study were distinguished using LCGA, resulting in six distinct trajectories of NSP.[30] This corroborates a study by Lövgren et al. (2014) which used Growth Mixture Modeling to identify six trajectory classes of NSP in nursing students entering working life. In contrast, the severity of NSP in the current sample of workers was much higher, perhaps due to the large proportion of blue-collar workers in this study.[1] The high prevalence of strong fluctuating (24%) and severe persistent NSP (9%), with mean pain intensities of 5 and 7 (scale 0-10), respectively, is noteworthy.

Trajectory class of NSP was strongly associated with the number of days on sick leave over the 1-year study period. Particularly, the fully adjusted model indicated an increased relative risk of sick leave in the trajectory class with severe persistent NSP (mean 1.5 days/month), compared with low NSP (mean 0.1 days/month). This result is in line with previous prospective studies showing a positive association between NSP intensity and sick leave.[4 6] This result persisted with adjustment for potential confounding by multisite pain, which was associated with NSP and sick leave in previous studies.[19 44 45] Thus, severe persistent NSP appears to be strongly associated with sick leave due to musculoskeletal pain, regardless of multisite pain and other personal and occupational factors.

The four trajectory classes of NSP were also associated with poor work ability over the year (Table 2). For instance, the probability of reporting reduced work ability was 13 times higher for the trajectory class with severe persistent NSP (median work ability 7.1 on the 0-10 scale), compared with low NSP (median work ability 9.5), regardless of inclusion of potential confounders in the model (Table 2, model 3). In agreement, previous studies have found that intense NSP is associated with reduced work ability in workers,[3 46] although none of these examined pain trajectories. Interestingly, including baseline intensity of NSP (i.e. past 3 months) as an additional covariate in model 3 did not reduce the estimated association for sick leave or work ability. In fact, this adjustment resulted in even stronger estimates for work ability, which clearly indicates that the LCGA-based trajectory classes of NSP have a predictive value beyond that explained by past pain intensity assessed at a single time point.

The observed consistent associations between the identified trajectories of NSP and the outcomes sick leave and work ability support the prognostic value of LCGA-based trajectories of NSP among workers, and suggests that such sub-populations can be of clinical and occupational relevance. Thus, this study supports using LCGA to identify distinct sub-populations of workers with different patterns of NSP. Further, the increase in relative risk of sick leave and poor work ability for severe persistent NSP points to the need for interventions and preventive strategies aiming at reducing severe persistent NSP in working populations.

Effect modification by physical work load

High physical work load is a known risk factor for incident NSP and has been associated with a poor prognosis.[47] Thus, the association for NSP trajectories with sick leave and work ability was expected to be modified by the level of self-reported physical work load at baseline. However, we could not confirm any interaction between trajectory class of NSP and physical work load neither for sick leave nor work ability. Still, it is possible that more precise technical measurements of physical work exposure would have yielded different results.

Association of temporal fluctuations in NSP with sick leave and work ability

NSP is often referred to as a recurrent and fluctuating condition.[11] However, the temporal fluctuations in NSP have rarely been investigated in detail, and few, if any, studies have

examined whether fluctuations in NSP are associated with sick leave and work ability. The frequent repeated measures allowed us to assess the within-person temporal association between fluctuations in the intensity of NSP and sick leave (every fourth week) and work ability (every twelfth week). We found that the within-person fluctuations in pain intensity were significantly associated with both sick leave and work ability, which persisted in the fully adjusted model (Table 3). That is, when the individual pain score increased, the likelihood of sick leave and poor work ability also increased. Thus, not only could we address the differences between workers in temporal patterns of NSP, but also whether the temporal fluctuations in NSP at the individual level are of predictive value.

Methodological discussion

As this study is limited to self-reported measures of pain and the outcomes sick leave and work ability, one cannot overlook the possibility of bias. Regarding self-reported sick leave, meta-analytic evidence indicates reasonably high convergent validity against organization and register-based records, although with a slight tendency for under-reporting.[37] Thus, there is a risk for underestimation of sick leave in this study. The question about days on sick leave the past month did not distinguish between work days and non-work days, which may have resulted in less precise estimates. Also, although both outcomes sick leave and work ability were assessed prospectively over 1 year, the NSP trajectories were determined during the same time period and thus causal inferences should be made with caution. Still, it seems most likely that pain preceded the occurrence of sick leave, rather than the reverse relationship. The compliance to text messages was very high on average (Table 1). Still, missing data increased slightly over time, which might have introduced some uncertainties in the models.

We addressed several relevant factors as confounders or effect modifiers (physical work load) of the association of pain trajectories with sick leave and work ability. However, as the causes of sick leave and poor work ability are likely multifactorial,[4 19 21] the focus on pain trajectories as predictors is a potential limitation because it does not inform about other potentially important prognostic factors. Also, the possibility of residual confounding by non-measured factors cannot be ruled out. For instance, we did not measure comorbidity of chronic conditions that might be associated with both NSP trajectories and the outcomes.

Since this study was conducted in a non-random sample with a predominance of blue-collar workers, it is important to verify the study findings in other working populations. The general notion of NSP as a fluctuating and reoccurring condition[11] is corroborated by our data, but this is rarely taken into account in observational studies on NSP. The inclusion of residual variance in the LCGA model allowed us to distinguish trajectory classes with more or less fluctuating patterns of NSP. Temporal fluctuations were more prominent in the NSP trajectories with moderate and strong pain, which may have contributed to the lower relative risk of sick leave and poor work ability compared to the trajectory class with severe persistent NSP.

Since the trajectories with lower intensities of NSP, i.e., including asymptomatic, very low NSP and low recovering NSP, did not differ regarding their low occurrence of sick leave and poor work ability, we decided to merge them into a single reference category in the prediction models. Still, it is possible that these three classes differ in other prognostic outcomes.

Conclusion

This longitudinal study shows that severe persistent NSP is associated with sick leave due to pain and reduced work ability over 1 year among workers. The high prevalence of severe persistent NSP and the increase in relative risk of sick leave and poor work ability point to the need for preventive strategies aiming at reducing severe persistent NSP among workers. Overall, our findings contribute with further understanding of the possible consequences of different time patterns and levels of NSP, which can be of general importance for researchers, practitioners and clinicians.

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Conflict of interest

The authors declare none.

Author contributions

DMH contributed to the statistical data analyses and drafting of the manuscript. AH and MBJ contributed to the conception, design, data collection and funding of the full DPhacto study. All authors (DMH, AH, SDL, MBJ, and CDNR) contributed to the conception of this study, discussed the results and commented on the manuscript.

Data sharing statement

Additional data can be accessed on request by email (aho@arbejdsmiljoforskning.dk).

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Tables

Table 1 Descriptive characteristics of the study population (n=748)

	N	Median	IQR	Mean	SD
Age (years)	748			44.8	9.6
Men N (%)	411 (55)				
BMI (kg×m^{-2})	732			27.3	4.8
Seniority (years)	722			13.5	10.3
Administration workers N (%)	128 (17)				
Blue-collar workers N (%)	620 (83)				
Cleaning	115 (15)				
Manufacturing	448 (60)				
Transportation	57 (8)				
Physical work load at baseline (scale 1-10)	723			5.3	2.4
Sick leave days					
Baseline (days/month)	741	0.0	0.0	0.3	1.9
Last follow-up (days/month)	655	0.0	0.0	0.4	2.5
Total days (over all time points)	746	0.0	3.0	5.8	20.9
Work ability (scale 0-10)					
Baseline	646	9.0	2.0	8.5	2.0
Last follow-up	671	9.0	2.0	8.2	2.4
Mean work ability (over all time points)	732	8.8	2.5	8.3	1.7
NSP intensity (scale 0-10)					
Baseline	748	2.0	5.0	3.0	2.7
Last follow-up	652	2.0	4.0	2.4	2.7
Mean NSP intensity (over all time points)	748	2.0	3.6	2.6	2.3
Number of pain regions at baseline (count)	745	1.0	3.0	1.7	1.5
Compliance to text messages (missing responses, count)					
NSP intensity	748	0.0	1.0	1.2	2.7
Sick leave	746	0.0	1.0	1.2	2.6
Work ability	732	0.0	1.0	0.4	0.7

Abbreviations: BMI, body mass index; NSP, neck-shoulder pain; IQR, inter quartile range.

Table 2. Association of neck-shoulder pain (NSP) trajectory class with sick leave (days/month) and work ability (ordinal scale 0-10) over 1 year, referencing low NSP.

		Sick leave				**Work ability**			
GEE models (classes)	N	p-value	RR	95%CI Lower	95%CI Upper	p-value	OR	95%CI Lower	95%CI Upper
Model 1									
Low NSP	292		1.00				1.00		
Moderate NSP	208	<0.001	3.28	1.89	5.68	<0.001	2.45	1.87	3.21
Strong NSP	178	<0.001	8.98	4.78	16.89	<0.001	8.64	6.38	11.69
Severe NSP	70	<0.001	17.64	9.36	33.23	<0.001	15.07	9.94	22.85
Model 2									
Low NSP	286		1.00				1.00		
Moderate NSP	204	<0.001	3.25	1.87	5.64	<0.001	2.40	1.83	3.16
Strong NSP	174	<0.001	8.61	4.54	16.33	<0.001	9.03	6.62	12.31
Severe NSP	68	<0.001	16.00	8.17	31.34	<0.001	14.77	9.63	22.66
Model 3									
Low NSP	277		1.00				1.00		
Moderate NSP	199	<0.001	3.11	1.75	5.52	<0.001	2.43	1.84	3.20
Strong NSP	165	<0.001	7.58	3.91	14.71	<0.001	8.12	5.91	11.16
Severe NSP	66	<0.001	13.83	6.72	28.49	<0.001	12.93	8.50	19.67

Relative risk (RR) estimates, indicating the relative increase in the number of days on sick leave per month, were obtained using Generalized Estimation Equation (GEE) with a Poisson distribution for days on sick-leave (measured at 4 week intervals). Odds ratios (OR), indicating the likelihood of a 1-unit reduction in work ability, were obtained using GEE with a multinomial distribution for work ability (measured at 12 week intervals).
Model 1: Unadjusted.
Model 2: Adjusted for age, gender and body mass index.
Model 3: Additionally adjusted for occupational sector (four categories, referencing administration) and physical work load.

Table 3. Within-person effect of temporal fluctuations in neck-shoulder pain intensity (scale 0-10) on sick leave (days/month) and work ability (scale 0-10) over 1 year

		Sick leave				**Work ability**			
				95% CI				95% CI	
GEE models	N	p-value	RR	Lower	Upper	p-value	OR	Lower	Upper
Model 1	248	0.008	1.12	1.03	1.21	0.005	1.11	1.03	1.19
Model 2	242	0.008	1.12	1.03	1.21	0.009	1.11	1.03	1.19
Model 3	231	0.011	1.11	1.02	1.21	0.002	1.13	1.04	1.21

Relative risk (RR) estimates, indicating the relative increase in the number of days on sick leave per month, were obtained using Generalized Estimation Equation (GEE) with a Poisson distribution for days on sick-leave (measured at 4 week intervals). Odds ratios (OR), indicating the likelihood of a 1-unit reduction in work ability, were obtained using GEE with a multinomial distribution for work ability (measured at 12 week intervals). Estimates indicate the within-person effect of change in pain intensity on change in sick leave and work ability per month.

Model 1: adjusted for the person mean pain intensity across time points.

Model 2: additionally adjusted for age, gender and BMI.

Model 3: additionally adjusted for occupational sector and physical work load.

Figure legends

Figure 1. Mean 1-year trajectories of days on sick leave obtained in the fully adjusted model in each trajectory class of neck-shoulder pain (NSP). The x-axis represents the 14 pain ratings over 1 year. The y-axis represents the mean predicted number of days on sick leave per month.

Figure 2. Association between temporal fluctuations in neck-shoulder pain intensity (NSP) and the outcomes sick leave and work ability. The x-axis represents the difference in pain intensity scores from the person mean pain intensity across time points. The y-axis represents the predicted number of days on sick leave per month (Fig. 2a) and the predicted cumulative probability of poor work ability (Fig. 2b), as defined by the cut-point ≤7 (scale 0-10).[39]

Supplemental Figures

Supplemental Figure A. Mean predicted intensity of neck-shoulder pain (NSP) over 1 year in the four trajectory classes of NSP obtained using Latent class growth analysis.

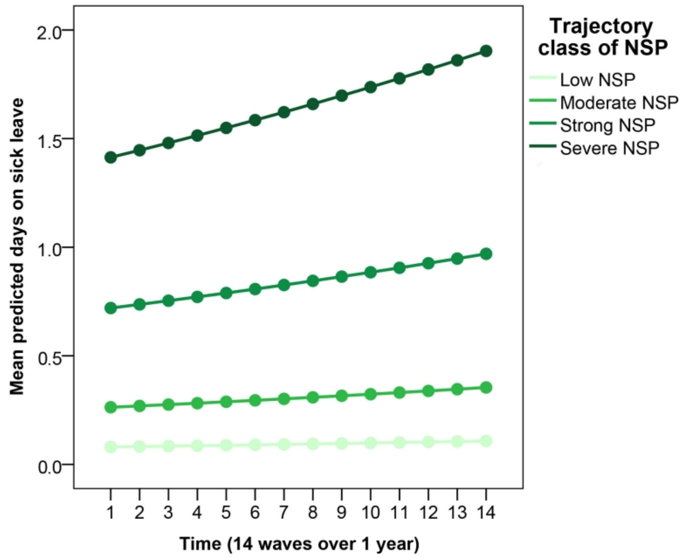


Figure 1.

Figure 1. Mean 1-year trajectories of days on sick leave obtained in the fully adjusted model in each trajectory class of neck-shoulder pain (NSP). The x-axis represents the 14 pain ratings over 1 year. The y-axis represents the mean predicted number of days on sick leave per month.

215x279mm (300 x 300 DPI)

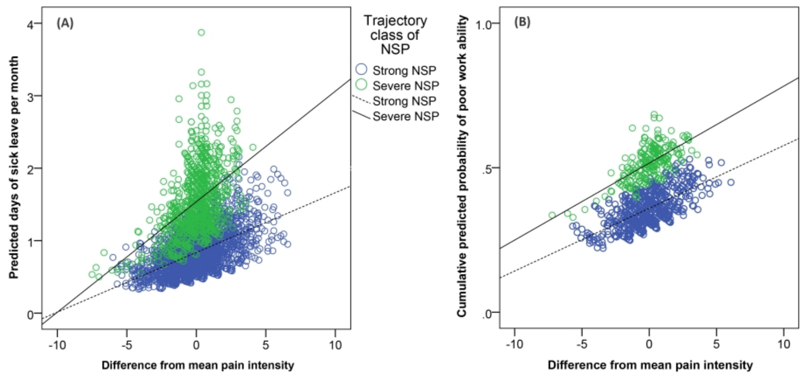
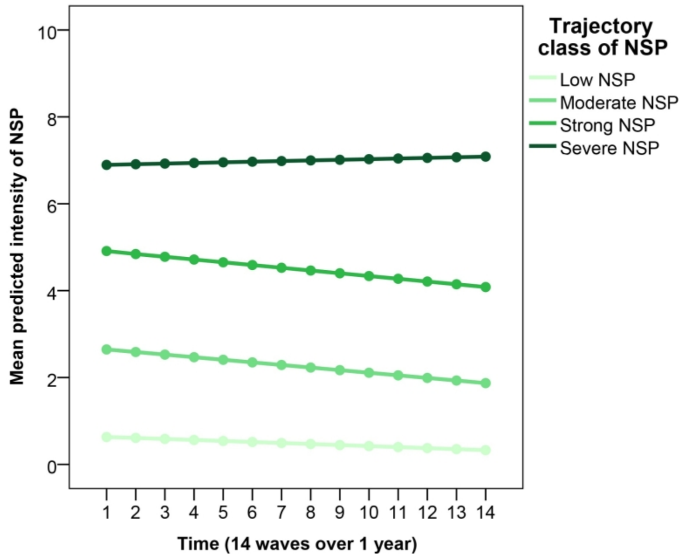


Figure 2

Figure 2. Association between temporal fluctuations in neck-shoulder pain (NSP) and the outcomes sick leave and work ability. The x-axis represents the difference in pain intensity scores from the person mean pain intensity across time points. The y-axis represents the predicted number of days on sick leave per month (Fig. 2a) and the predicted cumulative probability of poor work ability (Fig. 2b), as defined by the cut-point ≤7 (scale 0-10).

350x199mm (300 x 300 DPI)



Supplemental Figure A.

Supplemental Figure A. Mean predicted intensity of neck-shoulder pain (NSP) over 1 year in the four trajectory classes of NSP obtained using Latent class growth analysis.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Check yes/no
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	yes
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	yes, p4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	yes, p5
Methods			
Study design	4	Present key elements of study design early in the paper	yes, p5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	yes, p5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	a) yes, p5-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	yes, p6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	yes, p6-8
Bias	9	Describe any efforts to address potential sources of bias	yes, p7-8 and 9 (confounders and statistical analyses)
Study size	10	Explain how the study size was arrived at	yes, p6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	yes, p8-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	yes p8-9

	(*b*) Describe any methods used to examine subgroups and interactions	yes, p8-9
	(*c*) Explain how missing data were addressed	yes, p8
	(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	yes, p8; page 11
	(*e*) Describe any sensitivity analyses	

Continued on next page

Results			Yes/no
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes, p6 (flow) p 11 (compliance), and results tables 1-3.
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes, p11
		(b) Indicate number of participants with missing data for each variable of interest	Yes, p11 (table 1)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	yes, p 11 (table 1)
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Yes, tables 2-3
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	statistical methods and results
Discussion			
Key results	18	Summarise key results with reference to study objectives	yes, p15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	yes, p17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	yes, p18
Generalisability	21	Discuss the generalisability (external validity) of the study results	yes, p17 (last paragraph)
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	yes, p18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.