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Does the distribution of musculoskeletal pain shape the fate of long-term sick leave? A prospective cohort study with register follow-up

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Abstract

Although multisite pain can markedly reduce work ability, the relevance of the bodily pain distribution as a predictor of long-term sick leave is still unknown. This study aimed to investigate the association between musculoskeletal pain distributions and long-term sick leave in the general working population of Denmark and included 66,177 currently employed wage earners without long-term sick leave during the prior 52 weeks. Participants reported whether they had pain in the lower extremity (hips/knees), upper extremity (neck/shoulders), or the low back. The analysis controlled for age, sex, year of survey reply, educational level, occupational group, psychosocial work factors, body max index, smoking, leisure-time physical activity, and mental health confounders. The results demonstrated that the risk of long-term sick leave increased with the number of pain sites. Compared with no pain, localized pain in any body region increased the risk/hazard by 25% to 29% (HR [95% CI]: 1.29 [1.07-1.54] for pain only in the low back), whereas pain in 2 regions increased the risk by 39% to 44% (HR [95% CI]: 1.41 [1.18-1.69] for pain in the low back + hips/knees). Workers reporting pain in all 3 regions experienced a 72% increased risk (HR [95% CI]: 1.72 [1.55-1.91]). Thus, the number of pain regions seems to matter more than the exact pain location. The spatial extension of musculoskeletal pain in workers functions as a gradient system, where pain spread throughout the body is an independent indicator of the high risk of long-term sick leave.

Keywords: Musculoskeletal pain, Sick leave, Multisite pain, Public health, Pain distribution

1. Introduction

Musculoskeletal pain is a leading cause of disability[12] and reduced work capacity[16,47] and often comes with large negative consequences for working adults. Musculoskeletal pain also produces enormous costs for both workplaces/organizations and society as a whole because of, eg, work absence, productivity loss, increased healthcare utilization,[35] and disability pensions.[11,32] To address this problem, potentially modifiable pain-related predictive factors associated with long-term sick leave have been identified, including comorbidity,[9] as well as pain severity,[4] chronicity,[24] and location/body region.[4] From these, bodily pain distribution is of special interest because its easy assessment can provide relevant information regarding underlying mechanisms of pain,[41] associated disease burden,[30] and risk factors for pain in workers.[15] Localized work-related musculoskeletal pain may come from exposure to physical/ergonomic work factors overloading parts of the musculoskeletal system through, eg, repetitive forward bending of the trunk.[15,40] However, persistent musculoskeletal pain is often not isolated to a single anatomical site but rather expands to multiple body regions, a condition referred to as multisite pain.[13,26,31] Specifically, 16% of a large (working) population display 3 or more painful sites.[41] From a mechanistic perspective, multisite pain could indicate the progression from localized to widespread pain because of, eg, central sensitization[21,22] but also the accumulation of various localized musculoskeletal disorders. Compared with localized pain, multisite pain is more detrimental because of stronger associations with poor mental health,[61] higher use of health care,[37] reduced work ability,[10] and increased sick leave.[24,39] Traditionally, these studies have investigated the impact of multisite pain by counting the number of body sites affected by pain,[15,38] showing that the association between pain and decreased health-related functioning depends on the number of pain sites, irrespective of the location.[46] However, this method might be too simplistic as different pain patterns have shown different prognosis and treatment outcomes.[26] Furthermore, different bodily distributions of pain but with an equal number of body regions affected by pain have shown different impacts on physical function.[3] Still, however, it is unclear whether having pain in certain

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combinations of body regions, eg, the low back and the knee or the low back and the neck/shoulders, is particularly detrimental to the risk of long-term sick leave. Knowing whether assessing clustered bodily pain distributions yields greater insights than simply counting pain regions in their association with long-term sick leave can hold significant relevance for the occupational and research contexts. This knowledge could address the need for effective methods to stratify workers with common musculoskeletal pain locations,[29] potentially leading to improved clinical outcomes[19] and optimal resource use.[29] It could also deepen the understanding of whether multisite pain in workers primarily results from accumulating local musculoskeletal disorders or systemic mechanisms. This large-scale prospective cohort study with register follow-up aimed to investigate the association between 7 distinct combinations of musculoskeletal pain distributions and long-term sick leave in the general working population of Denmark.

2. Materials and methods

2.1. Study design and population

This is a prospective cohort study with register follow-up using data from the "Work Environment and Health in Denmark" (WEHD) survey.[7] Work environment and health in Denmark is a comprehensive questionnaire survey with data collected every 2 years from 2012 until 2018. In this study, data from all 4 waves of the survey were linked to the Danish Register for Evaluation of Marginalisation (DREAM).[5,8] Statistics Denmark drew probability samples of and invited Danish residents aged 18 to 64 years who had been employed for at least 35 hours per month and had a monthly income at or above 3000 Danish crowns (~€400) in the past 3 months. In total, 228,173 received an invitation, of which 127,882 (56%) replied. Afterwards, datasets were merged on a secure server using an anonymous code representing the unique personal identification number (CPR), which is given to all Danish citizens at birth or immigration. In the present study, we only included currently employed wage earners (based on survey reply, n = 110,357 responses) free of long-term sick leave during the year (52 weeks) until baseline,[44] first responses for individuals taking part in several WEHD waves (n = 73,298 unique individuals), and people replying to the questions about musculoskeletal pain distribution (n = 66,177 unique individuals). The definition of long-term sick leave is indicated further down. In the analyses, the exact number of participants varies because not all participants filled in all survey questions. This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines for cohort studies.[60]

2.2. Musculoskeletal pain distribution (predictor)

To assess body region–specific musculoskeletal pain, participants replied "yes" or "no" to the following question: "Within the past 3 months, have you had pain in," with the following response options: (1) hips, (2) knees, (3) arms and/or wrists, (4) neck and/or shoulders, and (5) low back. To limit the number of possible combinations, we merged options 1 and 2, as well as options 3 and 4, leaving 3 body regions: the lower extremity (hips or knees), upper extremity (arms, wrists, and neck/shoulders), and the low back. The decision to merge body regions was made a priori to limit the number of possible combinations and to thereby retain statistical power.

2.3. Long-term sick leave (outcome)

The risk of long-term sick leave was assessed by linking survey responses to the DREAM register using the unique personal identifier (CPR). In Denmark, the employer covers the first 30 days of sick leave from work, after which the municipality can provide reimbursement for additional days. Danish register for evaluation of marginalisation contains information about reimbursement of sick leave payments and is based on the municipalities' actual payments,[5,8] making it highly valid as the employer has a strong economic incentive to receive the reimbursement.[50] As previously, long-term sick leave was defined as having a period of ≥6 consecutive weeks of sick leave registered in DREAM for a period of up to 2 years after replying to the survey.[5,8] The follow-up period was restricted to about 1.5 years in the last WEHD wave in 2018 (~end of 2019) to end before the COVID-19 pandemic to avoid potential data contamination resulting from this.

2.4. Control variables

We controlled our analyses for a set of potential confounders, which have previously been associated with both musculoskeletal pain and sick leave.[5,8,34,52,59] Those confounders retrieved from national registers included age, gender, year of survey reply, educational attainment, and occupation (Danish version of the International Standard Classification of Occupations [DISCO]). We also included the following confounders from the WEHD: smoking, body mass index (BMI), leisure-time physical activity, and depressive symptoms. Based on information from the Central Person Register of Denmark, age was entered as a continuous variable, and gender was entered as a categorical variable (man and woman). Year of survey wave was entered as a categorical variable (2012, 2014, 2016, and 2018). Educational attainment and occupation were also obtained from a national register and included as categorical variables, eg, shorter education (unskilled and skilled work), and longer education (further education). Occupation was based on the Danish version of the International Standard Classification of Occupations (DISCO, first digit). Two psychosocial work factors adapted from the Copenhagen Psychosocial Questionnaire[43] were included and entered as continuous variables, ie, influence at work (2 items) and job strain (scale of 0-100, 100 = best). Smoking status was entered as a categorical variable ("Yes, daily," "Yes, once in a while," "Ex-smoker," "No, never"). Body mass index (kg/m^2), leisure-time physical activity (total weekly hours of leisure physical activity), and depressive symptoms (Major Depression Inventory, scale 0-50) were included as continuous variables. We present both minimally and fully adjusted models as some of these variables may be potential mediators and could lead to overadjustment.

2.5. Statistical analyses

We used the Proc SurveyPhreg (SAS version 9.4., SAS institute), which is a Cox proportional hazard model with weights. The reason for using weights is to make the estimates representative for the general working population without recent long-term sick leave. To ensure that the estimates were representative for wage earners in Denmark, each individual was assigned a weight value (model-assisted weights) based on information from high-quality national registers (gender, age, occupational industry, highest completed education, family income, family type, and origin). The weight variable was introduced in the SurveyPhreg procedure using the weight statement. Body region–specific

musculoskeletal pain was the predictor variable, and long-term sick leave during follow-up was the outcome variable (time to first event). We censored in case of reaching the end of the follow-up period, early retirement, disability pension, statutory retirement, emigration, or death. Model 1 was adjusted for age, gender, and year of survey reply. The fully adjusted model 2 was additionally adjusted for educational level, DISCO group, psychosocial work factors, BMI, smoking, leisure-time physical activity, and mental health (MDI). Results are reported as hazard ratio (HR) with 95% confidence intervals (CIs).

3. Results

3.1. Participants characteristics

Table 1 presents descriptive baseline characteristics of the included sample. The participants (n = 66,177) were, on average, 46 years, and 52% were female. During the maximal 2 years of follow-up, the weighted incidence of long-term sick leave was 9.3% (n = 5775).

Table 1

Descriptive baseline characteristics of the study sample.

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Variable	**n**	**%**	**Mean**	**SD**
WEHD wave	66,177			
2012	17,301	26.1		
2014	15,293	23.1		
2016	17,341	26.2		
2018	16,242	24.5		
Age (y)	66,177		46.0	10.8
Sex	66,177			
Men	31,489	47.6		
Women	34,688	52.4		
Smoking				
Yes, daily	9397	14.3		
Yes, once in a while	3393	5.2		
Ex-smoker	19,038	28.9		
No, never	33,985	51.6		
DISCO group				
Military work	422	0.7		
Work that requires knowledge at the highest	3302	5.2		
Work that requires intermediate level knowledge	22,178	35.0		
General office and customer service work	9001	14.2		
Service and sales work	5892	9.3		
Work in agriculture, forestry, and fishing excl. assistance	8985	14.2		
Craftsmanship	346	0.6		
Operator and assembly work as well as transport work	4964	7.8		
Other manual work	3795	6.0		
BMI (kg/m^2)	65,451		25.7	4.4
Major depression inventory (0-50)	65,886		8.0	7.4
Educational attainment	65,784			
Shorter education	35,618	54.1		
Longer education	30,166	45.9		
Psychosocial work factors (0-100)				
Job strain	66,115		46.2	16.3
Influence at work	66,055		78.9	18.9
Leisure-time physical activity (hours/wk)	65,811		5.2	3.3
Workers without pain at any region	20,556	31.1		
Workers presenting pain in at least one region	45,621	68.9		

BMI, body mass index; DISCO, Danish version of the International Standard Classification of Occupations; WEHD, work environment and health in Denmark.

Table 2 shows the minimally and fully adjusted association between localized and different body region–specific combinations of multisite pain and long-term sick leave. Compared with having pain in no region (20,556 workers, 31.1%; **Table 1**), the higher the number of sites with pain, the higher the risk of long-term sick leave. This was the case in both the minimally and the fully adjusted models. In the fully adjusted model, localized pain in the low back, neck/shoulder, or hip/knees increased the risk of long-term sick leave by 25% to 29% (from HRs of 1.25-1.29; **Table 2**), having pain in 2 body regions increased the risk by 39% to 44% (from HRs of 1.39-1.44; **Table 2**), whereas the risk of long-term sick leave was increased by 72% (from HRs of 1.72; **Table 2**) among workers reporting pain in both the low-back, neck and shoulder, and hip and knee regions. Weighted data showed that 17% of the population experienced pain at the 3 sites, whereas 25% and 26% experienced pain at 2 or one sites, respectively.

Figure 1 shows the survival probability for the 7 different pain distribution groups.

4. Discussion

This prospective cohort study with register follow-up found that multisite pain was associated with an increased risk of long-term sick leave compared with more localized and no pain. Additionally, the risk for long-term sick leave was comparable among workers with the same number of pain regions but with different distribution of pain across regions. These findings reinforce previous findings[15,41,46] and suggest spatial pain extension as a stronger risk factor for long-term sick leave than the specific pain location.

4.1. Pain distribution patterns and risk of long-term sick leave

The fully adjusted model in this study revealed that experiencing pain in only one body region was associated with a similarly increased risk of long-term sick leave (from 25% to 29%) regardless of location, be it in the neck/shoulder(s), low back, or hip(s)/knee(s). This finding indicates that experiencing pain is a detrimental factor for work capacity per se, with the body region of pain being less important. This finding is in accordance with previous research indicating a detrimental effect of pain on physical function independent of the bodily location of pain.[46] In line with this, a previous large-scale study demonstrated that different upper-body pain distributions extending down to the knees had a comparable negative impact on physical function.[3] Our data indicating a similar independence of body location of musculoskeletal pain on long-term sick leave risk was also observed for workers presenting with more expanded, multisite pain, showing from 39% to 44% increased risk for long-term sick leave in workers with pain in 2 body regions irrespective of combinations, as compared with workers without musculoskeletal pain.

Interestingly, workers with the most expanded multisite pain pattern (ie, pain in all investigated body regions) were at the highest risk for long-term sick leave (ie, 72% increased risk compared with workers without pain). For an unknown percentage of these workers with the most expanded multisite pain distribution, their pain pattern might meet the American College of Rheumatology criteria for widespread pain[63] (ie, axial and bilateral pain above and below the waist). Our finding aligns with previous

Table 2

Association between presenting pain in different distributions (low back, neck/shoulders, or hips/knees pain) and the risk of long-term sickness absence compared with workers presenting no musculoskeletal pain.

Body regions	Workers n (%)	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Absolute risk
Pain only in the low back	3712 (5.6)	1.30 (1.09-1.55)	1.29 (1.07-1.54)	6.9
Pain only in the neck/shoulder(s)	10,053 (15.2)	1.36 (1.22-1.52)	1.25 (1.11-1.40)	7.9
Pain only in the hip(s)/knee(s)	2725 (4.1)	1.43 (1.19-1.71)	1.28 (1.05-1.55)	7.0
Pain in the neck/shoulder(s) and the low back	9223 (14.1)	1.67 (1.50-1.86)	1.39 (1.24-1.56)	9.7
Pain in the low back and the hip(s)/knee(s)	2408 (3.6)	1.67 (1.41-1.99)	1.41 (1.18-1.69)	9.6
Pain in the neck/shoulder(s) and hip(s)/knee(s)	5581 (8.4)	1.85 (1.64-2.09)	1.44 (1.26-1.64)	10.5
Pain in all regions	11,819 (17.9)	2.51 (2.29-2.75)	1.72 (1.55-1.91)	13.9

Model 1: Adjusted for age, gender, and year of survey reply.
Model 2: Additionally adjusted for age, sex, year of survey reply, educational level, DISCO group, psychosocial work factors, body max index, smoking, leisure-time physical activity, and mental health (MDI).
The absolute risk of long-term sickness absence in the reference group (workers presenting no musculoskeletal pain) was 5.59.
95% CI, 95% confidence interval; HR, hazard ratio.

findings showing associations between the number of pain areas and risk of sick leave in workers[24] and that workers with the highest pain spread (ie, fibromyalgia) are also those with most accumulated sick leaves and at the highest risk of disability pension.[61] Despite the limitation that multisite and widespread pain are not necessarily the exact same entities, the overall data of the present study could suggest that pain expansion throughout the body is a continuum[42] where widespread pain increases the risk of long-term sick leave the most rather than being just the manifestation of accumulated several local musculoskeletal complaints. Some previous findings lead to a similar hypothesis. For example, although multisite pain is typically relatively stable over time, the spatial distribution of pain does fluctuate.[41] Fluctuation of pain distribution over time reinforces the idea that systemic mechanisms such as central sensitization and psychosocial factors affecting pain, such as depression, might be more important than other work-related factors affecting specific body parts (eg, local mechanical stressors because of occupation type).[41,55] Another example is that while mechanical exposures at work might be sufficient for the onset of local pain and, to some extent, widespread pain, psychosocial factors (eg, low social support) have been shown as the strongest predictors for the onset of widespread pain in workers.[25,55]

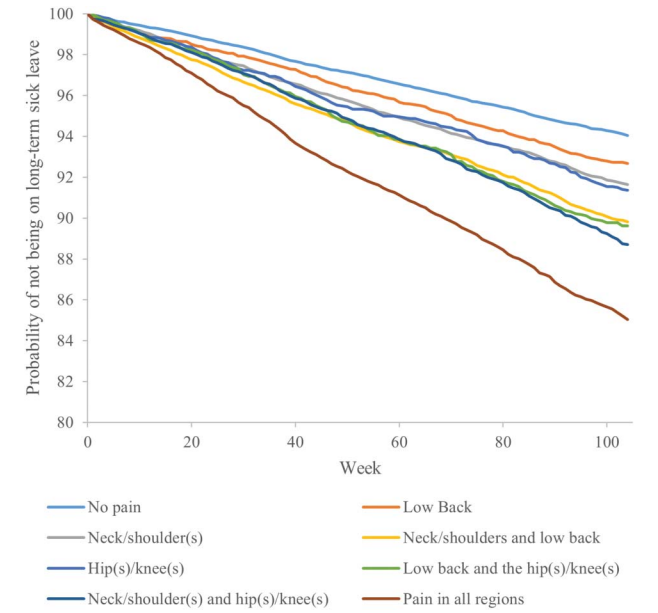

Figure 1. A survival plot representing the probability of groups with various pain distributions of staying working overtime (ie, not to be on long-term sick leave).

4.2. Mechanisms of multisite pain, comorbidities, and sick leave

Several reasons may explain why expanded multisite pain may "push" workers out of the labor market temporarily. For example, there is a consistent association between chronic widespread pain and common comorbidities of depression and cardiovascular disease[18,57] leading to disability. Indeed, the more expanded the pain, the stronger associations with health conditions such as mental health problems, hypertension, obesity, and cardiovascular diseases.[28,45] Furthermore, multimorbidity combined with reduced work ability (eg, because of musculoskeletal pain) increases the risk of long-term sick leave.[53] Therefore, in addition to considering the number of musculoskeletal pain sites when attempting to predict sick leave, it has been recommended that the coexistence of obesity and high levels of depressive symptoms should also be considered.[27] Interestingly, obesity and depression have also shown as the strongest predictors for spatial pain expansion over time.[55] Still, in the current study, even when adjusting for depressive symptoms (MDI), the association remained quite strong. We did not, however, adjust for other comorbidities typical for multisite and widespread pain, ie, cardiovascular disease, to avoid overadjustment. However, although having adjusted for cardiovascular disease could have lowered the significance of the associations, it is highly unlikely that such adjustment could affect the main finding of the study, which is that higher number of regions with pain increases the risk of long-term sick leave.

This co-occurrence of conditions has been partially explained by common underlying systemic mechanisms. For instance, increased basal (low-grade) inflammation has been proposed to explain the co-occurrence of multisite pain and other long-term health conditions.[20] Inflammation has also been proposed as a potential mechanism explaining both widespread pain and premature death because of cardiovascular diseases in a study involving 475,171 participants from the UK biobank.[45] The study revealed 14% and 48% increased hazard among individuals with localized and widespread pain, respectively, when compared with pain-free participants, after adjusting for age, gender, established cardiovascular risk factors, physical activity, anxiety, depression, cancer, chronic inflammatory/painful disease, pain/

anti-inflammatory medication, and socioeconomic status. With regards to pain distribution, there is recent and novel experimental evidence showing a direct mediation effect of inflammation in specific parts of the somatosensory nervous system on widespread pain in patients with fibromyalgia.[14] Furthermore, central sensitization has been pointed out as an important mechanism for the transition from localized to widespread pain,[21,23,58] individuals with pain located in the low back or neck regions compared with any other locations being at a higher risk of developing widespread pain.[33]

Overall, these findings suggest that in preventing long-term sick leave, efforts must be specially made to prevent individuals from developing widespread pain and the associated comorbidities, which are likely linked by common underlying pathophysiological mechanisms rather than just the accumulation of several independent localized musculoskeletal disorders. However, it is still possible that a more reduced pain distribution, affecting multiple sites but less extensively than widespread pain, may be caused by different underlying mechanisms. These could depend on the proximity of the different pain regions. For example, according to the understanding of pain distribution mechanisms, pain in both the neck and the knee likely indicates independent local musculoskeletal disorders. However, pain distributed across the back, neck, shoulder, and upper limb regions can be seen as the expansion of originally localized pain caused by sensitization mechanisms.[17] In this line, an alternative mechanism explaining the relationship between expanded pain distribution and the increased risk of long-term sick leave may be the spatial summation of pain. This summation involves the heightened perception of pain intensity when the source of nociception affects a larger body area[1,51] or there are more body sites affected by nociception.[2] This central mechanism would explain that the increased risk of long-term sick leave in workers with, for example, 2 nearby nonserious musculoskeletal disorders and an expanded area of pain, is primarily because of pain intensity rather than the extent or the number of painful areas. This hypothesis is in line with recent data demonstrating a clear dose–response relationship between spinal pain intensity in workers and the risk of long-term sick leave.[49]

Regardless the mechanism governing musculoskeletal pain distribution in workers, assessing spatial pain distribution is a simple screening tool easy to implement in the organizational context that could facilitate organizations to screen for those workers more vulnerable to labor maker marginalization and therefore adopt timely measures and inform decisions on different management strategies for localized and widespread pain, respectively.[15,25,28,62] In this regard and based on the results of this study, when screening for high risk of long-term sick leave in workers with musculoskeletal pain, the extension of pain should be prioritized over the specific location of pain. Thus, workers with musculoskeletal pain might obtain more benefit from occupational health policies primarily addressing biopsychosocial and general health factors (eg, depression or body mass index[55]) over approaches only focusing on physical/ergonomic work factors. Moreover, systematic reviews indicate that workplace-based physical exercise can effectively prevent and reduce pain[48,54,56] and reduce risk of long-term sickness absence.[6] Therefore, this prompts consideration that these interventions have worked through the systemic effects of exercise, such as reduction in low-grade inflammation,[36] which could potentially benefit individuals with more expanded pain distributions. Finally, the results warrant an investigation comparing the impact of the distribution in pain expansion vs the pain intensity on the incidence of long-term sick leave in workers with musculoskeletal pain.

4.3. Strength and limitations

The main strength of this study is the large cohort of workers assessed and the highly valid register used for the outcomes, which allowed adjusting the analysis for several confounders previously associated with pain and sick leave. However, there is still a chance for residual confounding bias because we did not adjust our models for other comorbidities, eg, cardiovascular disease; this issue represents a small limitation as pain spread has recently demonstrated a relationship with the risk of cardiovascular disease morbidity and mortality.[45] Also, because of self-reported exposure and covariates, there is a certain risk for recall bias, which, in turn, may lead to some degree of misclassification bias. Finally, this study grouped different body regions as if they were one body region (eg, neck and shoulder, hip, and knees) to simplify the analysis model. Furthermore, bilateral pain in the same region was not considered multisite pain because of the questionnaire format with which the data were collected. Beyond being considered a limitation, these facts would indicate that the study results have been obtained after a conservative analysis methodology, and the potential contribution of multisite pain to the risk of long-term sick leave in the real occupational context might be even more significant.

5. Conclusion

The spatial extension of musculoskeletal pain in workers functions as a gradient system, where widespread pain throughout the body is an independent indicator of the high risk of long-term sick leave. Future studies should investigate the mediation effect of common comorbidities and mechanisms of multisite pain on long-term sick leave.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Data availability: Data used in this study cannot be shared publicly because of the data protection regulation. All data are stored on a protected server hosted by Statistics Denmark and can be accessed by researchers registered with Statistics Denmark and meeting the criteria for access to confidential data. The data are available for research upon reasonable request and with permission from the Danish Data Protection Agency.

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