Master's thesis

NTNU
Norwegian University of Science and Technology
Faculty of Medicine and Health Sciences
Department of Public Health and Nursing

Ane-Lee Yung Hafstad

# Occupational Activity, Family History, and the Association with Chronic Neck/Shoulder and/or Spinal Pain

## A Prospective Cohort Study

Master's thesis in Public Health
Supervisor: Anne Lovise Nordstoga
Co-supervisor: Tom Ivar Lund Nilsen
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**Sammendrag**

**Introduksjon:** Kroniske muskel- og skjelettsmerter er et betydelig folkehelseproblem som påvirker individers helse og kan resultere i redusert arbeidsevne. Målet med denne studien var å undersøke sammenhengen mellom yrkesaktivitetsnivå, familiehistorie og risikoen for å utvikle kroniske muskel- og skjelettsmerter i nakke/skulder og/eller ryggrad. Å forstå hvordan familiehistorie og yrkesaktivitetsnivå samhandler med hverandre kan bidra til å identifisere individer med høyere risiko for kroniske muskel- og skjelettsmerter og kan bidra til å forbedre forebyggende tiltak

**Metode:** Studiepopulasjonen besto av 9.840 personer som deltok i tredje (2006-08) og fjerde (2017-19) bølge av HUNT-studien. Familiehistorie ble koblet gjennom familie-registeret og foreldrenes deltakelse i tidligere HUNT-bølger. Poisson-regresjonsanalyser ble brukt for å undersøke sammenhengen mellom yrkesaktivitetsnivå, familiehistorie og risikoen for å utvikle kronisk muskel-skjelett smerte. Resultatene ble presentert som relativ risiko (RR) med 95% konfidensintervaller (KI).

**Resultater:** Resultatene viste at personer med høyt yrkesaktivitetsnivå hadde høyere risiko for å utvikle kronisk muskel-skjelett smerte i skulder- og/eller rygg (RR = 1,25, 95% KI = 1,14-1,37) sammenlignet med personer med lavt aktivitetsnivå. Studien avdekket en sammenheng mellom familiehistorie og smerte. Mors smerte viste en relativ risiko (RR) på 1,23 (95% KI = 1,11-1,36), fars smerte hadde en RR på 1,25 (95% KI = 1,10-1,40), og når begge foreldrene hadde en historie med smerte, var RR 1,27 (95% KI = 1,14-1,43). Imidlertid ble det ikke funnet noen additiv interaksjon mellom yrkesaktivitetsnivå og familiehistorie i forhold til utvikling av smerte (RR = 1,78).

**Konklusjon:** Studien fant en sammenheng mellom yrkesaktivitetsnivå og risiko for utvikling av kroniske nakke/skulder eller/og ryggsmerter og at personer med familiehistorie med smerter har ytterligere høyere risiko. Mor mer kunnskap om denne sammenhengen vil det være nyttig å undersøke hvordan yrkesaktivitet påvirker spesifikke smerterelaterte epigenomer og å gjenta denne studien med bruk av genetiske data.

**Abstract**

**Introduction**: Chronic musculoskeletal pain is a significant public health concern that affects individuals' health and can result in reduced work capacity. The aim of this study was to investigate the association between occupational activity level, family history, and the risk of developing chronic musculoskeletal pain in the neck/shoulder and/or spinal area. Understanding how family history and occupational activity level interact with each other can help identify individuals at higher risk for chronic musculoskeletal pain and can help in creating preventative measures.

**Method**: The study population comprised of 9.840 individuals who participated in the third (2006–08) and fourth (2017–19) waves of the HUNT Study. Family history was linked through the family registry, and the parents' participation in previous HUNT waves. Poisson regression analyses was used to investigate the association between occupational activity level, family history, and the risk of developing chronic musculoskeletal pain. The results were presented as relative risk (RR) with 95% confidence intervals (CI).

**Results**: The results showed that individuals with high occupational activity levels had a higher risk of developing chronic musculoskeletal pain in the shoulder and/or back (RR = 1.25, 95% CI = 1.14-1.37) compared to individuals with low activity levels. The study revealed a correlation between family history and pain. Maternal pain showed a relative risk (RR) of 1.23 (95% CI = 1.11-1.36), paternal pain 1.25 (95% CI = 1.10-1.40), and when both parents had a history of pain, the RR was 1.27 (95% CI = 1.14-1.43). However, no additive interaction was found between occupational activity levels and family history regarding the development of pain (RR = 1.78).

**Conclusion**: The study found an association between physically demanding work and the risk of chronic neck/shoulder and spinal pain development and between family history of pain and risk of neck/shoulder and spinal pain. Further studies are recommended to investigate how occupational activity affects specific pain-related epigenomes and to repeat this study on a larger cohort with genetic data.

**Preface**

This master thesis represents the culmination of my Master of Public Health at NTNU. It is with great pleasure and a sense of accomplishment that I present this work. I would like to express my sincere gratitude to my supervisor, Anne Lovise Nordstoga for her invaluable guidance, encouragement, and support throughout this endeavour. Her expertise and feedback have been incredibly important in shaping the direction and quality of this thesis. I would also like to thank Tom Ivar Lund Nilsen as the co-supervisor, who helped me interpret and focus in on interesting points in my findings.

I would also like to thank the close friends that have helped me during the writing process, 'bonus supervisor' Gerard Clarke for his valuable insights and constructive suggestions, fellow students Benjamin Thomason for company during the last semester of writing, Jordan Mbote for teaching me about epigenetics and genetics and Bjørn Christian Lundberg for some final proofreading.

I extend my appreciation to my friends at NTNUI Dans and boyfriend Bjarke Lak Pettersen for their support and company that have helped me relax and take a break from the work and give me a good work/free time balance. I am deeply grateful to my family for their unwavering love and encouragement.

15th May 2023

Ane-Lee Yung Hafstad

# Contents

# Introduction

Understanding the factors that contribute to chronic musculoskeletal pain is crucial for developing effective preventative measures and treatments. Many potential risk factors for chronic musculoskeletal pain have been identified, two of these factors are occupational activity level and family history(Farioli et al., 2014; Lier et al., 2016; Veiersted et al., 2017; Zadro et al., 2018). Despite the importance of occupational activity level and family history of chronic musculoskeletal pain, previous studies have produced inconsistent findings such as disagreements on how important inherited pain-behaviour is to developing chronic musculoskeletal pain(Edwards et al., 2016; Jones, 2004), and there is a need for further research to understand the relationship between these factors and risk of chronic pain. Additionally, previous research in the field has mostly focused on either widespread general chronic pain, or lower back pain(Diatchenko et al., 2013; Matsudaira et al., 2014; Omair et al., 2019).

Although there has been an increase of office work in the last few decades and the pandemic has made home offices more common, research in this field is still relevant because we still are in need of active occupations such as cleaning staff, janitors, nurses and other physical occupations. In Norway, there is still a high number of people who apply for nursing degrees(Direktoratet for høyere utdanning og kompetanse, 2023), and in rural areas as much as 49% of high school students chose to pursue vocational school(Lervåg, 2023).

Investigating the associations between occupational activity level, family history, and chronic musculoskeletal pain in the neck/shoulder and/or spinal area is important for several reasons. Firstly, work is a major part of an individual’s adult life therefore being able to identify and adapt to potential risk factors that can reduce risk of pain. Secondly, studying the relationship between family history of pain and chronic musculoskeletal pain can provide insights into the mechanisms of pain development, which can inform the development of more targeted pain management. Lastly, understanding how family history and occupational activity level interact with each other can help identify individuals at higher risk for chronic musculoskeletal pain and can help in creating preventative measures.

This thesis aims to investigate the association between occupational activity level, family history, and chronic musculoskeletal pain in a large population-based sample.

# Background

Chronic musculoskeletal pain is one of the leading causes for disability in the world(Vos et al., 2020) with back pain having the highest proportion of years lost to disability, and other musculoskeletal pains is within the top 10 leading causes for disability(Bevan, 2015). Chronic musculoskeletal pain greatly affects the quality of life e.g., by increasing the risk of sleep disturbance(Skarpsno et al., 2018), fatigue(Løke et al., 2022), and mental health(Hooten, 2016) and in turn lead to a reduction in leisure-time activities and social contacts that the person usually participates in(Tüzün, 2007).

Chronic musculoskeletal pain poses a significant societal, medical and socioeconomical problem due to loss of productivity and the cost of medical care(Cimmino et al., 2011). In Europe the cost of absenteeism due to musculoskeletal disorders were estimated up to 2% of the gross domestic product(Bevan, 2015). In Norway, chronic musculoskeletal pain represents a significant and costly health problem of the working population, whereas 3 out of 10 adults report musculoskeletal pain(Nielsen et al., 2018). Approximately half of reported disability cases in Norway is attributed to chronic pain and is thus the largest cause for work-related disability(Nielsen et al., 2018). Every year in the period 2017-2021 over 2.5 million sick leaves certified by a doctor was attributed to musculoskeletal problems(NAV & SSB, 2022). In Norway, the cost of musculoskeletal disorders due to health services usage including primary healthcare service, special health service and pharmaceutical resources was 14 253 million kroner(Lærum et al., 2013). The cost of sick-leave-, and other musculoskeletal-related disability pay-outs from NAV(Arbeids- og velferdsetaten) were 116.5 billion in 2009(Lærum et al., 2013). Adjusting these numbers for inflation (average 2,4% a year), musculoskeletal disorders would directly cost the state 178 598 million kroner every year if the rate of musculoskeletal disorders and the treatment had gone unchanged since 2009.

## Occupational activity level and musculoskeletal pain

National and global recommendations on physical activity are well-known and are a central part of public health policies(Bull et al., 2020). Insufficient physical activity levels is one of the leading risk factors for non-communicable diseases(i.e., cardiovascular health and musculoskeletal disorders), and has a negative effect on mental health(Bertheussen et al., 2011) and quality of life(Guthold et al., 2018). Although leisure time physical activity is positively associated with less musculoskeletal pain and cardiovascular health benefits(Nordstoga et al., 2019), physical activity at work was linked with a negative outcome for cardiovascular health in Danish blue-collared workers(Holtermann et al., 2021). Some precautions have been put in place already, that can be seen in The Norwegian Working Environment Act § 4-4-2 states:

> “The workplace shall be equipped and arranged in such a way as to avoid adverse physical strain on the employees. Necessary aids shall be made available to the employees. Arrangements shall be made for variation in the work and to avoid heavy lifting and monotonous repetitive work. When machines and other work equipment are being installed and used, care shall be taken to ensure that employees are not subjected to undesirable strain as a result of vibration, uncomfortable working positions and the like.”(Arbeidsmiljøloven, 2005).

However, the laws currently written about the physical work requirements might be too vague to be enforced at the average workplace with specific interventions, there has yet to be an illustrative judgement on how the Norwegian state will deal with preventing physical strain and chronic musculoskeletal pain in active occupations(Benson, 2019).

The paradox of contradictory effects of physical activity at work vs. leisure physical activity on cardiovascular health has been investigated in several studies(Holtermann et al., 2021; Pieter et al., 2018). Workers with high level of physical activity at work had a higher risk of major adverse cardiovascular event and all-cause mortality, compared to the workers with low level of physical activity at work(Holtermann et al., 2021). There is a possibility that the differences in health outcomes between physical activity at work and physical activity in leisure time is due to different key characteristics of the physical activity(Holtermann et al., 2021), for instance different mechanics(i.e. no warm-up at work, not using full range of motion, few breaks, no restitution time) in leisure time exercise and occupational activity(Holtermann et al., 2021). These mechanical differences may result in tearing down the muscles and not allowing them to recover and rebuild properly, which in turn would cause the muscles to become less capable of withstanding additional workloads.

A working environment with moderate to high physical activity can increase the risk of developing chronic pain due to improper lifting, repetitive movements, and other ergonomic hazards that the workers can be more frequently exposed to. In an evaluation done by Oslo Economics(Oslo Economics, 2018) the work environment influence the employee’s health, work-participation, sick-leave and productivity. A non-optimal working environment is defined as:

> “Conditions with the working environment that prevent the workers to produce what they could otherwise have made or which exposes the workers or the businesses for something undesirable (e.g. damages and disease).”(Oslo Economics, 2018).

Non-optimal work environment costs has been estimated to cost 75 billion Norwegian kroner every year(Oslo Economics, 2018).

Physical occupational strain has been identified as a significant risk factor in the development of chronic musculoskeletal pain(Farioli et al., 2014), and several studies have found strong correlation between occupations with physically straining tasks and musculoskeletal pain(Veiersted et al., 2017). The most common occupational risk factors for musculoskeletal pain were excessive repetition, awkward postures and heavy lifting during work(Andersen et al., 2016; Veiersted et al., 2017) and the association between occupational strain and increased risk of musculoskeletal pain is different in occupations, e.g. those with high strain such as nurses have higher risk(Langballe et al., 2009). Workers that was exposed to repetitive movements for more than 25% of their workday had between 25% to 94% increased risk of developing long-term sickness absence depending on whether or not the worker had one or four or more physical workloads compared to no physical workloads (Andersen et al., 2016). Bending, twisting and turning the back during work time has been shown to be a strong risk factor for long-term sickness absence(Andersen et al., 2016). The occupations that was deemed to have a possible increased risk of musculoskeletal pain was occupations that had manual handling, pushing and pulling, non-neutral working positions, arms raised for a prolonged time, static muscle activity, standing position, physically heavy labour, repetitive motions and hand-arm vibrations(Veiersted et al., 2017). This risk of musculoskeletal pain has shown to be slightly higher among blue-collar workers compared to the general population in Denmark, possible due to the increased exposure to repetitive lifting above shoulder height and heavy lifting in this occupation group(Andersen et al., 2016).

### Armstrong dose-response model

There are several theories that aim to incorporate a multifactorial explanation of the process of developing musculoskeletal pain, for instance by including social and work-related factors and the process of developing musculoskeletal pain. For example, the biopsychosocial model proposed by Engel in 1977, is a model with a holistic view on health and illness through the combination of biological, psychological, and sociological factors(Schultz et al., 2007). In 2001 WHO developed: *International Classification of Functioning(ICF),* where an individual's capacity for their workload is described from the individual's state of health and contextual factors such as individual psychological and social/environmental factors(Costa-Black et al., 2013). Furthermore, in 1993 the dose-response theory on the development of musculoskeletal disorders were proposed by Armstrong(Armstrong et al., 1993). The dose-response theory has been used in many studies within the field of ergonomic and work-related health(Karsh, 2006).

The model tries to explain that while the amount of force is an important factor, a negative response can happen with a high amount of low-doses(Armstrong et al., 1993). The theory was developed to look at the multifactorial nature of developing musculoskeletal disorders(Armstrong et al., 1993). Armstrong looks at the interactions between factors in exposure, dose, capacity, and response; which could be in illustrated in the current study as the dose being a mechanical workload(i.e., heavy lifting, strenuous position). The dose-response theory propose that for each dose of external factors(i.e., heavy lifting at work)a body receives a new response(i.e., tearing muscle from lifting) will be generated due to the previous response(i.e., previous tearing not having finished healing) having changed the body's capacity(Armstrong et al., 1993) the subsequent response is whether or not the body develops chronic neck/shoulder and/or spinal pain, and the capacity is based on whether or not the individual has an increased risk due to family history of musculoskeletal pain. The example given by Armstrong is a mailman lifting a heavy parcel during work would be exposed to a dose, then their back muscles respond by breaking down the muscle tissue to eventually rebuild them. However, there is an additional dose soon after the first one, and instead of the rebuilt tissue resisting the heavy lifting(dose), it is the broken-down muscle tissue with a lower capacity that must respond to the dose, leading to a decreased capacity for each response.

## Family history of musculoskeletal pain

Several studies have investigated the risk of developing musculoskeletal pain and association with family history of pain. There has been found that family history of pain can be a risk factor for developing chronic musculoskeletal pain(Dario et al., 2019). There is evidence that certain chronic pain conditions, such as fibromyalgia(Omair et al., 2019), osteoarthritis(Spector & MacGregor, 2004), and rheumatoid arthritis(Frisell et al., 2016), have a familial component. Additionally, certain familial factors, such as genetics or shared home environment, may increase a person's susceptibility to developing chronic pain in response to environmental factors, such as physical stress or capability to adapt to injury(Collins et al., 2015).

The risk of developing chronic widespread pain increases when there is family history of chronic pain(Lier et al., 2014) compared to no family history of pain. The risk is amplified when both parents have a history of chronic musculoskeletal pain(Lier et al., 2016; Lier et al., 2014). A study in Japan found that there was a positive association between aggravated low backpain and family history of disabling low backpain(Matsudaira et al., 2014). The link between family history of pain and pain in adolescent and adult offspring may be due to several factors(Hoftun et al., 2013), such as genetics, shared environment, and shared behaviors(e.g., genetic vulnerability and lifestyle factors like leisure-time physical activity or diet)(Hoftun et al., 2013). In a Swedish study on sociodemographic factors and the risk of development of chronic musculoskeletal pain(Bergman et al., 2001), they found that people with a family history of pain(parents or siblings) had an almost three-fold higher odds ratio(OR) compared to people with no family history, on the risk of developing chronic widespread pain(Bergman et al., 2001).When the parents were separated, the chronic pain that the adolescents and young adult offspring reported was widely associated with the parent they lived with(Hoftun et al., 2013).

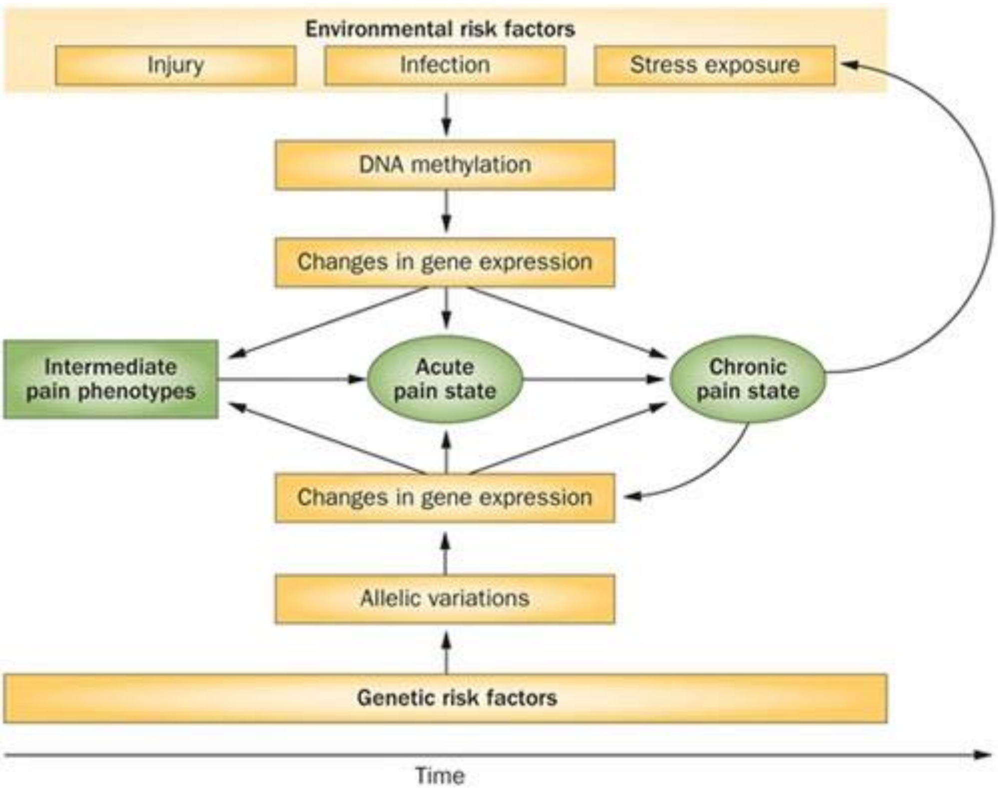
Most research on the association between family history of pain and risk of developing musculoskeletal pain focuses on general widespread pain and/or specific disorders (i.e., fibromyalgia or lower back pain). There is a lack of studies investigating other musculoskeletal conditions, such as neck/shoulder and back pain. Some limitations with these studies are that they are relatively small(Bergman had 3928 participants), and may be more difficult to generalize to a Norwegian context, due to specific cultural and ethnical factors(Matsudaira et al., 2014). Furthermore, some studies are using a cross-sectional design, making it impossible to observe whether or not the risk factors came before the development of pain.

## Occupational activity level, family history, and musculoskeletal pain

Previous research done on how family history affects an individual's sensitivity to pain suggests that lifestyle factors such as level of physical activity having a direct effect on inheritable epigenomes(Denham et al., 2014; Polli et al., 2019).

Common musculoskeletal pain disorders and the risk of developing it has been implicated in six identified genes or genetic regions(Diatchenko et al., 2013). There has been estimated that the inheritability of neck pain, fibromyalgia and pain at any site to be approximately 50%(Diatchenko et al., 2013). Epigenetics looks at how the environment changes our gene expression, which can have both a major or minor impact on our health(Denham et al., 2014).

A heuristic model was developed to look into the interaction between environmental risk factors and genetic risk factors (see fig. 1). The model shows how changes in the gene expression can come from both environmental risk factors and genetic risk factors(Diatchenko et al., 2013). In figure 1, the term "chronic pain state" refers to a stressor which poses an environmental risk and is both influenced by and influences changes in gene expression(Diatchenko et al., 2013).




From (Diatchenko et al., 2013), with permission from Nature Reviews Rheumatology. Figure 1: The phenotype of the pain receptors is impacted by both genetic factors and environmental factors. These factors lead to a differential gene expression of pain for the individual. Long lasting exposure to environmental risk factors can cause a physical change in the histones important for genetic regulation, depending upon the genetic susceptibility of the individual. This change can result in a chronic pain expression which can be experienced as greater sensitivity to pain, greater proneness to stress and can lead to genetic alterations, resulting in a feedback loop.

Physical exercise may be another environmental variable affecting the epigenetic changes and gene expression of not only the individual doing the physical exercise, but also their genes generations after(Denham et al., 2014). Epigenetics also has an effect on pain and physical exercise, and the effect is stronger the older the individual is and the intensity of the exercise(Polli et al., 2019). So far, research have shown that epigenomes' have a mediating and predicting role in different chronic pain conditions, such as chronic lower back pain and fibromyalgia(Polli et al., 2019).

As far as we are aware, there has not been done any research in Norway on the association between occupational activity level, family history of pain and interaction between these factors on the risk of developing neck/shoulder and spinal pain.

Although the current evidence indicates a relation between work-related physical strain and chronic musculoskeletal pain, it is not clear whether the strain at work have a long-term influence on neck/shoulder and/or spinal pain in a general population. Furthermore, it is possible that the family history of chronic pain may influence the association between work-related strain and risk of chronic spinal and shoulder pain. Investigating the risk of developing chronic spinal and shoulder pain in different occupational groups may be helpful to identify whether people in specific occupational groups is more vulnerable to developing chronic musculoskeletal pain and it can be used to develop preventative measures for these groups.

## Aim

The aim of this project is to investigate:

i. The association between moderate to high occupational activity level and the risk of neck/shoulder and spinal pain development.
ii. Is there an association between family history of pain and risk of neck/shoulder and spinal pain?
iii. Is there a joint effect of occupational activity and family history of pain on the risk of developing neck/shoulder and spinal pain?

## Method

This study is a prospective population-based observation study utilizing data from The Trøndelag Health Study (HUNT) linked with data from the Family registry at Statistics Norway.

### Participants

The Trøndelag Health Study (HUNT) is a large population-based health study that has been conducted in four waves: HUNT1 (1984-86), HUNT2 (1995-97), HUNT3 (2006-08) and HUNT4 (2017-19). (42). The entire adult population in former Nord-Trøndelag was from the age of 20 invited to participate in the HUNT Study. The HUNT Study includes data based on clinical examinations, self-reported health questionnaires, and biological samples. The participation rate was initially high in HUNT1(88%) to 70% in HUNT2 and subsequently 54% in HUNT3 and HUNT4. However, the people participating in the HUNT Study is considered fairly representative of the Norwegian population with the exception of large cities and immigrant population(Åsvold et al., 2022).

The study population in the current study consists of individuals that participated in both HUNT3 and HUNT4.

The inclusion criteria for this project are that the individual participated in both HUNT3 and HUNT4. They must have answered the question relating to physical activity at their workplace in HUNT3 and the question relating to musculoskeletal pain that has lasted longer than 3 months. Participants will be excluded if they have not answered either of those questions. Furthermore, participants will be excluded from the study if they answer “Yes” to having had bodily pains for more than 3 months on HUNT3, as we were interested in the risk of developing chronic pain in a chronic pain free population. Participants with lower body pains were also excluded, despite that they can develop upper body pain.

### Family Registry

Personal identification number was used to link each participant's record to information from the Family Registry at Statistics Central Bureau, and therefore establish a family link between parents and their offspring in the HUNT Study.

Participants that had missing family data or had parents that did not participate in any HUNT Study, were also excluded from the current study.

Variables

**Outcome variable:** Chronic neck/shoulder and/or spinal was assessed by the question: "During the last year, have you had pain and/or stiffness in your muscles and limbs that has lasted for at least 3 consecutive months?" with response options "Yes" and "No".

The pain afflicted areas were in HUNT3 and HUNT4 identified by a figure of the human body that the participants had to identify where they experienced the pain. The figure illustrates 13 areas that the participants could identify as painful. The 13 areas were: "Neck", "jaw", "chest", "shoulders", "upper back", "elbows", "lower back", "hips", "thigh", "wrist/fingers", "knees", "calves", and "ankles/feet". The participants were defined as having chronic spinal or shoulder pain if they reported pain in either the "neck", "shoulders", "upper back" and/or "lower back" areas.

**Exposure variables:** Physical activity at work was assessed with the question "If you have had paid or unpaid employment, how would you describe your job?" with response options "Work that mostly involves sitting (e.g. desktop work, assembly)", "work that requires much walking (e.g. clerk light industry work, teacher)", "work that requires much walking and lifting (e.g. postman, caregiver, building work) " and "heavy physical labour (e.g. forester, farmer, heavy construction work)"

The history of pain in parents was investigated in a dataset containing individuals who participated or were invited to participate in both HUNT3 and HUNT4. To begin, 'Maternal_pain' and 'Paternal_pain' were created using information from the first HUNT survey the mother and father answered. The influence of familiar history of general musculoskeletal pain was assessed by using information about the parents' history of pain. Mother/father pain was identified by using data from HUNT2, HUNT3 or HUNT4, where parental pain will be assessed by the question "During the last year, have you had pain and/or stiffness in your muscles and limbs that has lasted for at least 3 consecutive months?" with response options "Yes" and "No". These variables were used to create the variable 'parental_pain', which categorized participants based on whether both parents experienced pain(both), only the mother(maternal pain) or father(paternal pain) experienced pain, neither parent experienced pain(no pain), or there was no pain information available for either parent(none).. In this study the 'none' category and 'no pain' was merged into one category of 'no family history of pain'.

**Possible confounding variables**

Possible confounding variables has been identified and will be included in the analysis. The following variables have previously been associated with chronic musculoskeletal pain and work-related physical strain(Nielsen et al., 2018). The confounding variables that was taken into consideration in the current study was measured at HUNT3:

**Education level:** Education level was measured by the highest level of completed education that was recorded in Statistics Norway at the time of the HUNT3 survey(2006-08). Information on education was extracted only for those who took part in the surveys.

The education levels were categorized based on the Norwegian education system, with the following classifications: “0 No education and pre-school education”, “1 Primary school education”, “2 Junior high school education”, “3 Secondary education, basic education”, “4 Secondary, final education”, “5 Extension to upper secondary education”, “6 University and college education, lower level”, “7 University and college education, higher level”, “8 Research training”, and “9 Unspecified”

These education levels were collapsed into three categories in the analysis to investigate their association with other study variables. “Primary education” included education levels 0 to 4 “vocational” was made up of level 5 extension to upper secondary education, and “higher education” included education levels 6 to 8. Education level “9 unspecified” was excluded. It should be noted that education data for non-participants in the surveys were not included in this analysis.

**Leisure physical activity** was assessed by the questions: “How often do you exercise? (On average) By exercise we mean that you e.g. goes hiking, skiing, cycling, swimming or doing exercise / sports.” With the answer options: “never”, “less than once a week”, “once a week”, “2-3 times a week” and “approximately every day”. And the question "If you exercise like this, as often as once or several times a week; how hard do you exercise?" with the answers "Takes it easy without being out of breath or sweating", "Takes it so hard that I get out of breath and sweat" and "Takes me out almost completely" and the question "How long do you last each time?" with the answer options "Less than 15 minutes", "15-29 minutes", "30 minutes - 1 hour" and "More than 1 hour". Based on this information, the participants will be categorised into two levels of leisure time physical activity which is based on the guidelines for physical activity among adults by The Norwegian Institute of Public Health(Helsedirektoratet, 2019): Engage in physical activity for 150 to 300 minutes with moderate intensity or 75 to 150 minutes with high intensity or a combination of moderate and high intensity per week. The categories are: “Meeting the physical activity guidelines” and “Not meeting physical activity guidelines”.

**Insomnia** was assessed by the questions: “How often has it happened during the last 3 months that you”: "Has difficulty falling asleep at night", "Wakes up repeatedly at night", "Wakes up too early and cannot sleep again", "Works poorly during the day (socially or professionally) due to sleep problems", and "Approximately how many hours of night sleep do you get on a normal weekday?"

**Stress and/or anxiety** was assessed by the question: “In the last 2 weeks, have you felt:” with the answer options: "Safe and calm", "Happy and optimistic", "Nervous and restless", "Afflicted with anxiety", "Irritable", "Down/depressed", "Lonely", and "Generally tense". Participants who crossed off on any of "Nervous and restless", "Afflicted with anxiety", "Irritable", "Down/depressed", and/or "Generally tense" will be categorised separately from participants who did not cross off any of the listed options.

**Body mass index (BMI)** was calculated with weight/height based on clinical measurements performed during the data collection in HUNT3. The participants were grouped together into four groups: less than 18.5, (underweight), 18.5 to <25 (normal weight), 25.0 to <30 (overweight), 30.0 or higher(obese)

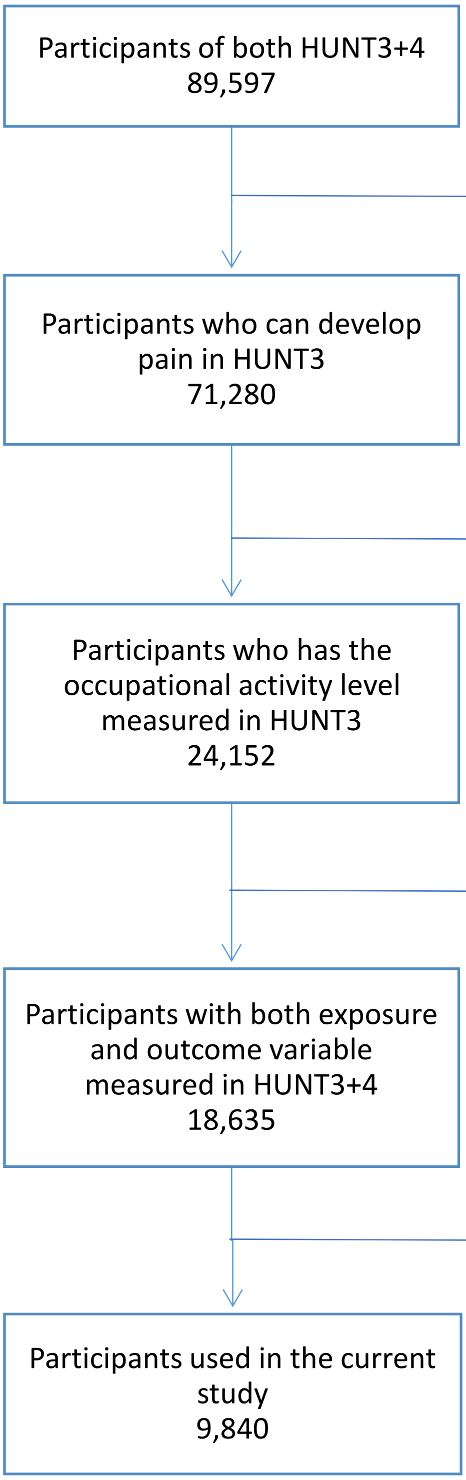



Figure 3, Flowchart showing the selection process, reasons for dropping observations, and final number of study population used in the analysis.

## Statistical analysis

The characteristics in the study population was presented in descriptive statistics with total mean and standard deviation.

The risk ratio (RR) for chronic spinal and/or shoulder pain and association with work-related physical strain was analysed using a generalised linear model of the Poisson family to estimate the difference between the two groups in relative risk of the outcome variable 'Chronic pain' or 'no chronic pain' at HUNT4.

The precision of the RRs was assessed by 95% CIs using robust variance estimation. Active workers were compared with the reference group of sedentary workers. All associations were adjusted for potential confounding by age (39 and younger, 40–49 and 50–59 years, 60-69 years and 70 and older), BMI (Underweight, normal weight, overweight, obese), leisure time physical activity (high activity, moderate activity and low activity), education (primary school, vocational school, university), insomnia (4 or more insomnia symptoms, less than 4 insomnia symptoms) and stress/anxiety (HADS no anxiety or depression, HADS anxiety and/or depression).

In the analyses of the joint effect of work-related physical activity and family history of musculoskeletal pain on the risk of musculoskeletal disorders in the neck/shoulder and spinal region, the sedentary workers without a family history of musculoskeletal pain served as the reference group.

Additionally, potential effect modification between occupational activity level and family history of pain was assessed by calculating the "Relative excess risk due to interaction" RERI, was performed to determine whether any interaction was additive or not. If the RERI is >0 (95% CI), this suggests the combination of familial history of chronic widespread pain and offspring occupational activity level are greater than what would be expected from an additive effect on the development of chronic neck/shoulder and spinal pain.

All statistical analyses were performed using Stata for Windows, V.17. (StataCorp LP, College Station, TX, USA).

## Results

The study population was made up of 9,840 participants, whereas 6,559(66.6%) were classified as having high enough occupational activity level to be in "Active work", while 3,281(33.3%) were classified as having sedentary work. There was fairly equal amount of males(44.9%) and females(55.0%) with an even distribution between male(50.2%) and female(49.7%) sedentary work, while there was a little difference between male(42.2%) and female(57.7%) in active work. Among the participants who had not yet developed pain by HUNT3(2006-2008), 20.2% (1 990) developed chronic pain in the neck/shoulder and spinal region(see tab.1) by the follow-up in HUNT4(2017-2019).

***Table 1** - Baseline characteristics of the study population stratified by occupational physical activity level*

| | Total | Active work | Sedentary work |
|---|---|---|---|
| **NO OF PARTICIPANTS** | N = 9 840 | N = 6 559 | N = 3 281 |
| **MATERNAL PAIN, NO (%)** | 3 050 (31.0%) | 2 013 (30.6%) | 1 037 (31.6%) |
| **PATERNAL PAIN, NO (%)** | 1 721 (17.4%) | 1 151 (17.5%) | 570 (17.3%) |
| **BOTH, NO (%)** | 1 996 (20.2%) | 1 356 (20.6%) | 640 (19.5%) |
| **NO PARENTAL PAIN, NO (%)** | 3 073 (31.2%) | 2 039 (31.0%) | 1 034 (31.5%) |
| **MALE, NO (%)** | 4 423 (44.9%) | 2 773 (42.2%) | 1 650 (50.2%) |
| **FEMALE, NO (%)** | 5 417 (55.0%) | 3 786 (57.7%) | 1 631 (49.7%) |
| **AGE (MEAN ± SD, YEARS)** | 51.9 (10.2) | 51.2 (10.4) | 53.2 (9.7) |
| **BMI (MEAN ± SD)** | 26.3 (4.2) | 26.2 (4.2) | 26.5 (4.2) |
| **OBESE, NO (%)** | 1 718 (17.4%) | 1 129 (17.2%) | 589 (17.9%) |
| **INSOMNIA, NO (%)** | 1 518 (15.6%) | 996 (15.4%) | 522 (16.1%) |
| **HADS THRESHOLD MET[1], NO (%)** | 1 307 (13.2%) | 901 (13.7%) | 406 (12.3%) |
| **HADS TRESHOLD NOT MET[1], NO (%)** | 8 533 (86.7%) | 5 658 (86.2%) | 2 875 (87.6%) |
| **LEISURE TIME ACTIVITY[2]** | | | |
| **INACTIVE, NO (%)** | 2 080 (22.3%) | 1474 (22.4%) | 606 (18.4%) |
| **UNDER RECOMMENDED, NO (%)** | 538 (5.8%) | 373 (5.6%) | 165 (5.0%) |
| **OVER RECOMMENDED, NO (%)** | 6 708 (71.9%) | 4346 (66.2%) | 2362 (71.9%) |
| **PRIMARY EDUCATION† , NO (%)** | 2 248 (22.8%) | 1 751 (26.7%) | 497 (15.1%) |
| **VOCATIONAL EDUCATION†, NO (%)** | 4 021 (40.8%) | 2 864 (43.6%) | 1 157 (35.2%) |
| **HIGHER EDUCATION†, NO (%)** | 3 570 (36.2%) | 1 943 (29.6%) | 1 627 (49.5%) |

Abbreviations: NO; Number, SD; standard deviation, HADS; Hospital Anxiety and Depression Scale
[1]HADS threshold is set at 8 points or more
[2]Categories based on recommendation from the Norwegian Institute of Public Health: Engage in physical activity for 150 to 300 minutes with moderate intensity or 75 to 150 minutes with high intensity per week.
†Primary= High school and lower, vocational=apprenticeship/journeyman letter and higher education=university/college degree

Table 2 shows that the participants that had an active job had a 1.25 times increased risk of developing chronic pain in the neck/shoulder and spinal area after 10-11 years, compared to the sedentary workers.

*Table 2 – Occupational activity level and the risk of developing chronic neck/shoulder and spinal pain at 11-year follow-up.*

| | Total | Cases | Crude RR (95% CI) | Adjusted RR (95% CI)[i] |
|---|---|---|---|---|
| **SEDENTARY†** | 3 281 | 572 | 1.00 (Reference) | 1.00 (Reference) |
| **ACTIVE‡** | 6 559 | 1 418 | 1.24 (1.13-1.35) | 1.25 (1.14-1.37) |

Abbreviations: RR; Relative Risk, CI; Confidence Interval

[i]Adjusted for age, sex, education, BMI, leisure physical activity, insomnia and stress/anxiety

†Participants who answered: "Mostly sedentary work (e.g. desktop work, assembly)" in HUNT3 when describing their work.

‡Participants who answered "work that requires you to walk a lot (e.g. cluster work, light industrial work, Teaching)", "work where you walk and lift a lot (e.g. postman, caregiver, building work) " and "heavy body work (e.g. forestry, heavy agricultural work, heavy construction work)" in HUNT3 when describing their work.

Table 3 shows a positive association between family history chronic widespread pain and the risk of the offspring developing neck/shoulder and/or spinal pain. Adjusted analysis showed that people with maternal pain had a RR of 1.23(95% CI 1.11-1.36), paternal pain to increase the risk with 1.25(95% CI 1.10-1.40), and parental pain to increase the risk with 1.27(95% CI 1.14-1.43), compared to people with no family history of pain.

***Table 3** – Family history of pain and the risk of developing chronic neck/shoulder and spinal pain at 11-year follow-up.*

| | Total | Cases | Crude RR (95% CI) | Adjusted RR (95% CI)[i] |
|---|---|---|---|---|
| **NO PARENTAL PAIN** | 3 073 | 519 | 1.00 (Reference) | 1.00 (Reference) |
| **MATERNAL PAIN** | 3 050 | 662 | 1.28 (1.15-1.42) | 1.23 (1.11-1.36) |
| **PATERNAL PAIN** | 1 721 | 364 | 1.25 (1.11-1.42) | 1.25 (1.10-1.40) |
| **PARENTAL PAIN** | 1 996 | 445 | 1.32 (1.17-1.47) | 1.27 (1.14-1.43) |

Abbreviations: RR; Relative Risk, CI; Confidence Interval

[i]Adjusted for age, sex, education, BMI, leisure physical activity, insomnia and stress/anxiety

Table 4 shows that the groups with a family history of pain had an increased RR for developing chronic neck/shoulder and/or spinal pain, compared to the group without family history of pain. The sedentary group had an RR of 1.28(95% CI 1.02-1.61) if both parents have pain, compared to the sedentary group with no parental pain. The group with an active job and a history of both parents having pain had an RR of 1.76(95% CI 1.46-2.11) compared to the sedentary group with no parental pain. Additionally, the active group with no family history of pain had an RR of 1.39(95% CI 1.16-1.66) compared to the sedentary group with no parental pain.

***Table 4** The joint effect of occupational physical activity and family history of pain on risk of developing chronic neck/shoulder and spinal pain at 11-year follow-up.*

| | **Sedentary†** | | | **Active‡** | | |
|---|---|---|---|---|---|---|
| **Family history** | **No. of persons** | **No. of cases** | **Adjusted RR (95%CI)[i]** | **No. of persons** | **No. of cases** | **Adjusted RR (95%CI)[i]** |
| **NO PARENTAL PAIN** | 1 034 | 139 | 1.00 (Reference) | 2 039 | 380 | 1.39 (1.16-1.66) |
| **MATERNAL PAIN** | 1 037 | 205 | 1.39 (1.14-1.69) | 2 013 | 457 | 1.62 (1.36-1.93) |
| **PATERNAL PAIN** | 570 | 114 | 1.46 (1.16-1.82) | 1 151 | 250 | 1.61 (1.33-1.95) |
| **PARENTAL PAIN** | 640 | 114 | 1.28 (1.02-1.61) | 1 356 | 331 | 1.76 (1.46-2.11) |

Abbreviations: RR; Relative Risk, CI; Confidence Interval

[i]Adjusted for age, sex, education, BMI, leisure physical activity, insomnia and stress/anxiety

†Participants who answered: “Mostly sedentary work (e.g. desktop work, assembly)" in HUNT3 when describing their work.
‡Participants who answered “work that requires you to walk a lot (e.g. cluster work, light industrial work, Teaching)", "work where you walk and lift a lot (e.g. postman, caregiver, building work) " and "heavy body work (e.g. forestry, heavy agricultural work, heavy construction work)” in HUNT3 when describing their work.

The RERI analysis showed that the interaction between occupational activity level and family history of pain was not likely an additive interaction. RERI estimate 0.082 (95% CI -0.287 to 0.451) indicates that there was little to no additive effect of parental chronic widespread pain and offspring occupational activity level on the risk of developing chronic neck/shoulder and spinal pain in offspring.

# Discussion

The result from this study indicates a positive association between occupational activity level and risk of developing neck/shoulder and/or spinal pain. Participants with a moderate to high occupational activity level had a 25% increased risk of developing neck/shoulder and/or spinal pain, compared to the participants with a sedentary job. Furthermore, it was found that participants with parental pain had a 27% increased risk of developing neck/shoulder and spinal pain compared to participants with no family history of pain. The analyses of the joint effects of occupational activity level and family history of pain on the risk of development of neck/shoulder and/or spinal pain showed that people with a physically demanding job and both parents having a history of pain had the highest risk for developing chronic shoulder/neck and/or spinal pain. However, we did not find any additive interaction between the variables.

## Occupational physical activity and musculoskeletal pain

Individuals with moderate to high occupational activity level had a 25% increased risk of developing pain compared to the sedentary group. The results can be explained by the Dose-response model, indicating that being more often exposed to physical strain can lead to pain(Armstrong et al., 1993). Individuals in active occupations is more often exposed to physical strain which may lead to a physiological reaction, which in turn affects how the next physical strain is handled. Repeated physical strain at work can start a bad loop, e.g., when external factors, such as heavy lifting leads to tissue load, which in turn leads to the muscle tissue being worn which can lead to a reduced capacity to withstand the next heavy lift at work(Armstrong et al., 1993).

The physical activity paradox at work vs. during leisure time, may also explain these findings. Some of the different biomechanics(i.e. no warm-up at work to avoid injury, not using full range of motion to stretch out the connective tissue, no breaks to recover, pleasure-oriented, etc) in leisure time exercise vs. occupational activity(Holtermann et al., 2021) could be an explanation for why occupational physical activity could lead to musculoskeletal pain disorders. It is shown to be a negative health related consequence of being in occupations with a high physical activity level, and that despite being physically active during leisure time, there was still an elevated risk for developing musculoskeletal pain associated with having a high occupational activity level(Holtermann et al., 2021).

The result of this study is in line with data from previous studies that investigate the association between physical strain at work and risk of musculoskeletal pain(Andersen et al., 2016; Farioli et al., 2014; Holtermann et al., 2021; Langballe et al., 2009; Veiersted et al., 2017). Mechanical factors such as “heavy lifting”, “repetitive arm movements”, “vibrations” and “standing” has been highlighted as central causal factors for developing musculoskeletal pain(Veiersted et al., 2017), where higher risk in the occupations that was exposed to these mechanical risk factors(Farioli et al., 2014; Sterud & Tynes, 2013; Veiersted et al., 2017). However, these studies are limited by relying on interview-administered questionnaire, which could make participants more prone to saying yes to the interviewer and being more sensitive to their pain than they otherwise would have been. However, the studies included many participants(Farioli had 43,816 participants) and accounted for many confounders that the current study considers to be possible confounders(Age, leisure-time physical activity)

## Family history and musculoskeletal pain

The current study found that participants with parental pain had a 27% increased risk of developing neck/shoulder and/or spinal pain compared to participants with no family history of pain. This is in line with previous studies(Bergman et al., 2001; Lier et al., 2016; Matsudaira et al., 2014).

Bergman found strong association between family history and chronic widespread pain and chronic regional pain in 2001(Bergman et al., 2001). Bergman showed the odds ratio of developing chronic regional pain in the two groups with family history to be significantly higher than in individuals with no family history of chronic pain. Where the individuals with family history had an OR of 1.70 compared to individuals with no family history(Bergman et al., 2001). Matsudaira also found a strong association between family history of lower back pain and the risk of the offspring developing lower back pain(Matsudaira et al., 2014). Matsudaira proposed that psychosocial factors could be a cause for family history to be a risk factor(Matsudaira et al., 2014).

The psychosocial environment in a family setting can have an influence on how an individual handles and perceives pain(Edwards et al., 2016). Family members can contribute by giving social help, and encouraging an individual to continue physical therapy and giving emotional support(Edwards et al., 2016), they can also be a detriment to an individual’s by catastrophizing and causing fear of moving due to pain(Luque-Suarez et al., 2019). However, a previous study looking at the association between parental chronic pain and socioeconomic and psychosocial factors with development of chronic pain in the adolescent and young adult offspring found that there was no markedly change after adjusting for psychosocial factors(Hoftun et al., 2013). This supports the belief of Jones(2004) who proposes that there is insufficient evidence to implicate parental pain behaviour as a central factor in the development of pain in offspring(Jones, 2004). Instead, a study found that family structure had an association with the risk of the offspring developing pain at one or multiple areas(Hoftun et al., 2013), it was found that if the parents were separated, then the offspring’s risk of developing chronic pain was more dependent on the pain status of the parent with whom they resided(Hoftun et al., 2013). The current research disagrees on the role of psychosocial environment and there should be conducted more studies.

Genetics refers to the study of genes and their inheritance, including variations that may influence pain susceptibility and response. Epigenetics, on the other hand, examines how gene expression is modified by environmental factors without altering the underlying DNA sequence(Campbell, 2018). Epigenetic modifications play a crucial role in regulating gene expression patterns without altering the DNA sequence. These modifications are influenced by environmental factors and have been implicated in exacerbating pain sensitivity(i.e., make an individual less equipped to handle pain), which could in turn lead to stress, which would lead to worsening of chronic pain due to stress(Diatchenko et al., 2013). Understanding the impact of changes in epigenetic gene expression on pain perception is important for improving pain management strategies.

Family history could be a multifactorial risk factor(inherited behaviours, shared environment and genetics) and needs to be split into different categories to be able to see the full extent on how family history affects the risk of developing chronic neck/shoulder and spinal pain. Both inherited pain behaviours and gene expressions seems to contribute to the development of chronic pain.

## The joint effect of occupational physical activity and family history of pain

Although we did not find any additive interaction effect between occupational activity level and family history of chronic musculoskeletal pain, we found that participants with an active job and with parental pain had the highest risk of developing chronic pain in the neck/shoulder and/or spinal area. Investigating the interplay between occupational physical activity and epigenetics can shed light on the mechanisms underlying pain sensitivity and identify potential avenues for intervention.

This result can partly be explained by physical activity on the gene expression(which can be passed down to offspring) which in turn can change how individuals experience and develop pain(Polli et al., 2019). Resistance training has been shown to have rapid benefits, such as increased muscle mass and reduced methylation in pain-related genes, after just a few weeks(Polli et al., 2019). The opposite effect can be possible for individuals who are in occupations with similar mechanisms, such as heavy lifting. Acute aerobic exercise has also demonstrated positive effects on gene expression related to skeletal muscle development, with changes observed up to 10 days following exercise(Denham et al., 2014). The amount of change in skeletal muscle-related gene expressions was found to be dose-dependent on the intensity and frequency of the physical activity(Denham et al., 2014). When viewed together with Armstrong's dose-response model, it is plausible that individuals may experience an immediate response in gene expression when exposed to high levels of occupational activity. It is possible that there is a similar, but detrimental, change in gene expression when individuals start being physically active in their occupations. However, this study did not have access to genetic data of the participants, and further research is needed to gain more insight into these mechanisms.

According to Diatchenko, approximately 50% of risk developing chronic pain condition is driven by an individual’s genetic background(Diatchenko et al., 2013). This number was found in the heritability of pain in twin studies performed in Sweden and Finland on neck pain and fibromyalgia(Diatchenko et al., 2013). This leaves the remaining 50% to driven by non-genetic factors, such as inherited behaviours from the parents, immediate environment, and external stressors an individual is exposed to in their lifetime.

As far as we know, this is the first study that has investigated the joint effect of occupational physical activity and family history of pain on the risk of developing neck/shoulder and/or spinal pain in the Norwegian population. Other studies have suggested that physical work demands and inherited pain-behaviour should both be taken into account when aiming to reduce lower back pain related disability(Matsudaira et al., 2014). Furthermore, manual work has been identified as an additional risk factor when looking at chronic widespread parental pain and chronic widespread pain in offspring(Lier et al., 2016). The offspring's occupational choice correlate with parent's occupation and education level(Whiston et al., 2004), which could influence the results by having the parent and offspring be exposed to similar occupational physical activities. The current study showed that individuals who had both active work and a family history of pain exhibited the highest risk among all the groups (RR = 1.76, 95% CI 1.46-2.11). This could indicate that inheritance of occupational factors from parents to offspring could be a central factor in the development of chronic neck/shoulder and/or spinal pain. It implies that both epigenetic factors and the influence of inherited occupations may contribute to the increased risk of musculoskeletal pain.

Strengths and weaknesses with the study

There are several strengths and weaknesses in the current study. A strength of the study is the data collected from the HUNT Study, which is a large population-based study with standardised measurement of height and weight, and a large amount of information on potentially confounding variables, as well as multiple follow-ups. Another important strength is that the data is linked to the family registry, which enabled us to make parental-offspring trios. Additionally, the large study sample allowed for analysis of joint effects of occupational physical activity and family history of chronic musculoskeletal pain on the risk of chronic neck/shoulder and/or spinal pain.

There are several weaknesses in this study that should be accounted for when interpreting the results. The relationship between developing chronic widespread pain and familial factors can be confounded, and we cannot be sure that we have adjusted for all possible confounders in the analysis. There could be a possibility that people who does not perform leisure-time physical activity have a tendency to consume more sugar and fat compared to the individuals who do(Elder & Roberts, 2007); sugar and fat consumption has a positive association with pain severity in osteoarthritis pain(Elma et al., 2020). Unfortunately, we have not used data on participants' diet, which could be a potential confounder. The analysis used in the current study can be sensitive to confounding, which occurs when an outside variable affects both the exposure and outcome, making it difficult to discern the effects of each factor. In medical studies it is almost impossible to account for every possible confounder. Failure to account for confounding can lead to biased estimates. Furthermore, the population included in the HUNT-study is vulnerable to selection bias, i.e., that less healthy individuals is less able to show up to the study or the follow-up. We cannot exclude the possibility that individuals with chronic musculoskeletal pain were either over- or under-represented in the study sample. This may influence the results of the current study by excluding individuals who have developed musculoskeletal pain that is severe enough that they were unable to show up to the study or subsequent follow-ups.  This could lead to this study underestimating the risk that was  shown in the results. Another weakness is the relative low response rate in both HUNT3 and HUNT4(response rate 54.1% and 54.0%) compared to the response rate in HUNT1 and HUNT2(response rate 88.1% and 70.0%).

Other potential weaknesses could be that the information on the participants' activity level at work was divided into four broad categories in the questionnaire, which can lead to misclassification bias(Pham et al., 2019). The occupation question used to categorise the groups into "work that involves a lot of sitting", "work that requires much walking", "work that requires a lot of walking and lifting, and "heavy physical labour" is prone to misclassification due to the grouping of different occupations; e.g., it grouped assembly worker with an office worker, light industrial work with teaching, etc. Assembly workers include lift fitter(heismontør) which could contain work-requirements such as heavy lifting and maintaining a strenuous position over a longer period of time; this is a work group that is not comparable to office workers in occupational activity level. A suggestion could be to update the example in the questionnaire to better reflect the average assumed occupational activity levels since work tasks change with technological developments. For example, farmers are using more heavy machinery to aid with harvesting, than they did a few decades ago(Weseth, 2007). This exposes farmers to less awkward positions(i.e., hunched over to pick up produce) and more to vibrations(i.e., sitting in a combine for long periods of time).

Additionally, if performing their work-tasks was made difficult by their musculoskeletal pains participants could be more likely to be aware of their pains, compared to individuals who are in work that does not require them to physically active to perform work-related tasks. While the clinical measurements can be assumed to be accurate, the self-reported information from the questionnaires can be susceptible to misinformation. Additionally, if musculoskeletal pain was exacerbated due to misjudgement of their occupational activity level, a suggestion to avoid this would be to either remove the examples given; this would put more weight on the participants giving accurate information about their activity level. Measurement error in either of these variables can lead to biased estimates, in the current study there is a risk of underestimating the risks of developing neck/shoulder and/or spinal pain, due to participants overestimating their occupational activity level(Korshøj et al., 2022) this could skew the data due to that people tend to overestimate their daily physical activity level(Korshøj et al., 2022).

Finally, there is a possibility of reverse-causation, where the individuals could quit their job or select a different type of occupation due to chronic pain. Or that they have pain during their adolescence that causes them to not pursue higher education. This could cause us to overestimate how important of a causal factor occupational activity level is, if the pain was already present when they started their occupation that had a moderate to high level of activity. More information whether previous and/or early life episodes of pain affected their life-choices could be useful.

The generalizability of the study can be improved by using data from HUNT4 and onwards due to HUNT4 adding South-Trøndelag which included Trondheim, a large city, to the cohort. It is therefore recommended to repeat this study on a cohort from HUNT4 and a potential HUNT5 to get both better representative data and to get genotype data on the participants.

The current study did not have access to genetic data of the participants, thus the epigenetic area lacks evidence and data to set up against previous research.

## Practical implication and Future Research

There are preventative measures already in place to minimise avoidable injuries at the workplace(Arbeidsmiljøloven, 2005). Preventing chronic musculoskeletal pains can be beneficial to both the employee and the employer, as seen in the "*Konduktørdommen*" where a conductor developed chronic hip pain due to the work-environment(swinging train) putting a strain on the their hips(Benson, 2019), thus they had to reduce their workload. It is recommended that workers are given information on the most common musculoskeletal disorders in their occupation(i.e., shoulder pain for hairdressers, hip pain for conductors).

The results from this current study could provide health care personnel and occupational health service(bedriftshelsetjenesten) that are directly involved with this target group, to identify and make preventative measures and treatments to the most vulnerable groups.

Due to the risk of developing chronic neck/shoulder and spinal pain when one is in a physically active job with a negative family history is higher(RR 1.39) than the people with sedentary jobs and a positive family history(RR 1.28), it is recommended and study more on the risks of physically active jobs when it comes to how to prevent the development of chronic musculoskeletal pain in the Norwegian working population.

It is recommended to further study more thorough how individuals with a genetic predisposition to pain can be at risk through environmental risk factors such as occupational activity levels. A study on how occupational activity changes specific pain-related epigenomes would be beneficial, such as gathering information on the parents' activity level and use it as a confounder in future studies.

# Conclusion

The result of this study shows that there is a positive association between physically demanding work and the long-term risk of chronic neck/shoulder and/or spinal pain development, and that having family history of pain increased the risk of developing neck/shoulder and/or spinal pain.

Although no additive interaction between occupational activity and family history of pain were found, this study shows that people with a physically demanding work and both parents having a history of musculoskeletal pain had the highest risk for developing chronic neck/shoulder and/or spinal pain. These findings may be helpful to identify people with particular risk of developing chronic pain, which is useful to further develop preventative measures.

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