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The influence of family history on prognosis of spinal pain and the role of leisure time physical activity and body mass index: family-linkage data from the Norwegian HUNT Study.

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ABSTRACT

Objectives: To investigate the influence of parental chronic spinal pain on prognosis of chronic spinal pain in adult offspring, and whether offspring physical activity level and body mass index (BMI) modified this association.

Design: Prospective cohort study.

Setting: We used family linked longitudinal data from the Norwegian HUNT study collected in HUNT2 (1995-97) and HUNT3 (2006-08).

Participants: A total of 1,529 offspring who reported spinal pain in HUNT2 were linked with parental data and followed-up in HUNT3.

Outcomes: We estimated relative risk (RR) with 95% confidence intervals (CIs) for recovery from chronic spinal pain, and also from activity limiting spinal pain, in offspring related to chronic spinal pain in parents. We also investigated whether offspring leisure time physical activity and BMI modified these intergenerational associations in spinal pain.

Results: Offspring with both parents reporting chronic spinal pain were less likely to recover from chronic spinal pain (RR: 0.83, 95% CI: 0.69, 0.99) and activity limiting spinal pain (RR: 0.71, 95% CI: 0.54, 0.94), compared to offspring of parents without chronic spinal pain. Analyses stratified by BMI and physical activity showed no strong evidence of effect modification on these associations. However, offspring who were overweight/obese and with both parents reporting spinal pain had particularly low probability of recovery from activity limiting spinal pain, compared those who were normal weight and had parents without spinal pain (RR: 0.57, 95% CI: 0.39-0.84).

Conclusion: Offspring with chronic spinal pain are less likely to recover if they have parents with chronic spinal pain, particularly if offspring are overweight/obese.

Key words: Low back pain, neck pain, chronic pain, obesity, family study, physical activity.

Strengths and limitations of this study

- The HUNT Study is a large population-based health study with longitudinal data that allows prospective analysis on the prognosis of chronic spinal pain.
- Chronic spinal pain was independently reported in parents and offspring; family relations was informed by a linkage with a national registry; and the data allowed us to control for a wide range of potential confounders.
- Information on pain status, physical activity, and body mass index was not updated throughout the follow-up period.

INTRODUCTION

Spinal pain that includes low back and neck pain is highly prevalent and a common cause of disability worldwide.[1] The natural history of spinal pain is extremely variable and may last a few days or persist for many years.[2] A substantial proportion of patients recover within the first three months of a spinal pain episode, but around three quarters of the remaining patients are likely to experience pain one year after onset.[3, 4] People who fail to recover in the first few months following an acute episode are at greater risk of poor prognosis.[5] Spinal pain, especially in its chronic and disabling form, could be a significant personal and financial burden,[6] and may also influence families and society.[1] It is therefore vital to identify factors that influence prognosis of spinal pain, which in turn can inform preventive interventions to reduce chronicity.

Parental pain is strongly associated with the increased risk of chronic musculoskeletal pain in offspring, both during adolescence[7], and in later adulthood.[8] Furthermore, there is preliminary evidence that treatment response in patients with chronic low back pain is influenced by genetic factors.[9] It is, therefore, possible that parental history of spinal pain influences the prognosis of spinal pain in offspring. Conversely, several studies have shown that engagement in moderate to vigorous-intensity leisure time physical activity and maintenance of a normal body mass index (BMI) are associated with better prognosis of spinal pain.[10-14] Thus, a healthy offspring lifestyle could modify a possible adverse effect of parental spinal pain on prognosis of offspring spinal pain. Currently, there is limited knowledge about the influence of parental spinal pain on prognosis of spinal pain in offspring and whether this association is modified by offspring lifestyle.

In this study, we have used population-based longitudinal data from the Norwegian HUNT Study to investigate the influence of parental spinal pain on the prognosis of chronic spinal pain regarding severity and activity limitation in the adult offspring. We have also investigated whether offspring leisure time physical activity and BMI modify any of these associations.

METHODS

Study population

The HUNT Study is a population-based health study conducted within the county of Nord-Trøndelag, Norway. The study was performed in three consecutive waves, first in 1984–1986 (HUNT1), then in 1995–1997 (HUNT2), and last in 2006–2008 (HUNT3). In all three surveys, all residents 20 years of age and older were invited to participate, and information on lifestyle and health-related factors were collected by questionnaires and a clinical examination. Information on musculoskeletal pain was not collected at HUNT1. Therefore, those who were eligible for inclusion in this study had participated at HUNT2 and HUNT3. At HUNT2, 93,898 individuals were invited to participate, and 65,237 (65.5%) joined the study, while at HUNT3 93,860 were invited and 50,807 (54.1%) agreed to participate.[15, 16] Each participant signed written consent, and the study was approved by the Regional Committee for Medical and Health Research Ethics Central Norway (ref. no. 2011/1455). Further information about selection procedures, participation and questionnaires used in the HUNT study can be found at http://www.ntnu.edu/hunt.

Patient involvement

Since historical cohort data was used in this study, patients were not involved in the conduct and design of the study.

Record linkage

The unique personal identification number held by all Norwegian citizens was used to link each participant's record to information from the Family Registry at Statistics Norway, and therefore establish a link between parents and offspring who participated in one or both of HUNT2 and HUNT3. A total of 11,483 offspring reported spinal pain at HUNT2, and of these, 6,662 could be followed-up on spinal pain status in HUNT3, approximately 11 years later. To be able to study the association between parental spinal pain and offspring prognosis of spinal pain, we selected all 1,529 parent–offspring trios (i.e., mother, father and adult offspring) where both the mother and the father had information on spinal pain from HUNT2.

Chronic spinal pain

At HUNT2 and HUNT3, participants were asked to complete the Standardized Nordic Questionnaire which has acceptable reliability and validity.[17] The question regarding musculoskeletal pain was as follows: "In the last year, have you had pain and/or stiffness in muscles or joints that have lasted at least 3 consecutive months?" (response options: "no" and "yes"). Participants who answered "yes" were asked to indicate the affected body area(s). Offspring who reported chronic neck and/or low back pain (spinal pain) at HUNT2 were included in this study, and offspring who also reported spinal pain at HUNT3 were considered not recovered (outcome measure). Offspring reporting spinal pain at HUNT2 were also asked to indicate if the pain had led to reduced leisure time activity (response options: "no", and "yes") or

reduced their work ability (response options: “no”, “to some extent”, “considerably”, or “don’t know”). Offspring who answered “yes” to the question on reduced leisure time activity and/or reported work ability to be reduced “to some extent” or “considerably”, were classified as having “activity limiting spinal pain”. In secondary analyses, we used this information to investigate the prognosis of activity limiting spinal pain; i.e., recovery was defined as not reporting activity limiting spinal pain at HUNT3. Based on the same question as described above, we obtained information on parental chronic spinal pain. Further, we created a variable with four mutually exclusive categories for presence of parental chronic spinal pain at baseline (exposure measure): “none”, “mother”, “father”, or “both parents”.

Leisure time physical activity

Leisure time physical activity was assessed by the following question “How much of your leisure time have you been physically active during the last year? (Think of a weekly average for the year. Your commute to work counts as leisure time)”. Participants reported the number of hours of either light (no sweating or heavy breathing) or hard (sweating and heavy breathing) activity using the response options “none”, “less than 1 hour”, “1–2 hours”, and “3 or more hours” for each type of activity. Based on this information, we constructed a variable with four categories (combining information on light and hard activity): 1) “inactive” (no light or hard activity), 2) “low activity” (<3 hours light and no hard activity), 3) “moderate activity” (≥3 hours light and/or <1 hour hard activity), and 4) “high activity” (any light and ≥1 hour hard activity). In the combined analyses of parental chronic spinal pain and offspring leisure time physical activity the categories “inactive” and “low activity” were collapsed into one category labelled “Physically inactive” and the categories “moderate activity” and “high activity” were collapsed into one

category labelled "Physically active". This categorization has been used previously in other studies based in data from HUNT.[18, 19]

Body mass index

Standardized measurements of body height (to the nearest centimetre) and body weight (to the nearest half kilogram) were obtained at clinical examination. BMI was calculated as weight divided by the square of height (kg/m^2), and classified into four BMI groups according to the cut-off points suggested by the World Health Organization:[20] underweight (BMI <18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25.0–29.9 kg/m^2), and obese (BMI ≥30.0 kg/m^2). Only 27 participants (1 %) were classified as "underweight", and the combined analysis of parental chronic spinal pain and offspring BMI, the categories "underweight" and "normal weight" were collapsed into one category labelled "normal weight". The categories "overweight" and "obese" were collapsed into one category labelled "overweight/obese".

Statistical analysis

We used a Poisson regression model [21-24] to estimate relative risk (RR) of chronic spinal pain and activity limiting spinal pain in offspring whose parents reported chronic spinal pain, using parents with no chronic spinal pain as the reference category. Precision of estimates was assessed by a 95% confidence interval (CI). All standard errors were adjusted for within-family clustering (i.e., siblings) using the vce (cluster) option in Stata, treating observations between families as independent and within families as dependent, and thus avoiding inflated precision of the estimated associations.[25]

Possible effect modification by offspring leisure time physical activity or offspring BMI was assessed by stratified analyses (i.e. physically active vs physically inactive and normal weight vs overweight/obese) as well as by tests of the estimated relative excess risk due to interaction (RERI) (i.e., departure from additive effects). We calculated RERI estimates with 95% CIs from the following equation: $RERI = RR_{\text{parental pain \& physically active/overweight and/or obese}} - RR_{\text{noparental pain \& physically activity/ overweight and/or obese}} - RR_{\text{parental pain \& physically inactivity/normal weight}} + 1$, [26] i.e., $RERI > 0$ indicate a synergistic effect beyond an additive effect. Statistical interaction was also evaluated on a multiplicative scale by a likelihood ratio test of a product term in the model (these likelihood ratio tests had to be run without cluster-adjusted standard errors to avoid misspecification of the model).

The main analyses (parental influence on risk of poor prognosis) were adjusted for possible confounding by offspring sex (male, female), age (continuous), BMI ("underweight", "normal weight", "overweight", "obese", or "unknown"), leisure time physical activity ("physically inactive" or "physically active", or "unknown"), education ("<10 years", "10–12 years", ">13 years", or "unknown"), and depression ("depressed", or "not depressed", or "unknown"). Depression was assessed using the depression subscale of the Hospital Anxiety and Depression Scale (HADs) using a score of 8 as a cut-off for a dichotomised variable.[27-29]

All statistical tests were two-sided, and all analyses were conducted using Stata statistical software (version 13.0, STATA Corp., College Station, TX, USA).

RESULTS

In this prospective study of 1,529 offspring with chronic spinal pain at baseline, a total of 540 (35%) offspring were defined as recovered after approximately 11 years of follow-up. Additionally, among 775 offspring with activity limiting spinal pain, 244 were defined as recovered at follow-up. Descriptive statistics of offspring, mothers, and fathers are shown in Table 1. The mean age at baseline was 32.8 (8.6) years among offspring. Most offspring were physically active (64.7%), and about half of the offspring (52.9%) were classified as overweight or obese. About one third (36.9%) of the offspring were current smokers, and just a small portion of offspring (18.7%) reported having a higher education degree. A small proportion (10.5%) of offspring had symptoms of depression according to the Hospital Anxiety and Depression Scale.

Table 1. Baseline characteristics of the study population at HUNT2

Variables	Offspring	Mothers	Fathers
Participants, no.	1,529	1,529	1,529
Age, mean (SD)	32.8 (8.6)	63.8 (9.4)	67.2 (9.5)
Body mass index, mean (SD)	25.9 (5.2)	28.3(7.3)	27.6 (6.9)
Overweight/obese, % (n)	42.3 (799)	70.6 (1,080)	72.2 (1,104)
Physically active[a], % (n)	63.9 (977)	43.0 (510)	57.7 (716)
Current smoker, % (n)*	33.1 (506)	26.3 (400)	28.5 (434)
Higher education[b], % (n)	20.7 (316)	4.5 (61)	6.0 (84)
Symptoms of depression[c], %, (n)	10.4 (155)	17.0 (225)	16.5 (215)

SD, standard deviation

[a] Engagement in moderate (≥3 hours light and/or <1 hour hard activity per week) or high leisure time physical activity (any light and ≥1 hour hard activity per week)

[b] University education or higher

[c] Score ≥8 on the Hospital Anxiety and Depression Scale

Chronic spinal pain and activity limiting spinal pain

Offspring with both parents reporting chronic spinal pain were less likely to recover from chronic spinal pain (RR: 0.83, 95% CI: 0.69, 0.99) and activity limiting spinal pain (RR: 0.71, 95% CI: 0.54-0.94) compared to offspring with no parents with chronic spinal pain (Table 2). These associations were weaker and less precise when chronic spinal pain was present in only one parent, with similar associations observed for maternal and paternal spinal pain.

Table 2. Relative risk (RR) of recovery from spinal pain and activity limiting spinal pain in adult offspring associated with parental spinal pain.

	Offspring spinal pain				Offspring activity limiting spinal pain			
Parental spinal pain	No. of persons	No. of cases	Crude RR	Adjusted RR[a] (95% CI)	No. of persons	No. of cases	Crude RR	Adjusted RR[a] (95% CI)
None	346	138	1.00	1.00 (Ref.)	163	66	1.00	1.00 (Ref.)
Mother	424	147	0.88	0.90 (0.75-1.07)	214	62	0.73	0.74 (0.56-0.98)
Father	272	97	0.90	0.91 (0.74-1.12)	127	40	0.77	0.78 (0.57-1.05)

Both	487	158	0.82	0.83 (0.69-0.99)	271	76	0.69	0.71 (0.54-0.94)

CI, confidence interval

[a]Adjusted for age, sex, BMI, smoking, leisure time physical activity, education and HADS score.

Physical activity

In the stratified analysis for physical activity, there was no strong evidence of effect modification for either physically active offspring (RR: 0.78; 95% CI: 0.62, 0.98), or physically inactive offspring (RR: 0.98; 95% CI: 0.71, 1.36) (Table 3). Tests of statistical interaction indicate no departure from neither multiplicative (p = 0.037) nor additive effects (RERI 0.19, 95% CI, -0.17, 0.55), data not shown.

Table 3. Relative risk (RR) of recovery from spinal pain in adult offspring associated with parental spinal pain; analysis stratified by leisure time physical activity.

	Physically active			Physical inactive		
Parental spinal pain	No. of persons	No. of cases	Adjusted RR[a] (95% CI)	No. of persons	No. of cases	Adjusted RR[a] (95% CI)
None	229	97	1.00 (Ref.)	111	40	1.00 (Ref.)
Mother or father	434	163	0.94 (0.77-1.14)	246	74	0.82 (0.60-1.11)
Both parents	314	100	0.78 (0.62-0.98)	166	58	0.98 (0.71-1.35)

CI: confidence interval

aAdjusted for age, sex, BMI, smoking, education and HADS score.

Body mass index

In the stratified analysis for body mass index, there was no strong evidence of effect modification. However, offspring who were overweight or obese had the lowest probability of recovery if both parents report activity limiting spinal pain or chronic spinal pain (RR: 0.57; 95% CI: 0.39, 0.84 and RR: 0.79; 95% CI: 0.61, 1.03 respectively) compared to normal weight (Table 4). In addition, there was no evidence of statistical interaction neither on the additive (estimates of RERI for chronic spinal pain and activity limiting spinal pain were -0.04; 95% CI: -0.38, 0.30 and -0.34; 95% CI: -0.91, 0.23, respectively) nor on the multiplicative scale (p = 0.131 and p = 0.048, respectively).

Table 4. Relative risk (RR) of recovery from spinal pain and activity limiting spinal pain in adult offspring associated with parental spinal pain; analysis stratified by BMI.

	Normal weight			Overweight/obese		
Variables	No. of persons	No. of cases	Adjusted RR[a] (95% CI)	No. of persons	No. of cases	Adjusted RR[a] (95% CI)
Offspring spinal pain						
Parental spinal pain						
None	168	68	1.00 (Ref.)	177	69	1.00 (Ref.)
Mother or father	316	111	0.88 (0.70-1.12)	380	133	0.89 (0.70-1.12)

Both parents	242	82	0.86 (0.66-1.11)	242	76	0.79 (0.61-1.03)
Offspring activity limiting spinal pain						
Parental spinal pain						
None	86	34	1.00 (Ref.)	130	50	1.00 (Ref.)
Mother or father	151	42	0.72 (0.49-1.04)	301	98	0.72 (0.51-0.99)
Both parents	129	41	0.84 (0.57-1.24)	188	52	0.57 (0.39-0.84)

CI: confidence interval.

aAdjusted for age, sex, leisure physical activity, smoking, education and depression.

DISCUSSION

Summary of findings

The findings of this large population-based prospective family-linkage study indicate that offspring with both parents reporting chronic spinal pain are less likely to recover from chronic spinal pain and activity limiting spinal pain compared with offspring with no parent with spinal pain. Overall, there was no strong evidence that physical activity or body mass index modified these associations, although the results suggest that the inverse association between parental spinal pain and recovery from activity limiting spinal pain was strongest among offspring with a high BMI. This study supports the evidence from twin studies that genetics potentially influences recovery from chronic spinal pain,[30] but these intergenerational associations incorporate

shared environmental factors and shared beliefs that could influence recovery. For instance, there is evidence showing that negative beliefs about pain and negative expectations about recovery predict chronic and disabling spinal pain.[31-33] It seems clear that it is important to consider the family history of chronic spinal pain as well as lifestyle behaviours when identifying people at higher risk of non-recovery.

Comparison of findings with previous research

A recent systematic review showed that offspring of parents with chronic pain have poorer outcomes regarding pain, general health, psychological, and family functioning as compared to offspring of parents without pain.[34] The inter-generational transmission of spinal pain could be explained by genetic heritability [35, 36] or a family shared environment.[37-40] Moreover, it has been suggested that the genetic influence is greater in more disabling pain conditions, such as chronic widespread pain and chronic activity limiting spinal pain, rather than in acute or sub-acute non-debilitating pain.[35, 36] It is widely accepted that lifestyle factors, such as physical activity and body weight, also play a significant role in the prognosis of chronic musculoskeletal pain.[41]

Some studies have suggested that people with chronic back pain who regularly engage in leisure time physical activity have better prognosis measured in terms of pain, disability, and quality of life than those who are sedentary.[18, 42] However, there remains conflicting evidence regarding how physical activity influences the prognosis of spinal pain,[43] with studies demonstrating that both low and high levels of physical activity can negatively influence the prognosis of spinal pain.[44, 45] For instance, a study found that high leisure time physical activity was related to

decreased prevalence of low back pain.[46] Whereas another study found that either high or low levels of leisure time physical activity was related to increased prevalence of low back pain.[44] In contrast, a prospective study did not find any significant association between moderate/high levels of leisure physical activity and low back pain in young adults.[47] Another follow-up study found that regular habits of leisure physical activity have no effect on recovery from low back pain.[48] The inconsistency in the literature is possibly attributed to the diverse definitions and classifications of levels of physical activity. If such divergent associations with leisure time physical activity exist this could mask a possible modifying effect of physical activity in our analyses.

The literature has provided evidence that obesity is associated with poor outcomes in people with chronic widespread pain,[49, 50] as well as chronic spinal pain [18, 51, 52] and also decreases the probability of recovery from chronic spinal pain regardless of the care they receive,[14] however, whether BMI could modify [19] the relationship between parental spinal pain on offspring recovery from chronic spinal pain has not been investigated before. Our results suggest that offspring BMI may modify on the parent-offspring association of spinal pain, with somewhat stronger associations among offspring who were classified as overweight or obese than those who were underweight or normal weight. Research has shown that inter-individual differences in pain sensitivity and endogenous pain-inhibitory capacity could reflect variations in the inherent susceptibility for chronic pain,[53, 54] but that a triggering exposure is required for the development of chronic pain.[55, 56] This could suggest that a possible genetic susceptibility for poor recovery from chronic pain [57, 58] as a higher penetrance between offspring who are overweight or obese.

Strengths and limitations

This study has several strengths including the prospective design utilising a large population-based sample with a long follow-up period. In addition, the registry based information on family relations allowed us to include information on chronic spinal pain obtained from parents and offspring independently and at different time points. An important aspect is that the offspring were adults at the time of data collection, indicating that the parent-to-offspring association of chronic spinal pain persists into adulthood when the offspring most likely live apart from their parents. Furthermore, we were able to adjust for several offspring characteristics that could confound the parent-offspring associations of chronic spinal pain, such as age,[59] BMI,[52] leisure physical activity,[60] smoking,[59] depression [59] and education.[36, 61] However, we cannot exclude the possible residual confounding attributable to unknown or unmeasured factors.

There are some limitations that should be taken into account. Firstly, information on chronic spinal pain was only reported at baseline and follow-up 10-11 years later, with no information on possible changes in chronic spinal pain during the follow-up period. Consequently, recovery measured at follow-up could have been related to another episode of chronic spinal pain rather than the one reported at baseline. However, it is unlikely that this was differential between offspring with parents who reported chronic spinal pain and those who did not. Likewise, information on leisure time physical activity and BMI was only assessed at baseline, with no information on possible changes during the follow-up period. Secondly, although the questions about leisure time physical activity used in this study have been reported to have good reliability and provide useful measures of leisure physical activity,[62] subjective interpretations of the

activity questions could have influenced the results. Besides, it is well known that self-reports may lead to under or overestimation of the variables of interest.[63] Thirdly, a premise for inclusion into this study was that the mother, father and offspring all had to participate in the health survey. To some extent, this may have resulted in a selected and more health conscious sample than the general population. Nevertheless, it is questionable whether representativeness is a prerequisite for making valid risk assessments in epidemiological studies.[57]

CONCLUSION

Offspring with chronic spinal pain are less likely to recover if they have parents with chronic spinal pain compared to offspring without parental chronic spinal pain. This association is stronger when the offspring present pain that interferes with their usual work and leisure activities (activity limiting spinal pain). The inverse association between parental chronic spinal pain on recovery was somewhat stronger among offspring who were overweight or obese. The association between parental chronic spinal pain and the prognosis of chronic spinal pain in the adult offspring underlines the importance of identifying those at high risk of non-recovery since they account for significant social and individual financial burden. Therefore, clinicians should consider family history of spinal pain when implementing strategies to improve recovery from chronic spinal pain, chronic spinal pain. For instance, the assessment of the potential risks of physical activity and education about the range of benefits, as well as highlights the importance of maintenance of a normal body weight.

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Author Contributions

All authors critically revised the manuscript for important intellectual content and approved the final manuscript. Please find below a detailed description of the role of each author:

- Anita B Amorim: conception and design, analysis and interpretation of data, drafting and revision of the manuscript, and final approval of the version to be published.
- Paulo H Ferreira: conception and design, interpretation of data, drafting and revision of the manuscript, and final approval of the version to be published.
- Manuela L Ferreira: conception and design, drafting and revision of the manuscript, and final approval of the version to be published.

- Ragnhild Lier: conception and design, drafting and revision of the manuscript, and final approval of the version to be published.
- Milena Simic: conception and design, drafting and revision of the manuscript, and final approval of the version to be published.
- Evangelos Pappas: conception and design, drafting and revision of the manuscript, and final approval of the version to be published.
- Joshua R Zadro: conception and design, interpretation of data, drafting and revision of the manuscript, and final approval of the version to be published.
- Paul Jarle Mork: conception and design, acquisition and interpretation of data, drafting and revision of the manuscript and final approval of the version to be published.
- Tom Ivar Lund Nilsen: conception and design, acquisition and interpretation of data, drafting and revision of the manuscript and final approval of the version to be published.

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Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

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		Reporting Item	Page Number
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	#3	State specific objectives, including any prespecified hypotheses	5
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	5

	#6b	For matched studies, give matching criteria and number of exposed and unexposed	6
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6, 7 and 8
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	See note 1
Bias	#9	Describe any efforts to address potential sources of bias	8
Study size	#10	Explain how the study size was arrived at	6
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	8
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	8 and 9
	#12b	Describe any methods used to examine subgroups and interactions	8 and 9
	#12c	Explain how missing data were addressed	8 and 9
	#12d	If applicable, explain how loss to follow-up was addressed	8 and 9
	#12e	Describe any sensitivity analyses	8 and 9
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	9 and 10
	#13b	Give reasons for non-participation at each stage	9 and 10
	#13c	Consider use of a flow diagram	n/a
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	9 and 10

		confounders. Give information separately for exposed and unexposed groups if applicable.	
	#14b	Indicate number of participants with missing data for each variable of interest	n/a
	#14c	Summarise follow-up time (eg, average and total amount)	9 and 10
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	10 and 11
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10 and 11
	#16b	Report category boundaries when continuous variables were categorized	10 and 11
	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	10 and 11
Key results	#18	Summarise key results with reference to study objectives	11 and 12
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	13
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	13 and 14
Generalisability	#21	Discuss the generalisability (external validity) of the study results	13 and 14
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15 and 16

Author notes

1. 6, 7 and 8

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The influence of family history on prognosis of spinal pain and the role of leisure time physical activity and body mass index: family-linkage data from the Norwegian HUNT Study.

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Keywords:	Low back pain, neck pain, chronic pain, obesity, family study, physical activity

The influence of family history on prognosis of spinal pain and the role of leisure time physical activity and body mass index: family-linkage data from the Norwegian HUNT Study.

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ABSTRACT

Objectives: To investigate the influence of parental chronic spinal pain on prognosis of chronic spinal pain in adult offspring, and whether offspring physical activity level and body mass index (BMI) modified this association.

Design: Prospective cohort study.

Setting: We used family linked longitudinal data from the Norwegian HUNT study collected in HUNT2 (1995-97) and HUNT3 (2006-08).

Participants: A total of 1,529 offspring who reported spinal pain in HUNT2 were linked with parental data and followed-up in HUNT3.

Outcomes: We estimated relative risk (RR) with 95% confidence intervals (CIs) for recovery from chronic spinal pain, and also from activity limiting spinal pain, in offspring related to chronic spinal pain in parents. We also investigated whether offspring leisure time physical activity and BMI modified these intergenerational associations in spinal pain.

Results: Offspring with both parents reporting chronic spinal pain were less likely to recover from chronic spinal pain (RR: 0.83, 95% CI: 0.69, 0.99) and activity limiting spinal pain (RR: 0.71, 95% CI: 0.54, 0.94), compared to offspring of parents without chronic spinal pain. Analyses stratified by BMI and physical activity showed no strong evidence of effect modification on these associations. However, offspring who were overweight/obese and with both parents reporting spinal pain had particularly low probability of recovery from activity limiting spinal pain, compared those who were normal weight and had parents without spinal pain (RR: 0.57, 95% CI: 0.39-0.84).

Conclusion: Offspring with chronic spinal pain are less likely to recover if they have parents with chronic spinal pain, particularly if offspring are overweight/obese.

Key words: Low back pain, neck pain, chronic pain, obesity, family study, physical activity.

Strengths and limitations of this study

- The HUNT Study is a large population-based health study with longitudinal data that allows prospective analysis on the prognosis of chronic spinal pain.
- Chronic spinal pain was independently reported in parents and offspring; family relations was informed by a linkage with a national registry; and the data allowed us to control for a wide range of potential confounders.
- Information on pain status, physical activity, and body mass index was not updated throughout the follow-up period.

INTRODUCTION

Spinal pain that includes low back and neck pain is highly prevalent and a common cause of disability worldwide.[1] The natural history of spinal pain is extremely variable and may last a few days or persist for many years.[2] A substantial proportion of patients recover within the first three months of a spinal pain episode, but around three quarters of the remaining patients are likely to experience pain one year after onset.[3, 4] People who fail to recover in the first few months following an acute episode are at greater risk of poor prognosis.[5] Spinal pain, especially in its chronic and disabling form, could be a significant personal and financial burden,[6] and may also influence families and society.[1] It is therefore vital to identify factors that influence prognosis of spinal pain, which in turn can inform preventive interventions to reduce chronicity.

Family studies have suggested that chronic pain aggregate in families,[7, 8] with the parent-offspring transmission of chronic pain explained by genetic heritability[9, 10] and shared environment factors.[11-14] The mean heritability of chronic low back pain is 67%,[10, 15] suggesting that a substantial proportion of the risk of developing chronic spinal pain is driven by genetics. However, families also share similar lifestyles and express similar health behaviours and beliefs. This suggests shared environmental factors[8, 16] could also have an important influence on the prognosis of spinal pain.[17, 18]

Parental pain is strongly associated with the increased risk of chronic musculoskeletal pain in offspring, both during adolescence,[7] and in later adulthood.[19] Furthermore, there is preliminary evidence that treatment response in patients with chronic low back pain is influenced by genetic factors.[20] It is, therefore, possible that parental history of spinal pain influences the

prognosis of spinal pain in offspring. Conversely, several studies have shown that engagement in moderate to vigorous-intensity leisure time physical activity and maintenance of a normal body mass index (BMI) are associated with better prognosis of spinal pain.[21-25] Thus, a healthy offspring lifestyle could modify a possible adverse effect of parental spinal pain on prognosis of offspring spinal pain. Currently, there is limited knowledge about the influence of parental spinal pain on prognosis of spinal pain in offspring and whether this association is modified by offspring lifestyle.

In this study, we have used population-based longitudinal data from the Norwegian HUNT Study to investigate the influence of parental spinal pain on the prognosis of chronic spinal pain regarding severity and activity limitation in the adult offspring. We have also investigated whether offspring leisure time physical activity and BMI modify any of these associations.

METHODS

Study population

The HUNT Study is a population-based health study conducted within the county of Nord-Trøndelag, Norway. The study was performed in three consecutive waves, first in 1984–1986 (HUNT1), then in 1995–1997 (HUNT2), and last in 2006–2008 (HUNT3). In all three surveys, all residents 20 years of age and older were invited to participate, and information on lifestyle and health-related factors were collected by questionnaires and a clinical examination. Information on musculoskeletal pain was not collected at HUNT1. Therefore, those who were eligible for inclusion in this study had participated at HUNT2 and HUNT3. At HUNT2, 93,898 individuals were invited to participate, and 65,237 (65.5%) joined the study, while at HUNT3

93,860 were invited and 50,807 (54.1%) agreed to participate.[26, 27] Each participant signed written consent, and the study was approved by the Regional Committee for Medical and Health Research Ethics Central Norway (ref. no. 2011/1455). Further information about selection procedures, participation and questionnaires used in the HUNT study can be found at http://www.ntnu.edu/hunt.

Patient involvement

Since historical cohort data was used in this study, patients were not involved in the conduct and design of the study.

Record linkage

The unique 11-digit personal identification number held by all Norwegian citizens was used to link each participant's record to information from the Family Registry at Statistics Norway, and there by establish a link between parents and offspring who participated in one or both of HUNT2 and HUNT3. The Family Registry provide data on persons registered as legal parents, either as biological parents or through adoption. A total of 11,483 offspring reported spinal pain at HUNT2, and of these, 6,662 could be followed-up on spinal pain status in HUNT3, approximately 11 years later. To be able to study the association between parental spinal pain and offspring prognosis of spinal pain, we selected all 1,529 parent–offspring trios (i.e., mother, father and adult offspring) where both the mother and the father had information on spinal pain from HUNT2.

Chronic spinal pain

At HUNT2 and HUNT3, participants were asked to complete the Standardized Nordic Questionnaire which has acceptable reliability and validity.[28] The question regarding musculoskeletal pain was as follows: "In the last year, have you had pain and/or stiffness in muscles or joints that have lasted at least 3 consecutive months?" (response options: "no" and "yes"). Participants who answered "yes" were asked to indicate the affected body area(s). Offspring who reported chronic neck and/or low back pain (spinal pain) at HUNT2 were included in this study, and offspring who also reported spinal pain at HUNT3 were considered not recovered (outcome measure). Offspring reporting spinal pain at HUNT2 were also asked to indicate if the pain had led to reduced leisure time activity (response options: "no", and "yes") or reduced their work ability (response options: "no", "to some extent", "considerably", or "don't know"). Offspring who answered "yes" to the question on reduced leisure time activity and/or reported work ability to be reduced "to some extent" or "considerably", were classified as having "activity limiting spinal pain". In secondary analyses, we used this information to investigate the prognosis of activity limiting spinal pain; i.e., recovery was defined as not reporting activity limiting spinal pain at HUNT3. Based on the same question as described above, we obtained information on parental chronic spinal pain. Further, we created a variable with four mutually exclusive categories for presence of parental chronic spinal pain at baseline (exposure measure): "none", "mother", "father", or "both parents".

Leisure time physical activity

Leisure time physical activity was assessed by the following question "How much of your leisure time have you been physically active during the last year? (Think of a weekly average for the

year. Your commute to work counts as leisure time)". Participants reported the number of hours of either light (no sweating or heavy breathing) or hard (sweating and heavy breathing) activity using the response options "none", "less than 1 hour", "1–2 hours", and "3 or more hours" for each type of activity. Based on this information, we constructed a variable with four categories (combining information on light and hard activity): 1) "inactive" (no light or hard activity), 2) "low activity" (<3 hours light and no hard activity), 3) "moderate activity" (≥3 hours light and/or <1 hour hard activity), and 4) "high activity" (any light and ≥1 hour hard activity). In the combined analyses of parental chronic spinal pain and offspring leisure time physical activity the categories "inactive" and "low activity" were collapsed into one category labelled "Physically inactive" and the categories "moderate activity" and "high activity" were collapsed into one category labelled "Physically active". This categorization has been used previously in other studies based in data from HUNT.[29, 30] We did not conduct analyses stratified by physical activity status on the outcome "activity limiting spinal pain", since people with activity limiting spinal pain are likely to have limited engagement in leisure and work activities.

Body mass index

Standardized measurements of body height (to the nearest centimetre) and body weight (to the nearest half kilogram) were obtained at clinical examination. BMI was calculated as weight divided by the square of height (kg/m^2), and classified into four BMI groups according to the cut-off points suggested by the World Health Organization:[31] underweight (BMI <18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25.0–29.9 kg/m^2), and obese (BMI ≥30.0 kg/m^2). Only 27 participants (1 %) were classified as "underweight", and the combined analysis of parental chronic spinal pain and offspring BMI, the categories "underweight" and

"normal weight" were collapsed into one category labelled "normal weight". The categories "overweight" and "obese" were collapsed into one category labelled "overweight/obese".

Statistical analysis

We used a Poisson regression model[32-35] to estimate relative risk (RR) of chronic spinal pain and activity limiting spinal pain in offspring whose parents reported chronic spinal pain, using parents with no chronic spinal pain as the reference category. Precision of estimates was assessed by a 95% confidence interval (CI). All standard errors were adjusted for within-family clustering (i.e., siblings) using the vce (cluster) option in Stata, treating observations between families as independent and within families as dependent, and thus avoiding inflated precision of the estimated associations.[36]

Possible effect modification by offspring leisure time physical activity or offspring BMI was assessed by stratified analyses (i.e. physically active vs physically inactive and normal weight vs overweight/obese) as well as by tests of the estimated relative excess risk due to interaction (RERI) (i.e., departure from additive effects). We calculated RERI estimates with 95% CIs from the following equation: $\text{RERI} = \text{RR}_{\text{parental pain \& physically active/overweight and/or obese}} - \text{RR}_{\text{noparental pain \& physically activity/ overweight and/or obese}} - \text{RR}_{\text{parental pain \& physically inactivity/normal weight}} + 1$,[37] i.e., RERI > 0 indicate a synergistic effect beyond an additive effect. Statistical interaction was also evaluated on a multiplicative scale by a likelihood ratio test of a product term in the model (these likelihood ratio tests had to be run without cluster-adjusted standard errors to avoid misspecification of the model).

The main analyses (parental influence on risk of poor prognosis) were adjusted for possible confounding by offspring sex (male, female), age (continuous), BMI ("underweight", "normal weight", "overweight", "obese", or "unknown"), leisure time physical activity ("physically inactive" or "physically active", or "unknown"), education ("<10 years", "10–12 years", ">13 years", or "unknown"), and depression ("depressed", or "not depressed", or "unknown"). Depression was assessed using the depression subscale of the Hospital Anxiety and Depression Scale (HADs) using a score of 8 as a cut-off for a dichotomised variable.[38-40]

All statistical tests were two-sided, and all analyses were conducted using Stata statistical software (version 13.0, STATA Corp., College Station, TX, USA).

RESULTS

In this prospective study of 1,529 offspring with chronic spinal pain at baseline, a total of 540 (35%) offspring were defined as recovered after approximately 11 years of follow-up. Additionally, among 775 offspring with activity limiting spinal pain, 244 were defined as recovered at follow-up. Descriptive statistics of offspring, mothers, and fathers are shown in Table 1. The mean age at baseline was 32.8 (8.6) years among offspring. Most offspring were physically active (63.9%), and nearly half of the offspring (42.3%) were classified as overweight or obese. About one third (33.1%) of the offspring were current smokers, and just a small portion of offspring (20.7%) reported having a higher education degree. A small proportion (10.4%) of offspring had symptoms of depression according to the Hospital Anxiety and Depression Scale.

Table 1. Baseline characteristics of the study population at HUNT2

Variables	Offspring	Mothers	Fathers
Participants, no.	1,529	1,529	1,529
Age, mean (SD)	32.8 (8.6)	63.8 (9.4)	67.2 (9.5)
Body mass index, mean (SD)	25.9 (5.2)	28.3(7.3)	27.6 (6.9)
Overweight/obese, % (n)	42.3 (799)	70.6 (1,080)	72.2 (1,104)
Physically active[a], % (n)	63.9 (977)	43.0 (510)	57.7 (716)
Current smoker, % (n)*	33.1 (506)	26.3 (400)	28.5 (434)
Higher education[b], % (n)	20.7 (316)	4.5 (61)	6.0 (84)
Symptoms of depression[c], %, (n)	10.4 (155)	17.0 (225)	16.5 (215)

SD, standard deviation

[a] Engagement in moderate (≥3 hours light and/or <1 hour hard activity per week) or high leisure time physical activity (any light and ≥1 hour hard activity per week)

[b] University education or higher

[c] Score ≥8 on the Hospital Anxiety and Depression Scale

Chronic spinal pain and activity limiting spinal pain

Offspring with both parents reporting chronic spinal pain were less likely to recover from chronic spinal pain (RR: 0.83, 95% CI: 0.69, 0.99) and activity limiting spinal pain (RR: 0.71, 95% CI: 0.54-0.94) compared to offspring with no parents with chronic spinal pain (Table 2). These associations were weaker and less precise when chronic spinal pain was present in only one parent, with similar associations observed for maternal and paternal spinal pain.

Table 2. Relative risk (RR) of recovery from spinal pain and activity limiting spinal pain in adult offspring associated with parental spinal pain.

	Offspring spinal pain				Offspring activity limiting spinal pain			
Parental spinal pain	No. of persons	No. of cases	Crude RR	Adjusted RR[a] (95% CI)	No. of persons	No. of cases	Crude RR	Adjusted RR[a] (95% CI)
None	346	138	1.00	1.00 (Ref.)	163	66	1.00	1.00 (Ref.)
Mother	424	147	0.88	0.90 (0.75-1.07)	214	62	0.73	0.74 (0.56-0.98)
Father	272	97	0.90	0.91 (0.74-1.12)	127	40	0.77	0.78 (0.57-1.05)
Both	487	158	0.82	0.83 (0.69-0.99)	271	76	0.69	0.71 (0.54-0.94)

CI, confidence interval

[a]Adjusted for age, sex, BMI, smoking, leisure time physical activity, education and HADS score.

Physical activity

In the stratified analysis for physical activity, there was no strong evidence of effect modification for either physically active offspring (RR: 0.78; 95% CI: 0.62, 0.98), or physically inactive offspring (RR: 0.98; 95% CI: 0.71, 1.36) (Table 3). Tests of statistical interaction indicate no departure from neither multiplicative (p = 0.11) nor additive effects (RERI 0.19, 95% CI, -0.17, 0.55), data not shown.

Table 3. Relative risk (RR) of recovery from spinal pain in adult offspring associated with parental spinal pain; analysis stratified by leisure time physical activity.

	Physically active			Physical inactive		
Parental spinal pain	No. of persons	No. of cases	Adjusted RR[a] (95% CI)	No. of persons	No. of cases	Adjusted RR[a] (95% CI)
None	229	97	1.00 (Ref.)	111	40	1.00 (Ref.)
Mother or father	434	163	0.94 (0.77-1.14)	246	74	0.82 (0.60-1.11)
Both parents	314	100	0.78 (0.62-0.98)	166	58	0.98 (0.71-1.35)

CI: confidence interval

aAdjusted for age, sex, BMI, smoking, education and HADS score.

Body mass index

In the stratified analysis for body mass index, there was no strong evidence of effect modification. However, offspring who were overweight or obese had the lowest probability of recovery if both parents report activity limiting spinal pain or chronic spinal pain (RR: 0.57; 95% CI: 0.39, 0.84 and RR: 0.79; 95% CI: 0.61, 1.03 respectively) compared to normal weight (Table 4). In addition, there was no clear evidence of statistical interaction neither on the additive (estimates of RERI for chronic spinal pain and activity limiting spinal pain were -0.04; 95% CI: -0.38, 0.30 and -0.34; 95% CI: -0.91, 0.23, respectively) nor on the multiplicative scale (p = 0.54 and p = 0.20, respectively).

Table 4. Relative risk (RR) of recovery from spinal pain and activity limiting spinal pain in adult offspring associated with parental spinal pain; analysis stratified by BMI.

Variables	Normal weight			Overweight/obese		
	No. of persons	No. of cases	Adjusted RR[a] (95% CI)	No. of persons	No. of cases	Adjusted RR[a] (95% CI)
Offspring spinal pain						
Parental spinal pain						
None	168	68	1.00 (Ref.)	177	69	1.00 (Ref.)
Mother or father	316	111	0.88 (0.70-1.12)	380	133	0.89 (0.70-1.12)
Both parents	242	82	0.86 (0.66-1.11)	242	76	0.79 (0.61-1.03)
Offspring activity limiting spinal pain						
Parental spinal pain						
None	86	34	1.00 (Ref.)	130	50	1.00 (Ref.)
Mother or father	151	42	0.72 (0.49-1.04)	301	98	0.72 (0.51-0.99)
Both parents	129	41	0.84 (0.57-1.24)	188	52	0.57 (0.39-0.84)

CI: confidence interval.

aAdjusted for age, sex, leisure physical activity, smoking, education and depression.

DISCUSSION

Summary of findings

The findings of this large population-based prospective family-linkage study indicate that offspring with both parents reporting chronic spinal pain are less likely to recover from chronic spinal pain and activity limiting spinal pain compared with offspring with no parent with spinal pain. Overall, there was no strong evidence that physical activity or body mass index modified these associations, although the results suggest that the inverse association between parental spinal pain and recovery from activity limiting spinal pain was strongest among offspring with a high BMI. This study supports the evidence from twin studies that genetics potentially influences recovery from chronic spinal pain,[41] but these intergenerational associations incorporate shared environmental factors and shared beliefs that could influence recovery. For instance, there is evidence showing that negative beliefs about pain and negative expectations about recovery predict chronic and disabling spinal pain.[42-44] It seems clear that it is important to consider the family history of chronic spinal pain as well as lifestyle behaviours when identifying people at higher risk of non-recovery.

Comparison of findings with previous research

A recent systematic review showed that offspring of parents with chronic pain have poorer outcomes regarding pain, general health, psychological, and family functioning as compared to offspring of parents without pain.[45] The inter-generational transmission of spinal pain could be explained by genetic heritability[9, 10] or a family shared environment.[11-14] Moreover, it has

been suggested that the genetic influence is greater in more disabling pain conditions, such as chronic widespread pain and chronic activity limiting spinal pain, rather than in acute or sub-acute non-debilitating pain.[9, 10] It is widely accepted that lifestyle factors, such as physical activity and body weight, also play a significant role in the prognosis of chronic musculoskeletal pain.[46]

Some studies have suggested that people with chronic back pain who regularly engage in leisure time physical activity have better prognosis measured in terms of pain, disability, and quality of life than those who are sedentary.[29, 47] However, there remains conflicting evidence regarding how physical activity influences the prognosis of spinal pain,[48] with studies demonstrating that both low and high levels of physical activity can negatively influence the prognosis of spinal pain.[49, 50] For instance, a study found that high leisure time physical activity was related to decreased prevalence of low back pain.[51] Whereas another study found that either high or low levels of leisure time physical activity was related to increased prevalence of low back pain.[49] In contrast, a prospective study did not find any significant association between moderate/high levels of leisure physical activity and low back pain in young adults.[52] Another follow-up study found that regular habits of leisure physical activity have no effect on recovery from low back pain.[53] The inconsistency in the literature is possibly attributed to the diverse definitions and classifications of levels of physical activity. If such divergent associations with leisure time physical activity exist this could mask a possible modifying effect of physical activity in our analyses.

The literature has provided evidence that obesity is associated with poor outcomes in people with chronic widespread pain,[54, 55] as well as chronic spinal pain[29, 56, 57] and also decreases the probability of recovery from chronic spinal pain regardless of the care they receive,[25] however, whether BMI could modify[30] the relationship between parental spinal pain on offspring recovery from chronic spinal pain has not been investigated before. Our results suggest that offspring BMI may modify on the parent-offspring association of spinal pain, with somewhat stronger associations among offspring who were classified as overweight or obese than those who were underweight or normal weight. Research has shown that inter-individual differences in pain sensitivity and endogenous pain-inhibitory capacity could reflect variations in the inherent susceptibility for chronic pain,[58, 59] but that a triggering exposure is required for the development of chronic pain.[60, 61] This could suggest that a possible genetic susceptibility for poor recovery from chronic pain[62, 63] as a higher penetrance between offspring who are overweight or obese.

Strengths and limitations

This study has several strengths including the prospective design utilising a large population-based sample with a long follow-up period. In addition, the registry based information on family relations allowed us to include information on chronic spinal pain obtained from parents and offspring independently and at different time points. An important aspect is that the offspring were adults at the time of data collection, indicating that the parent-to-offspring association of chronic spinal pain persists into adulthood when the offspring most likely live apart from their parents. Furthermore, we were able to adjust for several offspring characteristics that could confound the parent-offspring associations of chronic spinal pain, such as age,[64] BMI,[57]

leisure physical activity,[65] smoking,[64] depression[64] and education.[10, 66] However, we cannot exclude the possible residual confounding attributable to unknown or unmeasured factors.

There are some limitations that should be taken into account. First, information on chronic spinal pain was only reported at baseline and at follow-up 10-11 years later, with no information on possible changes in the status of chronic spinal pain during the follow-up period. Consequently, a person could have recovered from spinal pain at some time-point between the surveys, but still report pain at follow-up. However, if parental pain reflects an underlying heritable frailty, this may have an impact also on long-term recurrence and recovery from pain. Likewise, information on leisure time physical activity and BMI was only assessed at baseline, with no information on possible changes during the follow-up period. Second, although the questions about leisure time physical activity used in this study have been reported to have good reliability and provide useful measures of leisure physical activity,[67] subjective interpretations of the activity questions could have influenced the results. Besides, it is well known that self-reports may lead to under or overestimation of the variables of interest.[68] Third, a premise for inclusion into this study was that the mother, father and offspring all had to participate in the health survey. To some extent, this may have resulted in a selected and more health conscious sample than the general population. Nevertheless, it is questionable whether representativeness is a prerequisite for making valid risk assessments in epidemiological studies.[57] Fourth, although the Norwegian Family registry was used to identify family relations between parents and offspring, misclassification of biological family relations in the registry due to adoptions and non-paternity is possible. Although the influence on our results is likely to be small, such misclassification could give attenuated parent-offspring associations. Moreover, we had no information on

whether the offspring shared environment with none, one or both of their biological parents during childhood. Finally, residual confounding due to unmeasured or unknown factors cannot be ruled out.

CONCLUSION

Offspring with chronic spinal pain are less likely to recover if they have parents with chronic spinal pain compared to offspring without parental chronic spinal pain. This association is stronger when the offspring present pain that interferes with their usual work and leisure activities (activity limiting spinal pain). The inverse association between parental chronic spinal pain on recovery was somewhat stronger among offspring who were overweight or obese. The association between parental chronic spinal pain and the prognosis of chronic spinal pain in the adult offspring underlines the importance of identifying those at high risk of non-recovery since they account for significant social and individual financial burden. Therefore, clinicians should consider family history of spinal pain when implementing strategies to improve recovery from chronic spinal pain, chronic spinal pain. For instance, the assessment of the potential risks of physical activity and education about the range of benefits, as well as highlights the importance of maintenance of a normal body weight.

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Author Contributions

All authors critically revised the manuscript for important intellectual content and approved the final manuscript. Please find below a detailed description of the role of each author:

- Anita B Amorim: conception and design, analysis and interpretation of data, drafting and revision of the manuscript, and final approval of the version to be published.
- Paulo H Ferreira: conception and design, interpretation of data, drafting and revision of the manuscript, and final approval of the version to be published.
- Manuela L Ferreira: conception and design, drafting and revision of the manuscript, and final approval of the version to be published.
- Ragnhild Lier: conception and design, drafting and revision of the manuscript, and final approval of the version to be published.

- Milena Simic: conception and design, drafting and revision of the manuscript, and final approval of the version to be published.
- Evangelos Pappas: conception and design, drafting and revision of the manuscript, and final approval of the version to be published.
- Joshua R Zadro: conception and design, interpretation of data, drafting and revision of the manuscript, and final approval of the version to be published.
- Paul Jarle Mork: conception and design, acquisition and interpretation of data, drafting and revision of the manuscript and final approval of the version to be published.
- Tom Ivar Lund Nilsen: conception and design, acquisition and interpretation of data, drafting and revision of the manuscript and final approval of the version to be published.

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Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

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In your methods section, say that you used the STROBE cohort reporting guidelines, and cite them as:

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		Reporting Item	Page Number
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	#3	State specific objectives, including any prespecified hypotheses	5
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	5

	#6b	For matched studies, give matching criteria and number of exposed and unexposed	6
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6, 7 and 8
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	See note 1
Bias	#9	Describe any efforts to address potential sources of bias	8
Study size	#10	Explain how the study size was arrived at	6
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	8
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	8 and 9
	#12b	Describe any methods used to examine subgroups and interactions	8 and 9
	#12c	Explain how missing data were addressed	8 and 9
	#12d	If applicable, explain how loss to follow-up was addressed	8 and 9
	#12e	Describe any sensitivity analyses	8 and 9
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	9 and 10
	#13b	Give reasons for non-participation at each stage	9 and 10
	#13c	Consider use of a flow diagram	n/a
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	9 and 10

		confounders. Give information separately for exposed and unexposed groups if applicable.	
	#14b	Indicate number of participants with missing data for each variable of interest	n/a
	#14c	Summarise follow-up time (eg, average and total amount)	9 and 10
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	10 and 11
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10 and 11
	#16b	Report category boundaries when continuous variables were categorized	10 and 11
	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	10 and 11
Key results	#18	Summarise key results with reference to study objectives	11 and 12
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	13
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	13 and 14
Generalisability	#21	Discuss the generalisability (external validity) of the study results	13 and 14
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15 and 16

Author notes

1. 6, 7 and 8

BMJ Open

The influence of family history on prognosis of spinal pain and the role of leisure time physical activity and body mass index: a prospective study using family-linkage data from the Norwegian HUNT Study.

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The influence of family history on prognosis of spinal pain and the role of leisure time physical activity and body mass index: a prospective study using family-linkage data from the Norwegian HUNT Study.

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ABSTRACT

Objectives: To investigate the influence of parental chronic spinal pain on prognosis of chronic spinal pain in adult offspring, and whether offspring physical activity level and body mass index (BMI) modified this association.

Design: Prospective cohort study.

Setting: We used family linked longitudinal data from the Norwegian HUNT study collected in HUNT2 (1995-97) and HUNT3 (2006-08).

Participants: A total of 1,529 offspring who reported spinal pain in HUNT2 were linked with parental data and followed-up in HUNT3.

Outcomes: We estimated relative risk (RR) with 95% confidence intervals (CIs) for recovery from chronic spinal pain, and also from activity limiting spinal pain, in offspring related to chronic spinal pain in parents. We also investigated whether offspring leisure time physical activity and BMI modified these intergenerational associations in spinal pain.

Results: A total of 540 (35%) offspring were defined as recovered after approximately 11 years of follow-up. Offspring with both parents reporting chronic spinal pain were less likely to recover from chronic spinal pain (RR: 0.83, 95% CI: 0.69, 0.99) and activity limiting spinal pain (RR: 0.71, 95% CI: 0.54, 0.94), compared to offspring of parents without chronic spinal pain. Analyses stratified by BMI and physical activity showed no strong evidence of effect modification on these associations. However, offspring who were overweight/obese and with both parents reporting chronic spinal pain had particularly low probability of recovery from activity limiting spinal pain, compared to those who were normal weight and had parents without chronic spinal pain (RR: 0.57, 95% CI: 0.39-0.84).

Conclusion: Offspring with chronic spinal pain are less likely to recover if they have parents with chronic spinal pain, particularly if offspring are overweight/obese.

Key words: Low back pain, neck pain, chronic pain, obesity, family study, physical activity.

Strengths and limitations of this study

- The HUNT Study is a large population-based health study with longitudinal data that allows prospective analysis on the prognosis of chronic spinal pain.
- Chronic spinal pain was independently reported in parents and offspring; family relations was informed by a linkage with a national registry; and the data allowed us to control for a wide range of potential confounders.
- Information on pain status, physical activity, and body mass index was not updated throughout the follow-up period.

INTRODUCTION

Spinal pain that includes low back and neck pain is highly prevalent and a common cause of disability worldwide.[1] The natural history of spinal pain is extremely variable and may last a few days or persist for many years.[2] A substantial proportion of patients recover within the first three months of a spinal pain episode, but around three quarters of the remaining patients are likely to experience pain one year after onset.[3, 4] People who fail to recover in the first few months following an acute episode are at greater risk of poor prognosis.[5] Spinal pain, especially in its chronic and disabling form, could be a significant personal and financial burden,[6] and may also influence families and society.[1] It is therefore vital to identify factors that influence prognosis of spinal pain, which in turn can inform preventive interventions to reduce chronicity.

Family studies have suggested that chronic pain aggregate in families,[7, 8] with the parent-offspring transmission of chronic pain explained by genetic heritability[9, 10] and shared environment factors.[11-14] The mean heritability of chronic low back pain is 67%,[10, 15] suggesting that a substantial proportion of the risk of developing chronic spinal pain is driven by genetics. However, families also share similar lifestyles and express similar health behaviours and beliefs. This suggests shared environmental factors[8, 16] could also have an important influence on the prognosis of spinal pain.[17, 18]

Parental pain is strongly associated with the increased risk of chronic musculoskeletal pain in offspring, both during adolescence,[7] and in later adulthood.[19] Furthermore, there is preliminary evidence that treatment response in patients with chronic low back pain is influenced by genetic factors.[20] It is, therefore, possible that parental history of spinal pain influences the

prognosis of spinal pain in offspring. Conversely, several studies have shown that engagement in moderate to vigorous-intensity leisure time physical activity and maintenance of a normal body mass index (BMI) are associated with better prognosis of spinal pain.[21-25] Thus, a healthy offspring lifestyle could modify a possible adverse effect of parental spinal pain on prognosis of offspring spinal pain. Currently, there is limited knowledge about the influence of parental spinal pain on prognosis of spinal pain in offspring and whether this association is modified by offspring lifestyle.

In this study, we have used population-based longitudinal data from the Norwegian HUNT Study to investigate the influence of parental spinal pain on the prognosis of chronic spinal pain regarding severity and activity limitation in the adult offspring. We have also investigated whether offspring leisure time physical activity and BMI modify any of these associations.

METHODS

Study population

The HUNT Study is a population-based health study conducted within the county of Nord-Trøndelag, Norway. The study was performed in three consecutive waves, first in 1984–1986 (HUNT1), then in 1995–1997 (HUNT2), and last in 2006–2008 (HUNT3). In all three surveys, all residents 20 years of age and older were invited to participate, and information on lifestyle and health-related factors were collected by questionnaires and a clinical examination. Information on musculoskeletal pain was not collected at HUNT1. Therefore, those who were eligible for inclusion in this study had participated at HUNT2 and HUNT3. At HUNT2, 93,898 individuals were invited to participate, and 65,237 (65.5%) joined the study, while at HUNT3

93,860 were invited and 50,807 (54.1%) agreed to participate.[26, 27] Each participant signed written consent, and the study was approved by the Regional Committee for Medical and Health Research Ethics Central Norway (ref. no. 2011/1455). Further information about selection procedures, participation and questionnaires used in the HUNT study can be found at http://www.ntnu.edu/hunt.

Patient involvement

Since historical cohort data was used in this study, patients were not involved in the conduct and design of the study.

Record linkage

The unique 11-digit personal identification number held by all Norwegian citizens was used to link each participant's record to information from the Family Registry at Statistics Norway, and there by establish a link between parents and offspring who participated in one or both of HUNT2 and HUNT3. The Family Registry provide data on persons registered as legal parents, either as biological parents or through adoption. A total of 11,483 offspring reported spinal pain at HUNT2, and of these, 6,662 could be followed-up on spinal pain status in HUNT3, approximately 11 years later. To be able to study the association between parental spinal pain and offspring prognosis of spinal pain, we selected all 1,529 parent–offspring trios (i.e., mother, father and adult offspring) where both the mother and the father had information on spinal pain from HUNT2.

Chronic spinal pain

At HUNT2 and HUNT3, participants were asked to complete the Standardized Nordic Questionnaire which has acceptable reliability and validity.[28] The question regarding musculoskeletal pain was as follows: "In the last year, have you had pain and/or stiffness in muscles or joints that have lasted at least 3 consecutive months?" (response options: "no" and "yes"). Participants who answered "yes" were asked to indicate the affected body area(s). Offspring who reported chronic neck and/or low back pain (spinal pain) at HUNT2 were included in this study, and offspring who also reported spinal pain at HUNT3 were considered not recovered (outcome measure). Offspring reporting spinal pain at HUNT2 were also asked to indicate if the pain had led to reduced leisure time activity (response options: "no" and "yes") or reduced their work ability (response options: "no", "to some extent", "considerably" or "don't know"). Offspring who answered "yes" to the question on reduced leisure time activity and/or reported work ability to be reduced "to some extent" or "considerably", were classified as having "activity limiting spinal pain". In secondary analyses, we used this information to investigate the prognosis of activity limiting spinal pain; i.e., recovery was defined as not reporting activity limiting spinal pain at HUNT3. Based on the same question as described above, we obtained information on parental chronic spinal pain. Further, we created a variable with four mutually exclusive categories for presence of parental chronic spinal pain at baseline (exposure measure): "none", "mother", "father" or "both parents".

Leisure time physical activity

Leisure time physical activity was assessed by the following question "How much of your leisure time have you been physically active during the last year? (Think of a weekly average for the

year. Your commute to work counts as leisure time)". Participants reported the number of hours of either light (no sweating or heavy breathing) or hard (sweating and heavy breathing) activity using the response options "none", "less than 1 hour", "1–2 hours" and "3 or more hours" for each type of activity. Based on this information, we constructed a variable with four categories (combining information on light and hard activity): 1) "inactive" (no light or hard activity), 2) "low activity" (<3 hours light and no hard activity), 3) "moderate activity" (≥3 hours light and/or <1 hour hard activity), and 4) "high activity" (any light and ≥1 hour hard activity). In the combined analyses of parental chronic spinal pain and offspring leisure time physical activity the categories "inactive" and "low activity" were collapsed into one category labelled "Physically inactive" and the categories "moderate activity" and "high activity" were collapsed into one category labelled "Physically active". This categorization has been used previously in other studies based in data from HUNT.[29, 30] We did not conduct analyses stratified by physical activity status on the outcome "activity limiting spinal pain", since people with activity limiting spinal pain are likely to have limited engagement in leisure and work activities.

Body mass index

Standardized measurements of body height (to the nearest centimetre) and body weight (to the nearest half kilogram) were obtained at clinical examination. BMI was calculated as weight divided by the square of height (kg/m^2), and classified into four BMI groups according to the cut-off points suggested by the World Health Organization:[31] underweight (BMI <18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25.0–29.9 kg/m^2) and obese (BMI ≥30.0 kg/m^2). Only 27 participants (1 %) were classified as "underweight", and the combined analysis of parental chronic spinal pain and offspring BMI, the categories "underweight" and

"normal weight" were collapsed into one category labelled "normal weight". The categories "overweight" and "obese" were collapsed into one category labelled "overweight/obese".

Statistical analysis

We used a Poisson regression model[32-35] to estimate relative risk (RR) of chronic spinal pain and activity limiting spinal pain in offspring whose parents reported chronic spinal pain, using parents with no chronic spinal pain as the reference category. Precision of estimates was assessed by a 95% confidence interval (CI). All standard errors were adjusted for within-family clustering (i.e., siblings) using the vce (cluster) option in Stata, treating observations between families as independent and within families as dependent, and thus avoiding inflated precision of the estimated associations.[36]

Possible effect modification by offspring leisure time physical activity or offspring BMI was assessed by stratified analyses (i.e., physically active vs physically inactive and normal weight vs overweight/obese) as well as by tests of the estimated relative excess risk due to interaction (RERI) (i.e., departure from additive effects). We calculated RERI estimates with 95% CIs from the following equation: $\text{RERI} = \text{RR}_{\text{parental pain \& physically active/overweight and/or obese}} - \text{RR}_{\text{noparental pain \& physically activity/ overweight and/or obese}} - \text{RR}_{\text{parental pain \& physically inactivity/normal weight}} + 1$,[37] i.e., RERI > 0 indicate a synergistic effect beyond an additive effect. Statistical interaction was also evaluated on a multiplicative scale by a likelihood ratio test of a product term in the model (these likelihood ratio tests had to be run without cluster-adjusted standard errors to avoid misspecification of the model).

The main analyses (parental influence on risk of poor prognosis) were adjusted for possible confounding by offspring sex (male, female), age (continuous), BMI ("underweight", "normal weight", "overweight", "obese" or "unknown"), leisure time physical activity ("physically inactive", "physically active" or "unknown"), education ("<10 years", "10–12 years", ">13 years" or "unknown"), and depression ("depressed", "not depressed" or "unknown"). Depression was assessed using the depression subscale of the Hospital Anxiety and Depression Scale (HADs) using a score of 8 as a cut-off for a dichotomised variable.[38-40]

All statistical tests were two-sided, and all analyses were conducted using Stata statistical software (version 13.0, STATA Corp., College Station, TX, USA).

RESULTS

In this prospective study of 1,529 offspring with chronic spinal pain at baseline, a total of 540 (35%) offspring were defined as recovered after approximately 11 years of follow-up. Additionally, among 775 offspring with activity limiting spinal pain, 244 were defined as recovered at follow-up. Descriptive statistics of offspring, mothers and fathers are shown in Table 1. The mean age at baseline was 32.8 (8.6) years among offspring. Most offspring were physically active (63.9%), and nearly half of the offspring (42.3%) were classified as overweight or obese. About one third (33.1%) of the offspring were current smokers, and just a small portion of offspring (20.7%) reported having a higher education degree. A small proportion (10.4%) of offspring had symptoms of depression according to the Hospital Anxiety and Depression Scale.

Table 1. Baseline characteristics of the study population at HUNT2

Variables	Offspring	Mothers	Fathers
Participants, no.	1,529	1,529	1,529
Age, mean (SD)	32.8 (8.6)	63.8 (9.4)	67.2 (9.5)
Body mass index, mean (SD)	25.9 (5.2)	28.3(7.3)	27.6 (6.9)
Overweight/obese, % (n)	42.3 (799)	70.6 (1,080)	72.2 (1,104)
Physically active[a], % (n)	63.9 (977)	43.0 (510)	57.7 (716)
Current smoker, % (n)*	33.1 (506)	26.3 (400)	28.5 (434)
Higher education[b], % (n)	20.7 (316)	4.5 (61)	6.0 (84)
Symptoms of depression[c], %, (n)	10.4 (155)	17.0 (225)	16.5 (215)

SD, standard deviation

[a]Engagement in moderate (≥3 hours light and/or <1 hour hard activity per week) or high leisure time physical activity (any light and ≥1 hour hard activity per week)

[b]University education or higher

[c]Score ≥8 on the Hospital Anxiety and Depression Scale

Chronic spinal pain and activity limiting spinal pain

Offspring with both parents reporting chronic spinal pain were less likely to recover from chronic spinal pain (RR: 0.83, 95% CI: 0.69, 0.99) and activity limiting spinal pain (RR: 0.71, 95% CI: 0.54-0.94) compared to offspring with no parents with chronic spinal pain (Table 2). These associations were weaker and less precise when chronic spinal pain was present in only one parent, with similar associations observed for maternal and paternal spinal pain.

Table 2. Relative risk (RR) of recovery from spinal pain and activity limiting spinal pain in adult offspring associated with parental spinal pain.

	Offspring spinal pain				Offspring activity limiting spinal pain			
Parental spinal pain	No. of persons	No. of cases	Crude RR	Adjusted RR[a] (95% CI)	No. of persons	No. of cases	Crude RR	Adjusted RR[a] (95% CI)
None	346	138	1.00	1.00 (Ref.)	163	66	1.00	1.00 (Ref.)
Mother	424	147	0.88	0.90 (0.75-1.07)	214	62	0.73	0.74 (0.56-0.98)
Father	272	97	0.90	0.91 (0.74-1.12)	127	40	0.77	0.78 (0.57-1.05)
Both	487	158	0.82	0.83 (0.69-0.99)	271	76	0.69	0.71 (0.54-0.94)

CI, confidence interval

[a]Adjusted for age, sex, BMI, smoking, leisure time physical activity, education and HADS score.

Physical activity

In the stratified analysis for physical activity, there was no strong evidence of effect modification for either physically active offspring (RR: 0.78; 95% CI: 0.62, 0.98), or physically inactive offspring (RR: 0.98; 95% CI: 0.71, 1.36) (Table 3). Tests of statistical interaction indicate no departure from neither multiplicative (p = 0.11) nor additive effects (RERI: 0.19; 95% CI: -0.17, 0.55), data not shown.

Table 3. Relative risk (RR) of recovery from spinal pain in adult offspring associated with parental spinal pain; analysis stratified by leisure time physical activity.

	Physically active			Physical inactive		
Parental spinal pain	No. of persons	No. of cases	Adjusted RR[a] (95% CI)	No. of persons	No. of cases	Adjusted RR[a] (95% CI)
None	229	97	1.00 (Ref.)	111	40	1.00 (Ref.)
Mother or father	434	163	0.94 (0.77-1.14)	246	74	0.82 (0.60-1.11)
Both parents	314	100	0.78 (0.62-0.98)	166	58	0.98 (0.71-1.35)

CI: confidence interval

[a]Adjusted for age, sex, BMI, smoking, education and HADS score.

Body mass index

In the stratified analysis for body mass index, there was no strong evidence of effect modification. However, offspring who were overweight or obese and with both parents reporting chronic spinal pain had the lowest probability of recovery from activity limiting spinal pain or chronic spinal pain (RR: 0.57; 95% CI: 0.39, 0.84 and RR: 0.79; 95% CI: 0.61, 1.03, respectively), compared to those who were normal weight and had parents without chronic spinal pain (Table 4). In addition, there was no clear evidence of statistical interaction neither on the additive (estimates of RERI for chronic spinal pain and activity limiting spinal pain were -0.04; 95% CI: -0.38, 0.30 and -0.34; 95% CI: -0.91, 0.23, respectively) nor on the multiplicative scale ($p = 0.54$ and $p = 0.20$, respectively).

Table 4. Relative risk (RR) of recovery from spinal pain and activity limiting spinal pain in adult offspring associated with parental spinal pain; analysis stratified by BMI.

Variables	Normal weight			Overweight/obese		
	No. of persons	No. of cases	Adjusted RR[a] (95% CI)	No. of persons	No. of cases	Adjusted RR[a] (95% CI)
Offspring spinal pain						
Parental spinal pain						
None	168	68	1.00 (Ref.)	177	69	1.00 (Ref.)
Mother or father	316	111	0.88 (0.70-1.12)	380	133	0.89 (0.70-1.12)
Both parents	242	82	0.86 (0.66-1.11)	242	76	0.79 (0.61-1.03)
Offspring activity limiting spinal pain						
Parental spinal pain						
None	86	34	1.00 (Ref.)	130	50	1.00 (Ref.)
Mother or father	151	42	0.72 (0.49-1.04)	301	98	0.72 (0.51-0.99)
Both parents	129	41	0.84 (0.57-1.24)	188	52	0.57 (0.39-0.84)

CI: confidence interval.

[a]Adjusted for age, sex, leisure physical activity, smoking, education and depression.

DISCUSSION

Summary of findings

The findings of this large population-based prospective family-linkage study indicate that offspring with both parents reporting chronic spinal pain are less likely to recover from chronic spinal pain and activity limiting spinal pain compared with offspring with no parent with spinal pain. Overall, there was no strong evidence that physical activity or body mass index modified these associations, although the results suggest that the inverse association between parental spinal pain and recovery from activity limiting spinal pain was strongest among offspring with a high BMI. This study supports the evidence from twin studies that genetics potentially influences recovery from chronic spinal pain,[41] but these intergenerational associations incorporate shared environmental factors and shared beliefs that could influence recovery. For instance, there is evidence showing that negative beliefs about pain and negative expectations about recovery predict chronic and disabling spinal pain.[42-44] It seems clear that it is important to consider the family history of chronic spinal pain as well as lifestyle behaviours when identifying people at higher risk of non-recovery.

Comparison of findings with previous research

A recent systematic review showed that offspring of parents with chronic pain have poorer outcomes regarding pain, general health, psychological, and family functioning as compared to offspring of parents without pain.[45] The inter-generational transmission of spinal pain could be explained by genetic heritability[9, 10] or a family shared environment.[11-14] Moreover, it has

been suggested that the genetic influence is greater in more disabling pain conditions, such as chronic widespread pain and chronic activity limiting spinal pain, rather than in acute or sub-acute non-debilitating pain.[9, 10] It is widely accepted that lifestyle factors, such as physical activity and body weight, also play a significant role in the prognosis of chronic musculoskeletal pain.[46]

Some studies have suggested that people with chronic back pain who regularly engage in leisure time physical activity have better prognosis measured in terms of pain, disability, and quality of life than those who are sedentary.[29, 47] However, there remains conflicting evidence regarding how physical activity influences the prognosis of spinal pain,[48] with studies demonstrating that both low and high levels of physical activity can negatively influence the prognosis of spinal pain.[49, 50] For instance, a study found that high leisure time physical activity was related to decreased prevalence of low back pain.[51] Whereas another study found that either high or low levels of leisure time physical activity was related to increased prevalence of low back pain.[49] In contrast, a prospective study did not find any significant association between moderate/high levels of leisure physical activity and low back pain in young adults.[52] Another follow-up study found that regular habits of leisure physical activity have no effect on recovery from low back pain.[53] The inconsistency in the literature is possibly attributed to the diverse definitions and classifications of levels of physical activity. If such divergent associations with leisure time physical activity exist this could mask a possible modifying effect of physical activity in our analyses.

The literature has provided evidence that obesity is associated with poor outcomes in people with chronic widespread pain,[54, 55] as well as chronic spinal pain[29, 56, 57] and also decreases the probability of recovery from chronic spinal pain regardless of the care they receive,[25] however, whether BMI could modify[30] the relationship between parental spinal pain on offspring recovery from chronic spinal pain has not been investigated before. Our results suggest that offspring BMI may modify on the parent-offspring association of spinal pain, with somewhat stronger associations among offspring who were classified as overweight or obese than those who were underweight or normal weight. Research has shown that inter-individual differences in pain sensitivity and endogenous pain-inhibitory capacity could reflect variations in the inherent susceptibility for chronic pain,[58, 59] but that a triggering exposure is required for the development of chronic pain.[60, 61] This could suggest that a possible genetic susceptibility for poor recovery from chronic pain[62, 63] as a higher penetrance between offspring who are overweight or obese.

Strengths and limitations

This study has several strengths including the prospective design utilising a large population-based sample with a long follow-up period. In addition, the registry based information on family relations allowed us to include information on chronic spinal pain obtained from parents and offspring independently and at different time points. An important aspect is that the offspring were adults at the time of data collection, indicating that the parent-to-offspring association of chronic spinal pain persists into adulthood when the offspring most likely live apart from their parents. Furthermore, we were able to adjust for several offspring characteristics that could confound the parent-offspring associations of chronic spinal pain, such as age,[64] BMI,[57]

leisure physical activity,[65] smoking,[64] depression[64] and education.[10, 66] However, we cannot exclude the possible residual confounding attributable to unknown or unmeasured factors.

There are some limitations that should be taken into account. First, information on chronic spinal pain was only reported at baseline and at follow-up 10-11 years later, with no information on possible changes in the status of chronic spinal pain during the follow-up period. Consequently, a person could have recovered from spinal pain at some time-point between the surveys, but still report pain at follow-up. However, if parental pain reflects an underlying heritable frailty, this may have an impact also on long-term recurrence and recovery from pain. Likewise, information on leisure time physical activity and BMI was only assessed at baseline, with no information on possible changes during the follow-up period. Second, although the questions about leisure time physical activity used in this study have been reported to have good reliability and provide useful measures of leisure physical activity,[67] subjective interpretations of the activity questions could have influenced the results. Besides, it is well known that self-reports may lead to under or overestimation of the variables of interest.[68] Third, a premise for inclusion into this study was that the mother, father and offspring all had to participate in the health survey. To some extent, this may have resulted in a selected and more health conscious sample than the general population. Nevertheless, it is questionable whether representativeness is a prerequisite for making valid risk assessments in epidemiological studies.[57] Fourth, although the Norwegian Family registry was used to identify family relations between parents and offspring, misclassification of biological family relations in the registry due to adoptions and non-paternity is possible. Although the influence on our results is likely to be small, such misclassification could give attenuated parent-offspring associations. Moreover, we had no information on

whether the offspring shared environment with none, one or both of their biological parents during childhood. Finally, residual confounding due to unmeasured or unknown factors cannot be ruled out.

CONCLUSION

Offspring with chronic spinal pain are less likely to recover if they have parents with chronic spinal pain compared to offspring without parental chronic spinal pain. This association is stronger when the offspring present pain that interferes with their usual work and leisure activities (activity limiting spinal pain). The inverse association between parental chronic spinal pain on recovery was somewhat stronger among offspring who were overweight or obese. The association between parental chronic spinal pain and the prognosis of chronic spinal pain in the adult offspring underlines the importance of identifying those at high risk of non-recovery since they account for significant social and individual financial burden. Therefore, clinicians should consider family history of spinal pain when implementing strategies to improve recovery from chronic spinal pain, chronic spinal pain. For instance, the assessment of the potential risks of physical activity and education about the range of benefits, as well as highlights the importance of maintenance of a normal body weight.

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Author Contributions

All authors critically revised the manuscript for important intellectual content and approved the final manuscript. Please find below a detailed description of the role of each author:

- Anita B Amorim: conception and design, analysis and interpretation of data, drafting and revision of the manuscript, and final approval of the version to be published.
- Paulo H Ferreira: conception and design, interpretation of data, drafting and revision of the manuscript, and final approval of the version to be published.
- Manuela L Ferreira: conception and design, drafting and revision of the manuscript, and final approval of the version to be published.
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- Paul Jarle Mork: conception and design, acquisition and interpretation of data, drafting and revision of the manuscript and final approval of the version to be published.
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Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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In your methods section, say that you used the STROBE cohort reporting guidelines, and cite them as:

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		Reporting Item	Page Number
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	#3	State specific objectives, including any prespecified hypotheses	5
Study design	#4	Present key elements of study design early in the paper	5
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	5

	#6b	For matched studies, give matching criteria and number of exposed and unexposed	6
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6, 7 and 8
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	See note 1
Bias	#9	Describe any efforts to address potential sources of bias	8
Study size	#10	Explain how the study size was arrived at	6
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	8
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	8 and 9
	#12b	Describe any methods used to examine subgroups and interactions	8 and 9
	#12c	Explain how missing data were addressed	8 and 9
	#12d	If applicable, explain how loss to follow-up was addressed	8 and 9
	#12e	Describe any sensitivity analyses	8 and 9
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	9 and 10
	#13b	Give reasons for non-participation at each stage	9 and 10
	#13c	Consider use of a flow diagram	n/a
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	9 and 10

		confounders. Give information separately for exposed and unexposed groups if applicable.	
	#14b	Indicate number of participants with missing data for each variable of interest	n/a
	#14c	Summarise follow-up time (eg, average and total amount)	9 and 10
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	10 and 11
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10 and 11
	#16b	Report category boundaries when continuous variables were categorized	10 and 11
	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	10 and 11
Key results	#18	Summarise key results with reference to study objectives	11 and 12
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	13
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	13 and 14
Generalisability	#21	Discuss the generalisability (external validity) of the study results	13 and 14
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15 and 16

Author notes

1. 6, 7 and 8