OPEN

PAIN Publish Ahead of Print
DOI: 10.1097/j.pain.0000000000001062

Chronic pain in families: A cross-sectional study of shared social, behavioural, and environmental influences

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Key words

Chronic pain, Family, Multilevel Modelling, Social, Generation Scotland, Concordance

Pages – 21

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Abstract

Chronic pain is common and creates significant burden to the individual and society. Emerging research has shown the influence of the family environment on pain outcomes. However it is not clear what shared factors between family members associate with chronic pain. This study aimed to investigate the family level contribution to an individual's chronic pain status. This was a cross sectional study using the Generation Scotland: Scottish Family Health Study dataset. This study focused on a nested cohort of dyads (only 2 relatives per family, n = 2714). Multilevel modelling was first carried out to estimate the extent of variance in chronic pain at the family level. Then each member of the dyad was randomly assigned as either the exposure or outcome family member and logistic regression was used to identify shared factors associated with the outcome of chronic pain status. Multilevel modelling showed just under 10% of variation in chronic pain status was at a family level. There was an increase in odds of chronic pain if exposure family member had chronic pain (OR 1.30, 95% CI 1.02, 1.65), if both were female (OR 1.39, 95% CI 0.99, 1.94), both older age (OR 1.80, 95% CI 1.31, 2.48), and if both had low household income (OR 3.27, 95% CI 1.72, 6.21). These findings show that the majority of explanation for chronic pain is still at the individual level. However some significant shared effects between family members associate with chronic pain, and this highlights the influence of the family context.

1.0 Introduction

Chronic pain is common within the population and has an impact on the individual, their family, and wider society [3,50]. There are complex interactions between the individual with chronic pain and their family environment. Evidence shows the influence and impact of chronic pain on family members, in terms of the adjustments family members make (for example, possible employment changes),

relationship changes (for example, marital quality), and potential role changes (for example, becoming a caregiver for the person with pain and associated disability) [25,26,29,45]. The converse is also possible, that the family has an influence on the individual with chronic pain; numerous studies show the effects of family members, particularly partners, on the outcomes of those with chronic pain conditions, for example solicitous responses (e.g. being overly helpful with tasks and duties), mood influences and negative reactions (e.g. anger and frustration in partners) affecting relationship quality [6,8,9,49]. Evidence also exists of more direct influences and interactions at a biological/genetic level between family members. A number of twin and family studies have reported shared biological heritability concordance (shared risk) between family members for pain conditions [21,23,48]. For example Hocking et al [23] report that the genetic heritability estimate for chronic pain was 29% in a study of 2195 extended families, and another study [21] has shown a significant association between maternal and related adolescent chronic pain.

Research on specific conditions such as face pain, stomach pain, and headache has shown that family members are more likely to have similar symptoms, or have elevated levels of poor health compared to non-family members [11,28]. Families are also likely to share similar lifestyles, and express similar health behaviours and beliefs [18,30], and a significant amount of healthcare engagement can be explained at a family level [12,13]. Furthermore, families are likely to share the same environment, and so share similar economic status, educational status, and access to health services [10,35,40]. Recently a paper described concordance between partners (e.g. husband, wife) for musculoskeletal pain; concordance was partly explained in terms of the shared lifestyle and environment between couples [7]. Overall, this evidence suggests that, aside from biological and genetic propensity, there might be other important shared influences to explain concordance between family members. A recent heritability twin study carried out by Vehof et al [48] show that 7% to 10% of the variance in Chronic Pain Syndrome is explained by the common environment (i.e. shared social factors) over and above genetic and individual contribution. Clearly shared effects between family members are present, but currently we do not know what the specific shared factors are that may result in increased concordance for pain conditions. The aim of this study was to investigate the family

level contribution to chronic pain status within the individual, and describe which shared factors are associated with chronic pain.

2.0 Methods

2.1 Design and participants

This is a cross-sectional analysis of participants in the Generation Scotland: Scottish Family Health Survey (GS:SFHS [42]). Briefly the GS:SFHS identified potential participants at random from people aged 35 to 65 registered at collaborating primary care medical practices throughout areas of Scotland. Participants were invited to take part and to identify at least one first-degree relative (i.e. the index person's mother, father, sister, brother, adult child) aged 18 years or over to also take part. Volunteers from anywhere in Scotland were also welcomed to participate in GS: SFHS, again with the request that one or more first-degree relatives (aged 18 or over) also agree to take part. In total 126,000 probands were invited with 12.3% volunteering and meeting the Generation Scotland inclusion criteria [43].

Participants completed pre-clinic health questionnaires and attended research clinics for a physical examination, and mental health and cognitive function assessment. In total, at the time of this study, 21,327 individuals were participating forming 2195 family groups. Fuller details of the recruitment process are given elsewhere ([42,43], www.generationscotland.org). The GS: SFHS was approved by the Tayside Committee on Medical Research Ethics (reference 05/S1401/89).

The current study focuses on a nested cohort of the total population. We included index participants who only recruited one other first-degree relative (n = 2714 individuals forming 1357 family dyads). This strategy was specifically chosen on the basis of the analysis design where each member of the family dyad was randomly assigned as either the exposure or outcome. This ensured that each family member was a first degree relative, with the rationale that first-degree relatives (e.g. mother, father, brother, sister, adult child) would be more likely to experience, or have experienced, shared factors (e.g. economic, physical activity, health behaviour, psychological) compared to second degree or

more distant relatives. For example, first-degree relatives would most likely live or have lived in the same household as each other at some point, and have demonstrated continued contact with each other.

2.2. Measures

The outcome measure of chronic pain is based on the definition developed for the International Association for the Study of Pain (IASP) [34]. Chronic pain was assessed within the pre-clinic questionnaire, and participants were asked if they currently experienced continuous or intermittent pain, and if yes, whether this pain had lasted for at least 3 months or more. Those answering yes to both of these questions were classified as having chronic pain.

Potential shared physical factors include age (categorised in age bands 18 to 29, 30 to 49, 50 to 69, 70+ years), gender, weight (categorised as underweight/normal *versus* overweight/obese/severely obese using BMI cut-off ≥ 25). Potential shared health behavioural factors included smoking status (never smoked *versus* current smoker/ previously smoked), and whether the participant lived with someone who currently smokes. Education level was based on the number of years the participant was at school full time or in further study full time. Three categories were created to follow the UK's Educational system (UK Government [14]), compulsory education (e.g. primary/secondary education up to 11 years of education), further education (e.g. college education, 12 to 15 years), and higher education (e.g. university, > 15 years). Social environment measured whether the participant lived with a partner (e.g. husband, wife, cohabitee). Financial status was measured as annual household income (categorised as £0 < £30,000, £30,000 to £50,000, and > £50,000), and accommodation status categorised as: own home outright, current mortgage, currently rent, other. Finally, we measured potential shared psychological status using the general health questionnaire version 28 (GHQ 28, categorised using the recommended cut off score of 5 or above to indicate psychological morbidity [31,32,39]).

2.3. Statistical analysis

Analysis was conducted within the GS:SFHS dataset. The aim of this study did not overlap with any previous study using this data. A two-stage process was applied to address the research aim. The first stage investigated explanatory variables associated with the outcome of chronic pain across the cohort, with a multi-level model producing an estimation of the amount of variance in chronic pain status that was at the family rather than individual level. A two level hierarchical model was used, with individual participants (level 1) nested within their respective family dyads (level 2). An initial variance components model (i.e. no explanatory variables entered) was carried out to establish whether there was a significant effect at level 2 (family effect) using the Likelihood Ratio (LR) test [44]. A variance partition coefficient (VPC) was calculated (VPC = $\frac{\sigma_u^2}{\sigma_u^2 + \sigma_e^2}$ where σ_u^2 = residual variance (level 2), and σ_e^2 = 3.29 (logit), to estimate the proportion (%) of variance in chronic pain at the family level [1,44]. The use of a logit function is appropriate for a binary outcome multi-level model. The standard logistic distribution ($\pi^2/3$ = 3.29) is taken as the measure of level 1 variance, allowing for comparison on the same scale for level 2 variance, with VPC as the calculation of the ratio of level 2 variance to the sum of the level 1 and level 2 variances [43]. Then explanatory variables (individual's age, gender, weight, smoking status, live with smoker, education level, live with partner, household income, accommodation status, psychological status) were then entered into the model singularly (univariable multilevel logistic regression models) to estimate the significant factors associated with chronic pain. All variables were then placed within a final multivariable multilevel logistic regression model. This model was used to test the associations of the variables with chronic pain across the cohort (i.e. the general effect of variables on outcome) with a further VPC calculation carried out to produce an estimate of unexplained variance residing at level 2 (family) within the final multivariable model (i.e. proportion of variance in chronic pain status at a family level).

The second stage of the analysis considered how the significant explanatory variables from the first stage interrelate between family members to estimate the shared effect on chronic pain status. In order to model this, each participant within each family dyad was randomly assigned to be either an "index" family member (outcome being chronic pain status), or "exposure" family member following

previous methodology [7]. Variables significant from the multivariable multilevel model at the first stage were then entered as shared (i.e. using measures from both family members) potential predictors of chronic pain in the index participant using logistic regression producing Odds Ratios (ORs) and 95% confidence intervals (95% CI). Statistical adjustment was made for the age of both family members and the exposure family member's chronic pain status (to ensure shared effect was not an artefact of pain status). Using gender in association with the index family member's chronic pain outcome as an example; the analysis considered the independent association of the index family member's gender, then the independent association of the exposure family member's gender, and finally a shared analysis (i.e. index family member female and exposure family member male, index family member male and exposure family member female, both family members female compared to where both family members are male). Whilst the use of logistic regression is appropriate for this cross sectional design there are issues in the interpretation of effect size (relative effect) where the prevalence of the outcome is large. It is shown for example that the interpretation of ORs generated from populations where the prevalence of outcome is low (i.e. rare disease assumption) are comparable to estimates of relative risk (RR), however where prevalence of outcome is high (e.g. > 10%) the reported ORs can overestimate the relative effect [16,41]. Given that previous studies within the Generation Scotland population [23,43] have reported a high prevalence of chronic pain status (> 30%), this study will, alongside ORs, also report the prevalence percentage difference. The prevalence percentage difference will be calculated to show the difference from the reference category prevalence of chronic pain and the influence of exposure from both the index family member and the exposure family member. Complete case analysis was carried out due to the low level of missing data [42], and analysis was performed using SPSS version 21 and STATA 13 (STATA binary level multilevel modelling command *xtmelogit*).

To determine whether 2 member family dyads in this current study were different to those within Generation Scotland with more family members (e.g. 3, 4, 5, 6, 7 or more), we compared size of family block across a range of variables (chronic pain status, age, gender, BMI, smoking status, education level, lives with a partner, household income, accommodation status, psychological

morbidity) using one way ANOVA (continuous variables) or Chi Square (categorical) tests. These tests show no significant differences on any variables dependent on family size block (data not shown).

3.0 Results

Characteristics of the cohort are described in Table 1. The mean age was 47 years (standard deviation 15 years), 59% were female and just over 36% of the cohort indicated the presence of chronic pain.

Insert Table 1 about here

3.1 Stage 1: Multilevel modelling

Table 2 shows the results of the multilevel logistic regression analysis (stage 1). The multilevel univariable logistic regression results showed that age (being in older age bands), gender (being female), smoking status (currently or previously a smoker), living with a current smoker, educational level (having fewer years of education), household income (having less income), were all associated with increased odds of chronic pain. Having a mortgage (compared to owning your home outright) decreased the odds of reporting chronic pain. Being overweight or obese, not living with a partner, and having psychological morbidity were not significantly associated with chronic pain. The final multilevel multivariable logistic regression model showed that female gender, increased age, lower income, and smoking were significantly associated with increased odds of reporting chronic pain. The initial multilevel variance components model (i.e. no explanatory variables added) indicated a significant family level effect (LR test 4.81, p =0.01) with 8.1% of variation in chronic pain status residing at the family rather than individual level. LR tests for all univariable and multivariable models were significant, indicating the presence of a significant family level effect, and the final multilevel multivariable model VPC was 9.8% (LR test 4.15, p = 0.02, 9.8% unexplained variance at family level).

Insert Table 2 about here

3.2 Stage 2: shared effect analysis

Table 3 outlines the shared effects of the significant factors associated with chronic pain from stage 1. This shows that when the exposure family member indicates they have chronic pain, there is a 30% increase in odds of reported chronic pain in the index family member (after adjustment for both index and exposure family member age), prevalence percentage shows an increase of 5.9% addition due to the exposure having chronic pain. The effects of gender show, using both family members as male as the reference category, that being female (index family member) gives a prevalence percentage increase of 4.5%, but if the exposure family member is female (and index male) there is a reduction (-0.7%), both results were not significant within the logistic regression tests. However when both family members are female, independent of the exposure family members' chronic pain status, there was a non-significant trend (adjusted OR 1.39; 95% CI 0.99, 1.94) with a prevalence percentage increase of 9.1% which is a 4.6% increase on the effect if the index family member is female. Considering the shared effect of age, compared to when both family members are within the youngest categories (< 50 years) there was a significant effect when the index was older with a 16.9% increase in prevalence, but a non-significant effect when the exposure was older (3.0% increase in prevalence). There is a significant effect when both index and exposure were older, the percentage prevalence increase was 14.3%, which is a reduction of 2.6% prevalence compared to when only the index was older. For income, there is a significant effect when the index person is within the low income category, regardless of the exposure family members' income status. However the strength of effect is stronger when both exposure and index are low income (OR 3.27, prevalence increase of 28.2%) compared to when the index is low income and exposure is either medium income (OR 2.88, prevalence increase 25.5%) or high income (OR 2.84, prevalence increase 24.3%). There is also a significant effect when both the index and exposure are within the medium income category (OR 2.45, prevalence increase 18.6%) and this effect is stronger when the index is within the medium income category and the exposure is within the low income category (OR 2.80, prevalence increase 22.1%). Smoking only showed a significant effect if the index family member smoked or smokes (OR 1.41,

prevalence increase of 9.3%), with no significant effect found when both family members smoke or have smoked, compared to when they both have never smoked.

Insert Table 3 about here

4.0 Discussion

This multilevel modelling study shows that 8% of the variance in chronic pain status within a family health survey can be explained at a family level, and this rate increased slightly to 9.8% when introducing individual level variables associated with chronic pain. Overall this suggests that factors related to chronic pain status are mostly explained at the individual level, but that there is a modest level of shared effect present. The results of tests between family members on variables associated with chronic pain do show some effects; family members have increased odds of reporting chronic pain if they have another family member who also has chronic pain. Additional shared factors between family members that may contribute to chronic pain status were also identified, such as the shared gender status between family members, and also shared income status between family members. These findings show some potential shared effects beyond the individual that can contribute to chronic pain.

4.1 Comparison with other literature

In terms of generalisability the GS:SFHS has been compared to the Scottish general population [42,43], and it is reported that GS:SFHS participants are generally older, but have a lower prevalence of general illness; with lower levels of chronic pain status (32% versus 46%), less likely to smoke, more likely to have a better level of education, and less likely to be depressed. Similar trends are found in the nested cohort in this current study. A recent study using the GS:SFHS dataset that examined genetic heritability variance for chronic pain status report that 8% of the variance for chronic pain was explained by unmeasured “shared” environmental factors [23]. Similarly Vehof et al [48] found a range of 7% to 10% of the variance of chronic pain syndrome was explained by common shared environment factors, and both these figures are similar to the variances reported within this

current study. We have now added to this literature by investigating what shared factors contribute to this shared effect, and the size of the effect for each variable. This current study is also in accord with other chronic pain studies in identifying, age, sex, income, smoking status, and education level as factors associated with chronic pain [20,22,33,37,47]. Whilst the results report on significant shared effects in accord to previous literature, the actual contribution above and beyond the individual effects (i.e. the added effect) is small. For example the percentage prevalence of chronic pain status increased by only 5.9% if the exposure family member has chronic pain. The results for age actually show a reduction in the increase of prevalence when both family members are old (14.9%) compared to when the index family member is old (16.9%). Similarly for income, whilst there is an increase in chronic pain prevalence (increase of 28.2%) when both family members are low income, this is largely driven by the index individuals income status, for example we only see a 3.3% rise in prevalence if the exposure family member is low income and the index is high. Caution should be exercised on the interpretation of percentage prevalence increase in this context, as causation cannot be assumed within this cross sectional design. This current study did not find psychological morbidity (as measured by the GHQ-28) as a factor associated with chronic pain despite other epidemiological studies finding such an association [2,36]. This may be a reflection of the overall lower proportion of chronic pain and psychological distress within the GS:SFHS population, compared to Scottish population norms. For example the proportion of those depressed is double within the Scottish general population (8%) compared to GS:SFHS (4%), and the proportion of those with chronic pain at a Scottish national level is reported as 46%, whereas within the GS:SFHS it is lower at 32% for the full cohort [43], and 36% within this nested cohort.

4.2 Strengths and weaknesses

A key strength of this study is the recruitment of a random sample of families from a diverse range of areas within Scotland. Participants included within this analysis were not recruited on the basis of their chronic pain status, and so results would be less likely influenced by response bias. Furthermore we randomised which participant was assigned as the index family member, and which family member was assigned as the exposure family member, again to minimise bias. We also choose to

only include participants who had only one other family member within the dataset. This was for the analysis model whereby we randomly assigned each member to either exposure or outcome status with assumption that first degree relatives would have increased contact with each other (as evidenced by the invitation to take part in GS:SFHS from one family member to the other) as this would increase the likelihood that family members share a current relationship and probably share similar environmental influences [11]. However it is acknowledged that different analysis methods could have included all Generation Scotland participants.

There are some other limitations to this study. Firstly we have no information on the amount of time each family member spends with each other, and no information on the geographic location of each family member, and so no way of quantifying the amount of shared status between family members. We also have no information on the type of linkage between family members (i.e. brothers, sisters, mothers, and fathers). The study also lacks information on the family dynamics (e.g. relationship quality between family members, ethnic/cultural groups, social network and level of support) which may have contributed more explanation at the family level. Whilst this study used a valid question on chronic pain status [34], we did not carry out analysis based on the location of the pain, the duration of pain, the severity of pain, the impact on function, how the person views their pain, how they cope with their pain, or what medication or treatment they may be receiving for their pain. All of these factors may be more influenced by shared family effect, and further research is needed to look at these specific aspects between family members. Furthermore the effects reported for chronic pain may differ for other types of pain (e.g. back pain, or chronic widespread pain), recent research has shown different rates of concordance for consultations about musculoskeletal pain in couples dependent on which body region they consulted about [7], and further research is now required to understand potential differences on shared influence for different pain conditions. Lastly we have no information on which participant, within the family dyad, reported pain first, or how long each family member has had their chronic pain. Duration of pain is likely to be an influence in terms of a pain severity indicator, but also in terms of social learning influence (e.g. parents long term expression of

pain influencing child's reaction and coping with pain). Further longitudinal research would be required to help establish causal linkage factors between family members.

4.3 Clinical Relevance

The findings on family effects associated with chronic pain reported here are relatively small and unlikely to have direct clinical relevance. For example even though we present a 30% increase in odds for the influence of one family members' chronic pain status on another, this only translates to a modest percentage prevalence rise of 5.9%. Therefore we believe our findings have greatest relevance at a population level, given the very high proportion of the population who report chronic pain, for example 36% in this nested cohort, with general population estimates higher at 45% [4,15,43]. Buchbinder et al [5] demonstrated the effectiveness of a public health intervention designed to alter beliefs about back pain and report moderate success in changing back pain beliefs and pain related behaviours (e.g. disability) at a full population level. However subsequent attempts at population change have not been as successful, partly due to heterogeneity within the population, where people differ in their motivation, ability and opportunity to affect their outcome [19]. Perhaps one way of addressing chronic pain in this way (i.e. public health) is to target at a family level, where greater homogeneity will be found, in effect considering the "family case history". This may entail further research to ascertain shared family factors that are predictive of pain onset, and where identified, tailor interventions to reduce such risk factors at a family level. It may also be useful to examine the relationship between family members when they have pain; there is evidence of social learning influence on pain behaviour [46] and research has shown that interventions targeting modifiable lifestyle factors and beliefs at a family level can reduce the impact of other long term conditions such as heart disease and diabetes [27,38]. In addition there may be increased benefit combining the evidence we have at the individual, genetic and family level, and direct treatment towards those individuals where there is high risk of poor outcome.

4.4. Conclusion

There is an increasing research interest on shared experience and shared risk of illness with families. Studies have begun to report on genetic evidence associated with chronic pain. In this study we compliment such research by exploring the contribution of shared environmental factors. Taken together the evidence suggests family effects are present that impact on the individual. Further research is now required to understand the interaction of influence between family members.

Acknowledgements and conflicts of interest

Generation Scotland received core support from the Chief Scientist Office of the Scottish Government Health Directorates [CZD/16/6] and the Scottish Funding Council [HR03006]. We are grateful to all the families who took part, the general practitioners and the Scottish School of Primary Care for their help in recruiting them, and the whole Generation Scotland team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists, healthcare assistants and nurses. This research was supported and funded (e.g. access the Generation Scotland: Scottish Family Health Study dataset) by a Wellcome Trust Fellowship Grant to Professor Kate M Dunn [083572]. The funder played no role in the design or conduct of the study; the collection, management, analysis, or interpretation of the data; or preparation, review, or approval of the manuscript. The authors have no conflicts of interest.

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Table 1. Characteristics of cohort

Characteristics		Number (%)
Chronic pain	Yes	981 (36.1%)
Age bands	< 30 years old	421 (15.5%)
	30 years to 49 years	1048 (38.6%)
	50 years to 70 years	1058 (39.0%)
	> 70 years	187 (6.9%)
Gender	Female	1590 (58.6%)
Weight/BMI	Overweight/obese	1508 (59.2%)
Smoking status	Current/previous smoker	1265 (47.2%)
	Currently live with smoker	392 (15.0%)
Education level	Compulsory	793 (30.2%)
	Further education	927 (35.3%)
	Higher education	908 (34.6%)
Live with partner	Yes	1780 (67%)
Household income	< £30K per year	856 (35.3%)
	30K to 50K per year	642 (26.5%)
	> 50K per year	711 (29.3%)
	Not reported	216 (8.9%)
Accommodation status	Own outright	804 (30.0%)
	Current mortgage	1338 (49.9%)
	Rent	448 (16.7%)
	Other	90 (3.4%)

Psychological morbidity	Yes	480 (19.0%)

K = £1000

Table 2. Logistic regression multilevel model of factors associated with chronic pain status

Explanatory variable	Univariate model OR (95% CI)	Multivariable model OR (95% CI)
Gender (being female)	1.46 (1.23, 1.73)*	1.55 (1.25, 1.91)*
Age (reference 18yrs to 29yrs)		
30yrs to 49yrs	2.05 (1.53, 2.75)*	2.10 (1.45, 3.03)*
50yrs to 70yrs	4.17 (3.10, 5.60)*	3.98 (2.68, 5.92)*
Over 70yrs	2.82 (1.88, 4.24)*	2.23 (1.26, 3.93)*
Weight (being overweight/obese)	1.04 (0.87, 1.23)	0.98 (0.79, 1.20)
Smoking (yes or previous)	1.56 (1.32, 1.84)*	1.32 (1.07, 1.64)*
Live with smoker (yes)	1.28 (1.01, 1.62)*	0.98 (0.73, 1.33)
Education level (reference University)		
College	1.41 (1.14, 1.74)*	1.15 (0.90, 1.47)
Compulsory	1.99 (1.61, 2.48)*	1.18 (0.89, 1.56)
Live with partner/as couple (no)	0.85 (0.71, 1.02)	0.85 (0.66, 1.09)
Household income (reference > £50K)		
£30K to £50K	1.67 (1.30, 2.13)*	1.50 (1.13, 1.98)*
< £30K	2.40 (1.91, 3.03)*	2.10 (1.54, 2.85)*
Not reported	1.63 (1.15, 2.30)*	1.47 (0.95, 2.26)
Accommodation (reference own outright)		
Current mortgage	0.67 (0.55, 0.82)*	1.01 (0.77, 1.33)
Rent	1.01 (0.79, 1.30)	1.33 (0.94, 1.89)

Other	0.57 (0.34, 0.94)*	1.39 (0.68, 2.82)
Psychological morbidity (yes)	1.01 (0.80, 1.26)	0.99 (0.79, 1.20)

OR – Odds ratio, CI – Confidence Interval, * $p < 0.05$

Table 3. Influence of shared gender, age, income and smoking status on chronic pain status in index family member

Influence		Influence present	Percentage index family member with chronic pain	Unadjusted OR (95% CI)	OR (95% CI) adjusted for index and exposure age and exposure chronic pain status	% difference[§]
Presence of chronic pain in exposure family member		No	33.3%	1.29 (1.03, 1.63)	1.30 (1.02, 1.65)[#]	5.9%
		Yes	39.2%			
Gender	Both male	Yes	31.4%	**Reference**	**Reference**	
	Index female, exposure male	Yes	35.9%	1.23 (0.86, 1.76)	1.22 (0.85, 1.75)	4.5%
	Index male, exposure female	Yes	30.7%	0.97 (0.68, 1.39)	0.90 (0.62, 1.30)	-0.7%
	Both female	Yes	40.5%	1.49 (1.07, 2.08)	1.39 (0.99, 1.94)	9.1%
Age	Both younger (< 30 and 30 to 49)	Yes	27.6%	**Reference**	**Reference**	
	Index old, exposure young	Yes	44.5%	2.11 (1.55, 2.87)	2.10 (1.54, 2.86)*	16.9%
	Index young, exposure old	Yes	30.6%	1.16 (0.84, 1.60)	1.09 (0.78, 1.50)*	3.0%
	Both older (50 to 70 and > 70)	Yes	41.9%	1.90 (1.39, 2.61)	1.80 (1.31, 2.48)*	14.3%
Income	Both high income	Yes	19.1%	**Reference**	**Reference**	
	Index medium and exposure high income	Yes	27.3%	1.59 (0.78, 3.22)	1.53 (0.75, 3.11)	8.2%
	Index low and exposure high income	Yes	43.4%	3.25 (1.73, 6.12)	2.84 (1.49, 5.40)	24.3%
	Index high and exposure medium income	Yes	25.0%	1.41 (0.69, 2.91)	1.38 (0.67, 2.86)	5.9%
	Both medium income	Yes	37.7%	2.56 (1.25, 5.25)	2.45 (1.19, 5.04)	18.6%
	Index low and exposure medium income	Yes	44.6%	3.41 (1.74, 6.65)	2.88 (1.46, 5.68)	25.5%
	Index high and exposure low income	Yes	22.4%	1.23 (0.60, 2.49)	1.14 (0.56, 2.33)	3.3%
	Index medium and exposure low	Yes	41.2%	2.97 (1.56, 5.67)	2.80 (1.45, 5.41)	22.1%

	income					
	Both low income	Yes	47.3%	3.80 (2.02, 7.14)	3.27 (1.72, 6.21)	28.2%
Smoking status	Both never smoked	Yes	32.3%	**Reference**	**Reference**	
	Index smoker, exposure never	Yes	41.6%	1.50 (1.10, 2.04)	1.41 (1.03, 1.93)	9.3%
	Index never, exposure smoker	Yes	31.0%	0.95 (0.69, 1.30)	0.88 (0.64, 1.22)	-1.3%
	Both smoke or smoked	Yes	39.7%	1.38 (1.01, 1.90)	1.19 (0.85, 1.64)	7.4%

OR – Odds Ratio, CI – Confidence interval, [#] Adjustment for index and exposure family member age only, * Adjustment for exposure chronic pain status only, [§] Percentage difference from reference category.