Title: Social integration of adolescents with chronic pain: a social network analysis.

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Introduction

During adolescence, building relationships with peers and developing social competencies are of crucial importance for well-being. However, adolescents with chronic pain (ACPs) often experience impairments in their social functioning [26,35]. They report more frequent school absence and greater social isolation, be it through social exclusion by others or self-withdrawal [54]. This isolation may install a sense of loneliness, often associated with perceived lack of understanding from peers who do not know what it is like to have chronic pain [28,25]. However, little is known about the consequences of ACPs' reduced social functioning on their relationships with peers. Indeed, adolescents' social networks are complex and consist of multiple peer dyads in which each member has their own perspective on the same relationship.

A social network approach provides a valuable framework to assess both self- and peer-perceptions of adolescents' dyadic relationships within their social network [26,53]. Social network analysis (SNA) adds an advantage over traditional respondent-centered approaches, as it allows for the identification of peer relationships' structural characteristics within specific environments (e.g., a class or school) [53]. Earlier network research in other contexts has identified three characteristics, namely popularity, homophily, and relationship quality, that may be crucial in understanding ACPs' social networks [8,23].

First, peer relationships involve an individual's ***popularity***, referring to how often one is nominated as a friend by peers. As ACPs' perception of their own popularity may be biased, for instance, by negative attribution styles, including a peer perspective is important [28]. Studies examining popularity in ecologically valid contexts (e.g., a school) are sparse. Second, individuals show a tendency to maintain relationships with others who resemble them in terms of relevant characteristics, which is described as the ***homophily*** principle (similarity-attraction theory) [11,45]. A perceived lack of understanding from peers without pain may motivate ACPs to interact with peers who also experience pain, because ACPs may feel better understood by them. Nonetheless, it is still unclear whether this hypothesis holds true. Finally, examining the ***quality*** of relationships is also crucial [14]. Perceived positive friendship quality has been associated with reduced feelings of depression and loneliness [34] [47]. However, friendships may act as a source of stress as well as support [12], which may also have an impact on adolescents' ***mental distress***. Research into these characteristics from a social network perspective is largely lacking.

Considering these knowledge gaps, the current study used SNA to examine structural social network characteristics in ACP's peer relationships and addressed four research questions: (RQ1) Are adolescents with higher pain grades (i.e., pain frequency and disability) less often nominated by others as being part of a peer group? (popularity) (RQ2) Do adolescents with similar pain grades name each other more often as being part of the same peer group? (homophily) (RQ3) Do dyads with an adolescent having a higher pain grade report less positive (e.g., support) and more negative (e.g., conflict) friendship quality? (relationship quality) and (RQ4) Does perceived positive or negative friendship

quality moderate the relationship between pain and emotional distress? (relationship quality and mental distress) As sex is important for individual consequences of pain (e.g., [8]), we additionally explored the role of sex in RQ1-4.

Methods

Participants

The present study utilized data from the first wave (in 2014) of a larger longitudinal study (i.e., The Three Cities Study) examining risks and buffers influencing well-being throughout adolescence [9]. This study followed adolescents from 19 public schools. The schools were a mix of urban and rural schools, situated in one midsize city (156 000 inhabitants) and two small towns (26 000 and 30 000 inhabitants) in middle Sweden. All schools were public schools, broadly representing Swedish demographics. Data collection took place between 2014 and 2018, whereby only adolescents from grades 7 (13 years) and 8 (14 years) were included in the first wave of 2014.

Adolescents as well as their parents provided informed consent to participate in the longitudinal study. Parents of 3336 students were informed about the study via a written letter, after which parents who declined participation could send a form in a prepaid envelope indicating that they did not want their child to participate (N= 122; 3.6%). Consequently, not returning the form was regarded as passive informed consent. Adolescents actively provided informed consent prior to completing the questionnaires, after first receiving oral and written information about the study in the classroom. Four hundred forty-seven students did not agree to participate or were absent on the day of the data collection, resulting in a sample of 2767 (82.9%) adolescents. They completed the questionnaires in the classroom in the presence of a trained test leader. No teachers were present in the room. Adolescents were given 90 minutes to complete the survey. As a compensation, each class received 300 Swedish crowns. The regional Ethical Board of Uppsala gave ethical approval for the study (No 2013/384).

Measures

Sociodemographic characteristics

Adolescents answered questions about their sex, age, class, school grade, immigrant background, divorcement of parents, socioeconomic status, and which of the 19 schools they attended. Immigrant status was dichotomized as being born outside of Sweden or having both parents born outside of Sweden, following the official Swedish definition of immigrant background [66]. Socioeconomic status (SES) was assessed using the Family Affluence Scale, version 2 (FAS-II), from WHO's Health Behavior in School-aged Children (HBSC) survey [1], which includes 4 items by which adolescents assessed their family's affluence. The cut-off score for low SES was set to 4.61, which is one SD below the mean M= 6.28 (SD= 1.67) of FAS-II in the Swedish HBSC survey (N= 23 088) [1]. These scores were already used in a previous study on the same dataset [4].

Pain characteristics

The current study focused on musculoskeletal pain, which was assessed via the following question: "How often during the last six months have you suffered from pain in the back/neck/shoulders?". This item was derived from the Health Behavior in School-Aged Children Checklist [33] and rated on a scale from 1 (= Rarely or never) to 5 (= About every day). Afterwards, they were asked how painful their back/neck/shoulder pain was on average, ranging from 1 (= Not at all painful) to 10 (= Very painful). Pain interference was assessed by means of three items in which they were asked whether the pain had impaired their functioning during the last six months 1) at school, 2) during leisure activities, and 3) during contact with friends. Items were rated on a scale from 1 to 3 (1= No; 2= Yes, some; 3= Yes, definitely). A sum score was calculated for pain interference. Cronbach's alpha in this study was .74.

Adolescents were categorized according to 5 pain grades [38,63]: Grade 0 (i.e., pain frequency rarely or never), Grade I (i.e., pain at least every month, low pain intensity (score 1-5), no or low pain interference (score 3-5)); Grade II (i.e., pain at least every month, high pain intensity (score 6-10), no or low pain interference (score 3-5)), Grade III (i.e., pain at least every month, high pain intensity (score 6-10), medium impairment (score 6-7)), and Grade IV (i.e., pain at least every month, high pain intensity (score 6-10), high impairment (score 8-9)). These pain questions and grades were validated in a study among the same Swedish adolescents from 7th to 9th grade [65].

Social network questionnaire

To assess social networks within each school, adolescents were asked to think about the group of peers with whom they spent time at school. Adolescents could name up to three peers. This name generator approach has been previously used in research examining friendship relationships (e.g., [43]). Afterwards, several questions were asked about the peers they had named. First, adolescents indicated the class of each peer they mentioned. Second, they answered three questions about how positive the friendship quality was: "Supports you if you have fought with your parents or teacher", "Stands up for you when others talk behind your back", and "Cares about your feelings". Finally, they also indicated how negative the relationship was by means of three questions: "Argues a lot", "Get angry at each other often", and "Often gets irritated with each other". These six items were rated on a scale from 1 (= Don't agree at all) to 5 (= Agree completely). The positive and negative friendship quality items were derived from the Friendship Quality Questionnaire of Parker and Asher's [51]. A sum score was calculated for positive (range: 3-15) and negative friendship quality (range: 3-15). Cronbach's alpha for the positive and negative friendship quality scale was .88 and .67 respectively.

Emotional distress

Emotional distress was assessed by means of two constructs, namely stress and depressive symptoms. We opted for depression and stress because friendship quality may be protective against depression and the negative effects of stress-inducing events such as peer victimization (e.g., see [50]).

The degree to which situations in adolescent's lives during the last month are appraised as stressful was assessed by means of the Perceived Stress Scale (PSS) [56,13]. Since we examined friendships and friendship quality among adolescents with and without pain, a more general measure of distress, such as the PSS would allow for a broader understanding of the associations amongst pain, friendship quality and distress compared to specific forms of distress such as anxiety. The PSS includes 14 items, which are rated on a scale from 0 (= Never) to 4 (= Very often). The PSS has been found to be a reliable measure of stress in adolescents (e.g., [48]). A total sum score (range: 0-56) was calculated. Cronbach's alpha in this study was .98.

The Center for Epidemiologic Studies Depression scale (CES-D) [64] was used to assess depressive symptoms. The CES-D includes 20 items and adolescents rated these items on a 5-point scale from 0 (= Not at all) to 4 (= A lot). This scaling was adapted to the original 4-point scale using a standard transformation (see [61]). The CES-D has been validated in the current sample of Swedish adolescents [49]. A sum score (range: 0-60) was calculated. Cronbach's alpha in this study was .94.

Analyses

Because of the nature of the data collection process (i.e., questioning all people in a specific context about their relationships with each other), statistical methods such as linear regression, which assume independent error terms between observations, cannot be applied [22]. For one, because observations in social networks are interdependent (and not randomly sampled from the general population) as they can affect each other (e.g., through reciprocity, transitivity) and are part of the same social system (here: schools). Secondly, because the data are collected in multiple schools and thus have a multilevel/multigroup structure.

Taking into account that observations are interdependent, a *multiple regression quadratic assignment procedure* (MRQAP) [40] was used to test the research questions regarding ACPs' social networks (RQ 1-3). MRQAP analysis is a state-of-the-art SNA method used to investigate associations between characteristics of dyads (e.g., the level of pain homophily) and a binary or continuous tie variable (e.g., friendship nomination, level of perceived positive or negative friendship quality) [15,40,39]. MRQAP provides a solution for the violation of the independence assumption, by permuting the random dependent network matrices and thereby generating a reference null distribution that controls for the network structure. Four steps are taken in an MRQAP analysis: (1) First, a classic linear or logistic regression is run with the values of the network matrix as a dependent variable and predictors of interest (e.g., level of homophily) as independent variables. The regression coefficients are stored, as only the estimated standard errors are affected by the violation of the independence assumption. (2) Second, the network matrix that constitutes the dependent variable is permuted[1], which means that row

[1] In a simulation study, it was reported that permuting the dependent variable is the most conservative method to obtain statistical inference—other methods permute, for example, the independent variables or the residuals [15].

and column orders are shuffled simultaneously. This way, a large set of networks (in our case 2000) is created, where (on average) there should be no association between the dependent network and independent variables. (3) Third, on each of these permuted dependent networks, a regression model is run with specifications identical to those in step one. (4) In step four, regression coefficients obtained in the analyses carried out in step three (i.e., the null distribution) are compared to the observed regression coefficients obtained in step one. We can calculate, for example, the 97.5% / 2.5% percentiles of the null distribution to obtain a measure similar to the 95% confidence interval. Furthermore, we can compute a p-value by assessing how many coefficients from the null-distribution are larger or equally large than the observed value. For instance, a p-value of .99 indicates that 99 percent of the coefficients based on permuted networks are smaller or equal to the observed estimates. The probability of observing a larger estimate under the null-hypothesis is thus p = .01 (for further details see [41]). It is important to note that the level of analysis is the dyadic relationship, and not (as usual) the individual. In that sense, we aimed at predicting the presence of a friendship nomination (RQ1, RQ2) and the level of perceived positive friendship quality and negative friendship quality (RQ3) between two adolescents.

To take the multilevel/multigroup data structure into account, we applied a multigroup extension of the MRQAP framework. Similar to a multilevel analysis, all levels (i.e., schools) are analyzed simultaneously [55]. The only difference to the general MRQAP framework is that the permutations (step three above) are carried out within each group (i.e., within each school) [10,19]. This way, the baseline characteristics within each school (e.g., the distribution of adolescents with pain) are preserved allowing observations to be compared to alternative scenarios (i.e., null-distribution) in which ties would be randomly distributed within each school (and not among all schools). Because of this, the skewed distribution of the pain grades was also considered in the analytic procedure.

To examine research questions 1 and 2, a MRQAP model was specified with the presence of a tie (i.e., friendship nomination) between two adolescents as the dependent variable and independent variables in the form of matrices representing predictors related to the research questions and control variables (school class and grade). These key predictors were *pain sender*, *pain receiver*, and *pain similarity* (see Table 1). The term 'sender' refers to the adolescent sending a tie, in other words an adolescent who nominated peers (for an illustration see Figure 1). The pain sender effect thus captures the association between an adolescent's pain grade (see lightning flash on Figure 1) and the tendency to nominate other peers (irrespective of their pain grade). Analogously, 'receiver' refers to the adolescent receiving a tie, so an adolescent who was nominated as a friend by another adolescent (Figure 1). In that sense, the pain of receiver effect captures the association between an adolescent's pain level (see lightning flash on Figure 1) and the tendency to be nominated by others (irrespective of the adolescent's own pain level). The pain of receiver effect thus captures how pain is associated with being popular (RQ1). For the model testing the second research question, we included a variable indicating the level of pain similarity between adolescents (i.e., the pain similarity effect). Pain similarity is defined as

$P_{sim} = -1 * |P_{sender} - P_{receiver}|$, where P_{sender} and $P_{receiver}$ represent the pain values of every dyad in the dataset. Higher values represent a higher level of pain similarity. Further, this model also included an interaction effect between pain of the sender and pain of the receiver, which assessed whether the effect of pain similarity was differently expressed at the lower or high end of the pain scale (see Table 1). Simply put, this interaction effect assessed whether the effect of pain similarity was different for adolescents with a lower pain grade versus adolescents with a higher pain grade. Higher values for this effect correspond with homophily at the higher end of the pain scale. In this statistical interaction, dyads in which both individuals have a high pain grade (e.g., 4) have a high value (i.e., 4*4 = 16). Dyads with low pain grades (e.g., 0 and 1), on the other hand, have a low value (0*1 = 0). In this way, we can also assess in a multivariate model if the level of homophily is related to the dyad's level of pain. A positive estimate of the $P_{sender} * P_{receiver}$ interaction would indicate that dyads with high pain levels are more likely to be friends than those with low pain levels (i.e., that the homophily effect is stronger at the higher end of the scale than at the lower end of the scale).

** Insert Table 1 **

** Insert Figure 1 **

MRQAP also allows us to analyze weighted networks, which means that the degree of positive and negative friendship quality with peers can be included as continuous dependent measures in the analyses. To examine research question 3, a MRQAP model was fitted with the degree of positive friendship quality or negative friendship quality as the dependent network. In this model, the pain sender effect reflects the association between the adolescents' own level of pain and their self-perception of the dyadic relationship with their peers. The pain receiver effect reflects the association between the receiver's level of pain and the (sending) adolescents' self-perception of the dyadic relationship.

In the models testing research questions 1, 2, and 3, we further controlled for effects of sex (sex sender, sex receiver, same sex; see Table 1), being in the same school grade (grade homophily), and being in the same class (class homophily). We further controlled for differences in baseline levels of nominations (model for RQ1, RQ2) and baseline levels of positive/negative friendship quality (model for RQ3) between the 19 schools. For RQ1-3 estimates cannot be standardized as the standardization requires a standard error of the estimate. In the case of social networks, this standard error is biased due to the violation of the independence assumption, which states that observations are independent of each other. For reasons of consistency, we also reported unstandardized estimates for RQ4.

Finally, to examine research question 4, two standard multilevel models with observations of adolescents nested within schools were estimated [55]. Two moderation models were tested, one with stress as dependent variable and one with depressive symptoms as dependent variable. Main effects of pain grade, positive and negative friendship quality, and sex were included in the model. The main interests in this analysis are the interaction effects between pain grades on the one hand and

positive/negative friendship quality on the other hand with stress and depressive symptoms as dependent variables, testing research question 4. In this model, we also included two-way interaction effects between sex and positive/negative friendship quality, and three-way interactions between sex, pain grade, and positive/negative friendship quality.

The analyses were performed in the statistical programming language R [60] using the netglm [18] and the lme4 [6] package.

Results

Sociodemographic and pain characteristics

Table 2 shows the sociodemographic information and the distribution of the pain grades in the final sample.

** Insert Table 2 **

Social Network characteristics

In total, 6489 social network nominations were recorded. On average, adolescents nominated 2.34 (*SD* = 0.89) others. As an illustration, Figure 2 shows a network plot of one randomly selected school. The figure shows that few adolescents reported pain grade 3 or 4. Some were reciprocally connected to each other, meaning that they nominated each other as being part of the same peer group. Additionally, Figure 2 shows isolated adolescents, who were not nominated by others as being part of a peer group and also did not nominate others themselves. Network figures of all other schools can be found in the Supplementary Materials.

** Insert Figure 2 **

RQ1: Are adolescents with higher pain grades less often nominated as being part of a peer group?

Table 3 shows the results of a multigroup Multiple Regression Quadratic Assignment Procedure model with the presence of a friendship nomination as the dependent variable. The results showed that the effect of pain grade on nominations from peers (i.e., pain receiver effect) was not significant (*B*= -0.003, *p*= .470), indicating that the number of nominations was not lower for adolescents with higher pain grades.

Insert Table 3

RQ2: Do adolescents with similar pain grades name each other more often as being part of the same peer group?

Table 3 also shows the results regarding research question 2. These results indicated a significant effect of pain similarity on presence of a friendship tie between adolescents (*B*= 0.075, *p*= .004), which means that adolescents with a similar pain grade named each other more often as being part of the same peer group. The interaction between pain sender and pain receiver was not significant, indicating that

there was no difference in the effect of pain similarity across pain grades (B= -0.002, p= .472). In other words, adolescents with similar pain grades named each other more often regardless of their specific pain grade. So, the homophily effect was equally driven by dyads of low and high pain grades. Figure 3 and 4 show these results visually. Figure 3 shows the predicted probabilities of friendship ties (nominations) with varying levels of pain grades of senders and receivers, in other words it shows the chance of a friendship nomination considering both adolescents their pain grade. Figure 3 suggests that the probability of a friendship tie between adolescents was highest (dark red) when they reported similar pain grades, regardless of the level of their similar pain grade. Figure 4 shows the number of observed ties or friendship nominations (red dots) in comparison with a reference null-distribution (white violin distribution) by pain similarity and adolescent's pain grade. The null-distribution represents the number of nominations in a network in which ties would be randomly distributed. Figure 4 suggests that higher difference scores in pain grades were related to lower likelihood to nominate each other, so it was less likely that adolescents with different pain grades nominated each other (regardless of the specific pain grade).

** Insert figure 3 **

** Insert figure 4**

Further, the MRQAP results in Table 3 indicated a significant effect of sex similarity, which means that same sex adolescents named each other more often (B= 3.058, p< .001). Being in the same class (B= 3.049, p< .001) or school grade (B= 4.320, p< .001) was also highly significant, indicating that adolescents in the same class or school grade named each other more often as being part of the same peer group. Effect sizes of the latter three effects were very high, for instance the likelihood of a same sex friendship was 21 times (= Exp (3.058)) larger than a non-same sex friendship.

RQ3: Do dyads with an adolescent having a higher pain grade report less positive friendship quality and more negative friendship quality?

** Insert Table 4 **

Positive friendship quality. Table 4 shows the results of a multigroup MRQAP model with perceived positive friendship quality as the dependent variable. We focus on direct effects of friendship quality because of a weak correlation (r= -.15) between positive and negative friendship quality. The effect of pain sender on positive friendship quality was significant (B= -0.059, p= .023), indicating that adolescents with a higher pain grade perceived the relationship with their friends as less positive in terms of friendship quality than adolescents with lower pain grades. The effect of pain receiver was not significant (B= -0.035, p= .126), indicating that adolescents (who may or may not have pain) perceived relationships with friends with higher pain grades as equally positive as they perceived relationships with friends with lower pain grades.

Further, the effect of pain similarity within dyads was not significant in this model (B= -0.018, p= .250), indicating that adolescents with similar pain grades did not report higher or lower levels of positive friendship quality.

Finally, results also showed that male adolescents perceived the relationship as less positive than female adolescents (B= -0.362, p< .001) and that adolescents (irrespective of their own sex) perceived relationships with males as less positive than relationships with females (B= -0.400, p< .001). Peer relationships between adolescents of the same sex were perceived as less positive in terms of friendship quality (B= -0.257, p< .001). Similarly, adolescents of the same class (B= -0.171, p< .001) or school grade (B= -0.089, p< .001) perceived the dyadic relationship as less positive. These tendencies may result from rare relationships that cut across the boundaries of sex, class, and grade, but being perceived as highly positive by adolescents.

**Insert Table 5 **

Negative friendship quality. Table 5 shows the results of a multigroup MRQAP model with perceived negative friendship quality as the dependent variable. The effect of pain sender on negative friendship quality was significant, indicating that adolescents with higher pain grades perceive the relationship with their friends as more negative (B= 0.134, p< .001). The effect of pain receiver was also significant (B= 0.064, p= .002), which means that adolescents perceived relationships with peers with higher pain grades as more negative as compared to relationships with peers having lower pain grades. Interestingly, the effect of pain sender is twice as large as the effect of pain receiver on negative friendship quality, indicating that higher pain grades have a larger effect on one's own perception of relationships than the perception from others.

Furthermore, the effect of pain similarity was also significant, indicating that adolescents with similar pain grades reported more negative friendship quality in their relationships (B= 0.034, p= .044). This effect was not differently expressed at the lower or high end of the pain scale (B= -0.025, p= .061), indicating that school friends with similar pain grades perceived their relationship as more negative regardless of their specific pain grade. However, the latter two effects, need to be interpreted with caution, as both of them are close to the α value of .05.

Finally, male adolescents perceived the relationship as less negative (B= -0.040, p= .019) and relationships with males were also perceived as less negative (B= 0.047, p= .011). However these effect sizes were very small. Friendships between adolescents of the same sex were perceived as more negative (B= 0.087, p< .001). Nonetheless, most friendships were same sex (94.88%) and as such, the latter effect included almost all friendships. Similarly, adolescents of the same class (B= 0.072, p= .003) perceived the dyadic relationship as more negative, but adolescents of the same school grade perceived the relationship as less negative (B= -0.034, p= .044).

RQ4: Is positive or negative friendship quality with peers a moderator for the relationship between pain and emotional distress?

Perceived stress as dependent variable

** Insert Table 6**

Table 6 shows the results of the multilevel model with perceived stress as the dependent variable. As expected, the interaction effect between pain grade and positive friendship quality was significant (*B*= -1.55, *CI* [-2.68 – -0.42], *p*= .007), indicating that more positive friendship quality with self-nominated peers was buffering the negative effect of having a higher pain grade on stress. The interaction effect between pain grade and negative friendship quality was also significant (*B*= -1.53, *CI* [-2.84 – -0.22], *p*= .022), indicating that the relationship between negative friendship quality and stress was dependent on adolescents' pain grade. Simply put, the stress levels of adolescents with higher pain grades were less negatively affected by negative friendship quality than the stress levels of adolescents with lower pain grades. Those two effects together suggest that ACPs profit more from positive friendships and suffer less from negative friendships than non-ACP adolescents.

The latter two-way interaction effects are differently expressed in male and female adolescents as both three-way interactions between pain grade, positive friendship quality, and sex (*B*= 0.97, *CI* [0.29 – 1.65], *p*= .005) and between pain grade, negative friendship quality, and sex (*B*= 1.09, *CI* [0.25 – 1.93], *p*= .011) were significant. Because three-way interactions are not straightforward to interpret, we aid this process with an illustrative figure. Figure 5 shows the plot of the moderation model with pain grade, sex, and positive and negative friendship quality as independent variables and perceived stress as dependent variable. The plot shows that the buffering effect of positive friendship quality against the negative effect of higher pain levels on stress especially applied for female adolescents. More specifically, results show that female adolescents with a high pain grade greatly benefited from higher levels of positive friendship quality, while this mattered less for adolescents with a lower pain grade (B= -1.55, p= .007). In contrast, levels of stress were less negatively affected by negative friendship quality for female adolescents with a high pain grade (*B*= -1.53, *CI* [-2.84 – -0.22], *p*= .022), while negative friendship quality had a detrimental effect on levels of stress for male and female adolescents with a low pain grade (*B*= 4.45, *CI* [2.59 – 6.31], *p*< .001). Figure 5 also shows that stress levels of male adolescents with a high pain grade were more negatively affected by negative friendship quality than male adolescents with a lower pain grade.

** Insert Figure 5 **

Depressive symptoms as dependent variable

Insert Table 7

Table 7 shows the results of the multilevel model with depressive symptoms as the dependent variable. As expected, the interaction effect between pain grade and positive friendship quality was

significant (*B*= -4.45, *p*< .001), indicating that higher positive friendship quality levels were buffering the negative effect of having a higher pain grade on depressive symptoms. The interaction effect between pain grade and negative friendship quality was also significant (*B*= -2.29, *p*= .024), indicating that the negative effect of higher levels of negative friendship quality on depressive symptoms was lower for male and female adolescents with higher pain grades. Higher levels of negative friendship quality had primarily unfavorable effects on depressive symptoms in adolescents with lower pain grades.

The three-way interaction between pain grade, negative friendship quality, and sex was not significant (*B*= 1.16, *p*= .067), indicating that the interaction effect of negative friendship quality and pain grade on stress was not dependent on sex. In contrast, the interaction effect between pain grade and positive friendship quality was differently expressed in male and female adolescents as the three-way interaction between pain grade, positive friendship quality, and sex was significant (*B*= 2.43, *p*< .001). Once again, we aid the interpretation with an illustrative figure. Figure 6 shows the plot of the moderation model with pain grade, sex, and positive/negative friendship quality as independent variables and depressive symptoms as dependent variable. The plot showed that the buffering effect of positive friendship quality against the negative effect of higher pain levels on depressive symptoms especially applied for female adolescents (twice as large compared with male adolescents) and that this buffering effect is greatest for adolescents with higher pain grades. So, female adolescents with a high pain grade benefitted a lot from higher levels of positive friendship quality.

** Insert Figure 6 **

Discussion

The present study applied Social Network Analysis (SNA) to examine structural social network characteristics of adolescents with chronic pain's (ACP's) friendships. Specifically, popularity, homophily, and friendship quality were examined. Further, the moderating role of friendship quality on emotional distress was examined. The results can be summarized as follows. First, ACPs were not less popular than adolescents without chronic pain. Second, the homophily hypothesis was supported as ACPs nominated each other more often as being part of the same peer group. Third, the results regarding friendship quality showed that adolescents with higher pain grades (pain frequency and disability) perceived the relationship with their friends as less positive and more negative than adolescents with lower pain grades. Finally, positive and negative friendship quality moderated the relationship between pain grade and emotional distress (stress and depressive symptoms).

First, it was examined whether ACPs were less **popular** than other adolescents. Previous research demonstrated that lower popularity levels within adolescents' social networks are associated with psychological distress [59,42]. Social equity theory describes that people expect others to provide equal benefits as they provide for others [37]. This reciprocity may be violated in friendships with ACPs as arrangements with them are less predictable and as such, these friendships may entail more costs

compared with benefits. However, the current study did not find lower popularity levels in ACPs. This contrasts with a study in adolescents with fibromyalgia, indicating that they were less well liked and less often nominated as best friends [36]. Another study, in which real-world social interactions were examined, found that adolescents reporting acute pain, experienced decreasing popularity levels [8]. It could be that our sample consisted of ACPs who managed to establish reciprocal school friendships. It is also possible that adolescents in other studies experienced more disability, resulting in lower popularity levels. Alternatively, limiting the friendship nominations to three, may have impacted the current results if the effects of pain on popularity are at the larger friend group level versus the fewer friend group level.

Second, **homophily (**similarity in personal characteristics) at multiple dimensions (e.g., sex, ethnicity) has been shown to be beneficial in friendships [7]. Research showed that homophilous adolescent friendships are more stable over time [32]. This tendency may also hold for the dimension of chronic pain. In the current study, ACPs nominated each other more often as being part of the same peer group. This accords with previous research in which ACPs indicated that they would like to meet other ACPs on a regular basis [24]. A previous study found that ACPs search for informational and appraisal support from fellow ACPs [27], which could explain their homophily tendency. However, it was not solely the experience of pain that mattered for homophilous friendship nominations in this this study, but how similar each other's pain grade was for them to befriend, suggesting that a similar impact of pain on adolescents' lives is important. Interestingly, in a study examining real-world social interactions, no evidence was found for homophily in adolescents experiencing pain [8], so future research is needed.

Further, it is important to consider the **quality of friendships**. In the present study, adolescents with higher pain grades perceived the relationship with their friends as less positive (less supporting, standing up for you, caring) and more negative (more arguments, anger, irritation) than adolescents with lower pain grades, though effect sizes for positive friendship quality were relatively small. A previous study showed that ACPs perceive non-supportive situations with friends as more distressing than other adolescents [28]. ACPs may also experience a lack of support from peers because peers lack insight into what it is to have chronic pain [30]. Further, current results showed that peers perceived friendships with adolescents with a higher pain grade as equally positive, but also more negative. Perhaps, this is related to the unpredictable nature of friendships with ACPs, requiring further study.

In general, boys perceived their friendships as less positive in terms of quality and conversely, adolescents perceived friendships with boys less positively. These effects also hold for negative friendship quality, but those effect sizes were small. These findings are in line with numerous studies (e.g., [5]) showing that friendships among males are experienced as less supportive and intimate, regardless of the presence of pain in adolescents. This finding suggests that interventions to maintain and strengthen friendships for ACPs need to be cognizant of these sex differences.

Finally, the relationship between sex, pain, quality of friendships and **emotional distress** was examined. Friendship quality enhances psychosocial well-being, especially during adolescence [20]. Previous research showed that friendship quality and quantity buffer against emotional distress (loneliness and depression) [47] and the current findings show that friendships have an added benefit by protecting ACPs against the negative effects of pain on emotional distress. Research also showed that perceived quality of friendships was associated with psychological well-being and girls especially benefitted from high quality friendships [3]. Similarly, the current study found that the buffering effect of positive friendship quality against the negative effect of pain on emotional distress especially applied for females (but also for males), suggesting that emotional sharing within friendships are protective for female ACPs. The moderating effect of negative friendship quality on the relationship between pain grade and perceived stress applied for both females and males, but the effect was also stronger in females. Interestingly, adolescents with higher pain grades greatly benefitted from positive friendship quality while this was less the case for adolescents without pain. This was not applicable for negative friendship quality, which had a negative effect on emotional distress for all adolescents, with the exception for girls in the highest pain grade whose emotional distress was less negatively affected by higher levels of negative friendship quality. It could be that having a friend despite the presence of conflicts is better than not having a friend for girls in the highest pain grade.

The current results may have clinical implications. Assessing ACPs' friendships should become a standard practice of chronic pain management. Numerous measures have been developed to measure different aspects of peer relationships which could be used in clinical settings. Only one has been specifically developed for ACPs, the Bath Adolescent Pain Questionnaire, social functioning subscale [17,31], assessing positive and negative perceptions of friendships and engagement in social activities. Further, the PROMIS Pediatric Peer Relationships Scale [16] has been validated with children and adolescents from diverse backgrounds, but only a minority suffered from chronic illness. Clearly, establishing and maintaining friendships are critical for all adolescents, but friendships' quality may have additional therapeutic value for ACPs as these may buffer the negative impact of chronic pain on emotional distress. Clinicians should collaborate with teachers to become aware of the role of friendships in schools, especially for adolescents experiencing stress, such as ACPs. Isolated ACPs might need a particular attention to enhance their social integration in school. The homophily tendency suggests that ACPs perceive understanding and acceptance from each other. Clinically, ACPs may benefit (e.g., decreased loneliness, better self-management) from peer support groups due to the understanding from alike peers [2,29,58], however research is needed to examine if peer support programs reduce pain intensity [62] and enhance friendship functioning, and how these programs can be implemented in clinical settings [21].

This study has some limitations. First, adolescents were allowed to name up to three friends with whom they hang out in school, so we do not know their social networks as a whole. Conducting larger

social network research using paper-and-pencil surveys is a burden for respondents as they answer the same questions for each named peer. Computer-based (e.g. [57]) surveys diminish this burden and could be used in future research. Furthermore, it may be that some adolescents named more friends than they actually have as not all of their nominations were reciprocated. Second, the cross-sectional design does not allow to examine the direction of relationships and changes in networks over time. For example, we cannot statistically differentiate whether friendship quality or pain takes the moderating role. Third, we did not perform corrections for multiple testing, in line with recommendations of Perneger [52] and Nakawaga [46]. However, the findings' robustness in the outcomes is reassuring and we mentioned differences in effect sizes in the results. Fourth, the study focused on musculoskeletal pain, thereby excluding other forms of pain as well as consisting of a non-clinical population. It is unclear if our results are generalizable to adolescents with other forms of pain (e.g., abdominal pain). However, the method to determine pain grades (pain frequency and interference) would apply equally to other pain types. Moreover, musculoskeletal pain is the most common pain condition among adolescents [44]. Finally, this study focused on early adolescence (13-14 years) and it remains unclear if friendship quality changes as adolescents and their friendships mature.

Future research may benefit from examining extended social networks questioning more than three friends and allowing to nominate peers from other schools or broader contexts, resulting in even more ecologically valid data. ACPs generally report more loneliness than their healthy peers, so future studies could assess loneliness and examine whether befriending with fellow ACPs decreases loneliness. Studies could also examine the effect of friendship quality in pain-related situations, which may be more influential than general friendship quality as well as the effect of (in)validating responses from peers on emotional distress. Finally, longitudinal studies examining changes in ACPs' social networks over time and mediating processes are necessitated.

In conclusion, ACPs appear to be as popular as those without pain. Furthermore, ACPs tend to befriend each other when pain similarly impacts their lives. The need for qualitative friendships for ACPs cannot be underestimated as friendship quality buffered the impact of pain on emotional distress. Research to inform social interventions for ACP management is warranted.

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Table 1. Definition of network variables.

Variables	Definition
Pain sender	Pain of an adolescent who named peers
Pain receiver	Pain of an adolescent who is named by other adolescents
Pain similarity	Level of pain similarity between adolescents of a dyad
Pain sender * Pain receiver	Indicates whether the effect of pain similarity was different for adolescents without pain and adolescents with a higher pain grade
Sex sender	Sex of an adolescent who named peers
Sex receiver	Sex of an adolescent who is named by other adolescents
Sex same	Adolescents of a dyad have the same sex

Table 2. Descriptive statistics of the sample.

Variables	**Percentage (N)**
Sex, girls	47.6% (1316)
Age, 13 or 14	91.0% (2518)
Immigrant background	24.0% (664)
Low socioeconomic status	18.3% (506)
Divorced parents	32.9% (909)
Pain grade	
0	48.2% (1335)
1	30.6% (848)
2	8.8% (243)
3	6.4% (178)
4	2.0% (54)

Table 3. Results of Multiple Regression Quadratic Assignment Procedure model for Research Question 1 & 2.

				Percentiles	
	B	**p-value**	**E(Est.)**	**2.5th**	**97.5th**
Intercept	-11.658***	<.001	-4.420	-4.553	-4.296
Pain sender	0.017	.306	0.001	-0.059	0.063
Pain receiver	-0.003	.470	-0.001	-0.066	0.061
Pain similarity	0.075**	.004	0.000	-0.056	0.057
Pain sender * Pain receiver	-0.002	.472	0.000	-0.042	0.044
Sex sender (ref. female)	0.063*	.011	-0.002	-0.052	0.051
Sex receiver	-0.216***	<.001	0.001	-0.051	0.054
Sex same	3.058***	<.001	0.000	-0.051	0.052
Class same	3.049***	<.001	-0.002	-0.065	0.063
Grade same	4.320***	<.001	0.000	-0.049	0.052

*p < 0.05; **p ≤ 0.01; *** p ≤ 0.001. The reference category is female adolescents. E(Est)= Expected value of the estimate under the null distribution (i.e., the mean value of regression coefficients in the permuted scenarios).

Table 4. Results of Multiple Regression Quadratic Assignment Procedure model for Research Question 3 with positive friendship quality as dependent variable.

				Percentiles	
	B	**p-value**	**E(Est.)**	**2.5th**	**97.5th**
Intercept	5.686***	<.001	4.013	3.887	4.144
Pain sender	-0.059*	.023	0.000	-0.058	0.058
Pain receiver	-0.035	.126	0.000	-0.059	0.058
Pain similarity	-0.018	.250	0.000	-0.052	0.052
Pain sender * Pain receiver	0.025	.121	0.000	-0.040	0.040
Sex sender (ref. female)	-0.362***	<.001	0.000	-0.053	0.053
Sex receiver	-0.400***	<.001	0.000	-0.050	0.048
Sex same	-0.257***	<.001	0.000	-0.048	0.051
Class same	-0.171***	<.001	0.001	-0.061	0.060
Grade same	-0.089***	<.001	0.000	-0.048	0.049

*p < 0.05; **p ≤ 0.01; *** p ≤ 0.001. The reference category is female adolescents. E(Est)= Expected value of the estimate under the null distribution (i.e., the mean value of regression coefficients in the permuted scenarios).

Table 5. Results of Multiple Regression Quadratic Assignment Procedure model for Research Question 3 with negative friendship quality as dependent variable.

				Percentiles	
	B	**p-value**	**E(Est.)**	**2.5th**	**97.5th**
Intercept	1.360***	<.001	1.591	1.500	1.680
Pain sender	0.134***	<.001	0.000	-0.044	0.045
Pain receiver	0.064**	.002	0.000	-0.045	0.044
Pain similarity	0.034*	.044	0.000	-0.040	0.040
Pain sender * Pain receiver	-0.025	.061	0.000	-0.032	0.031
Sex sender (ref. female)	-0.040*	.019	0.001	-0.038	0.040
Sex receiver	0.047*	.011	0.001	-0.039	0.039
Sex same	0.087***	<.001	0.000	-0.037	0.038
Class same	0.072**	.003	0.000	-0.047	0.048
Grade same	-0.034*	.044	0.000	-0.038	0.037

*p < 0.05; **p ≤ 0.01; *** p ≤ 0.001. The reference category is female adolescents. E(Est)= Expected value of the estimate under the null distribution (i.e., the mean value of regression coefficients in the permuted scenarios).

Table 6. Results of multilevel model for Research Question 4 with pain grade, perceived positive and negative friendship quality, and sex as independent variables, and perceived stress as dependent variable.

	B	**95% CI**	**p-value**
Intercept	20.84***	12.52 – 29.16	<.001
Pain grade	9.49**	3.34 – 15.65	.002
Negative friendship quality	4.45***	2.59 – 6.31	<.001
Positive friendship quality	0.42	-1.10 – 1.95	.589
Pain grade * Negative friendship quality	-1.53*	-2.84 – -0.22	.022
Pain grade * Positive friendship quality	-1.55**	-2.68 – -0.42	.007
Sex (ref. female)	1.50	-3.24 – 6.24	.535
Pain grade * Sex	-5.36**	-9.01 – -1.72	.004
Negative friendship quality * Sex	-1.99**	-3.15 – -0.84	.001
Positive friendship quality * Sex	-0.48	-1.37 – 0.40	.283
(Pain grade * Negative friendship quality) * Sex	1.09*	0.25 – 1.93	.011
(Pain grade * Positive friendship quality) * Sex	0.97**	0.29 – 1.65	.005

*p < 0.05; **p ≤ 0.01; *** p ≤ 0.001. The reference category is female adolescents. E(Est)= Expected value of the estimate under the null distribution (i.e., the mean value of regression coefficients in the permuted scenarios).

Table 7. Results of multilevel model for Research Question 4 with pain grade, perceived positive and negative friendship quality, and sex as independent variables, and depressive symptoms as dependent variable.

	B	**95% CI**	**p-value**
Intercept	11.46***	-1.12 – 24.04	.074
Pain grade	26.82***	17.78 – 35.85	<.001
Negative friendship quality	7.66***	4.93 – 10.40	<.001
Positive friendship quality	0.01	-2.29 – 2.31	.994
Pain grade * Negative friendship quality	-2.29*	-4.27 – -0.30	.024
Pain grade * Positive friendship quality	-4.45***	-6.12 – -2.79	<.001
Sex (ref. female)	-2.38	-9.46 – 4.71	.551
Pain grade * Sex	-13.01***	-18.33 – -7.69	<.001
Negative friendship quality * Sex	-2.41**	-4.08 – -0.74	.005
Positive friendship quality * Sex	-0.67	-1.97 – 0.64	.316
(Pain grade * Negative friendship quality) * Sex	1.16	-0.08 – 2.41	.067
(Pain grade * Positive friendship quality) * Sex	2.43***	1.45 – 3.42	<.001

*p < 0.05; **p ≤ 0.01; *** p ≤ 0.001. The reference category is female adolescents. E(Est)= Expected value of the estimate under the null distribution (i.e., the mean value of regression coefficients in the permuted scenarios).

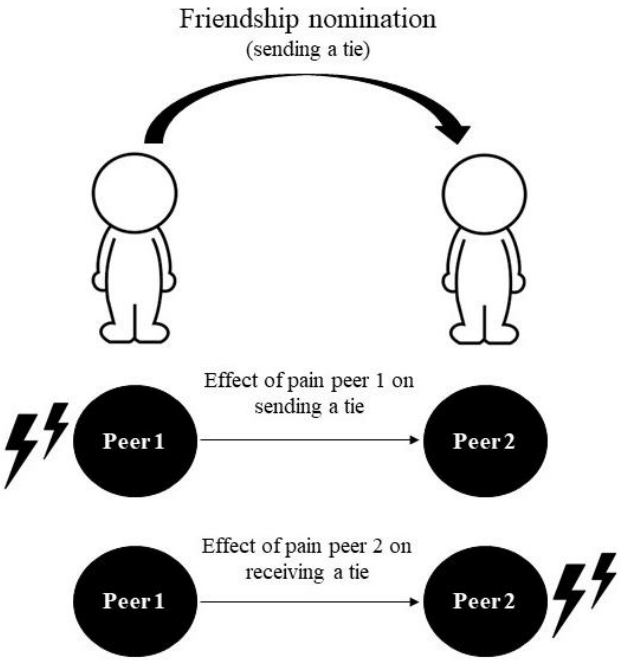

Figure 1. Illustration of sender and receiver effect. P1 sends a tie to P2 (P1 nominates P2 as a friend). The (pain) sender effect refers to the association between (pain) characteristics of the sender of the tie (P1) with the appearance of a tie. The (pain) receiver effect refers to the association between (pain) characteristics of the receiver of a tie (P2) with the appearance of a tie. Lightning signs represent high levels of peer's pain.

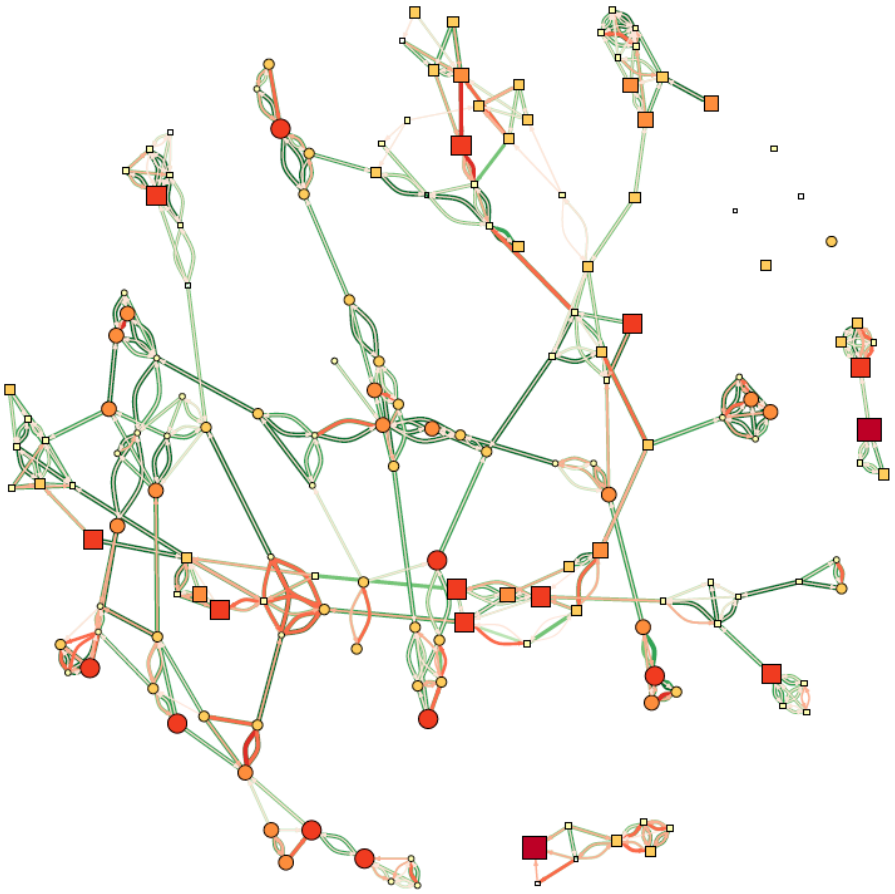

Figure 2. Plot of network in school 8. Circles = females, rectangles = males. Color and size of nodes represent pain grade, darker and bigger nodes represent higher pain grades (dark red = pain grade 4; yellow = pain grade 0). Color and width of ties represent higher positive (green) or higher negative (orange) friendship quality.

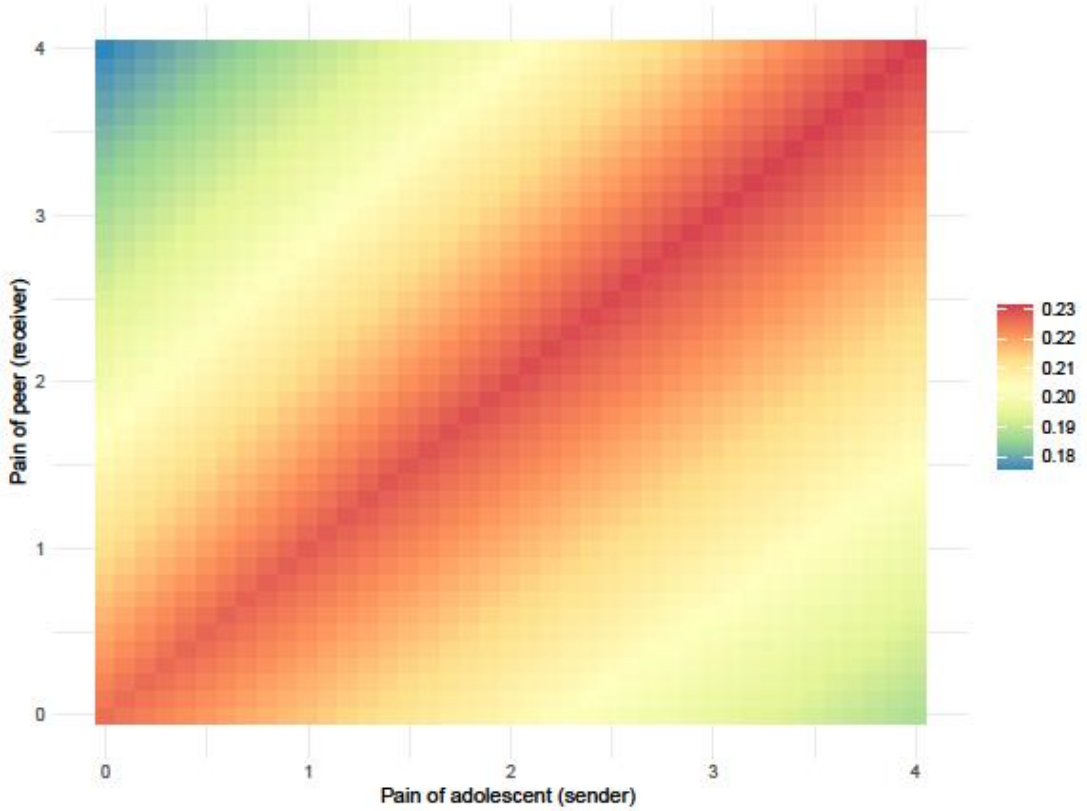

Figure 3. Predicted probabilities of friendship ties between adolescents with different pain grades. Darker red squares represent higher probabilities than darker blue squares. Predicted probabilities are computed based on the model estimates in Table 2.

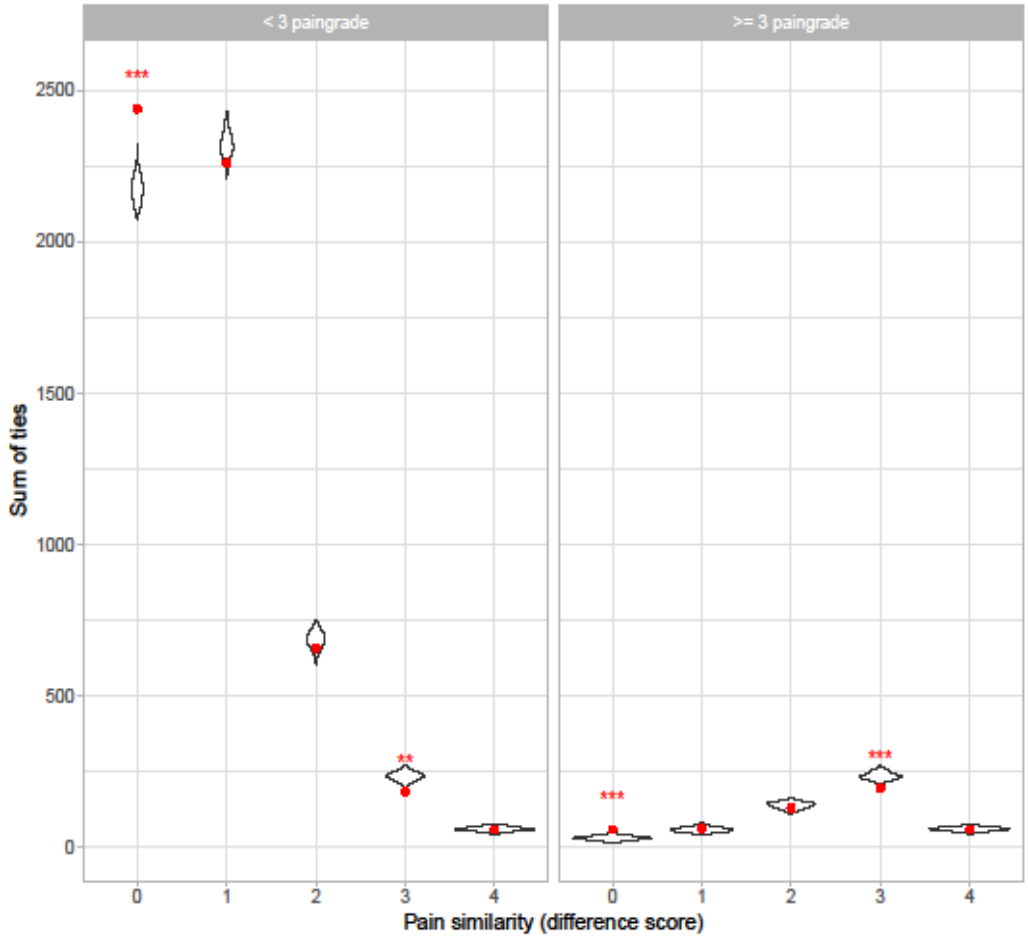

Figure 4. Number of ties by pain similarity and pain grade (<3 less than pain grade 3; >=3 more than pain grade 3). Difference score 0 represents similar pain grades.

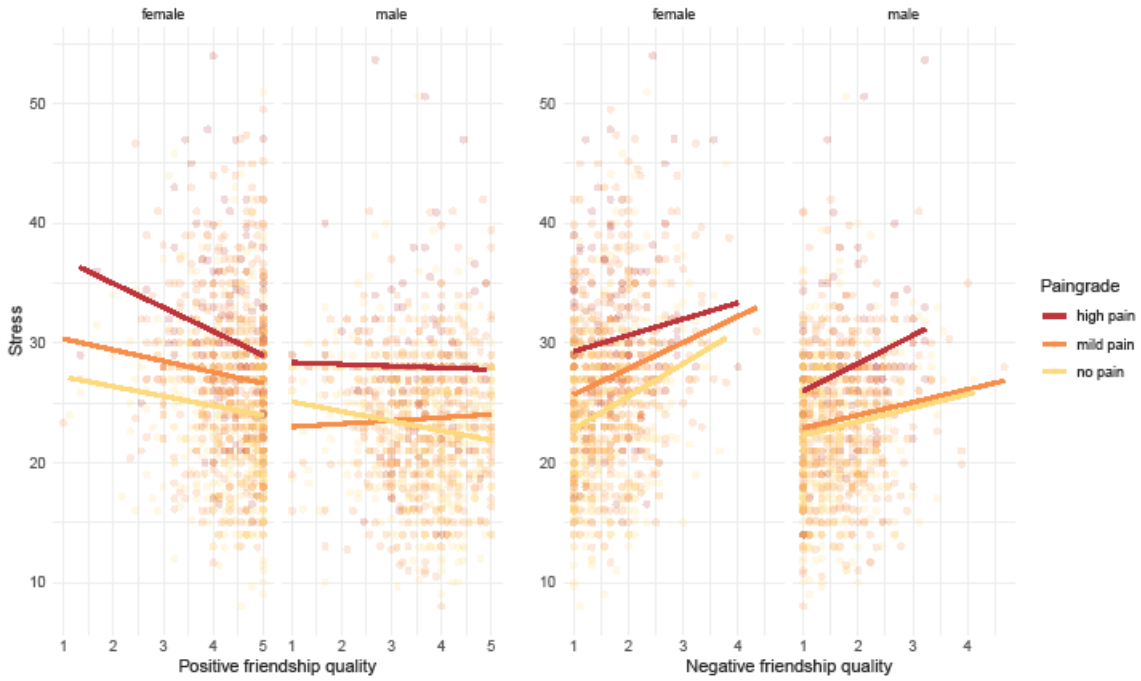

Figure 5. Plot of moderation model with pain grade, sex, and positive and negative friendship quality as independent variables and perceived stress as dependent variable. High pain represents pain grade 3 and 4. Mild pain represents pain grade 1 and 2. No pain represents pain grade 0.

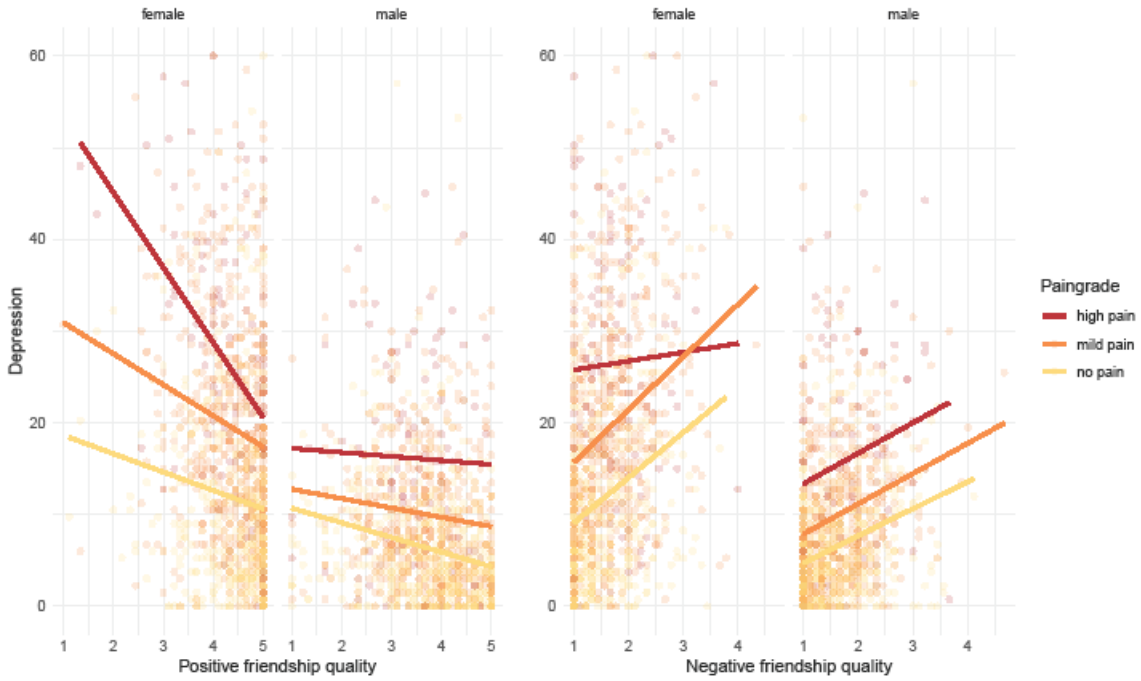

Figure 6. Plot of moderation model with pain grade, sex, and positive and negative friendship quality as independent variables and depressive symptoms as dependent variable. High pain represents pain grade 3 and 4. Mild pain represents pain grade 1 and 2. No pain represents pain grade 0.