

This is a repository copy of *The associations between loneliness, social exclusion and pain in the general population: a N=502,528 cross-sectional UK Biobank study*.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/id/eprint/163103/>

Version: Accepted Version

Article:

Allen, Sarah F, Gilbody, Simon orcid.org/0000-0002-8236-6983, Atkin, Karl Michael orcid.org/0000-0003-1070-8670 et al. (1 more author) (2020) The associations between loneliness, social exclusion and pain in the general population: a N=502,528 cross-sectional UK Biobank study. *Journal of Psychiatric Research*. pp. 68-74. ISSN: 0022-3956

<https://doi.org/10.1016/j.jpsychires.2020.06.028>

Reuse

This article is distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) licence. This licence only allows you to download this work and share it with others as long as you credit the authors, but you can't change the article in any way or use it commercially. More information and the full terms of the licence here: <https://creativecommons.org/licenses/>

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

The associations between loneliness, social exclusion and pain in the general population: A N=502,528 cross-sectional UK Biobank study.

Authors: Sarah F. Allen PhD^{a,b,*}; Simon Gilbody PhD^{ac}; Karl Atkin PhD^a & Christina van der Feltz-Cornelis PhD^{a,c,d}

Affiliations:

^a Department of Health Sciences, University of York, York; UK

^b Department of Psychology, School of Social Sciences, Humanities and Law, Teesside University, Middlesbrough, UK

^c Hull York Medical School, University of York, York; UK

^d York Biomedical Research Institute, University of York, York; UK

***Corresponding Author:**

Dr Sarah Allen

Department of Psychology

School of Social Sciences, Humanities and Law

Teesside University

Middlesbrough, UK.

Email: s.allen@tees.ac.uk

Words: 4324

References: 32

UKBiobank ref no: 49442

Abstract

Chronic pain presents a huge burden for individuals and society and evidence suggests intrinsic links with loneliness, social exclusion and sleep. Research examining how these factors interact is warranted. We aimed to explore the relationships between social exclusion, loneliness, acute and chronic pain, and the influence of poor sleep, in the general UK population. A cross-sectional analysis of UKBiobank participants with baseline data for acute and chronic pain, loneliness and sleep. Principal components analysis (PCA) used data relating to social isolation and deprivation to establish a composite measure of social exclusion. Binary logistic regression analyses were performed. 502,528 UKBiobank participants (mean age=56.6years, 54.4%female, 94.6%white) were included in the analysis. PCA suggested three social exclusion factors “social participation”, “individual deprivation” and “area deprivation”. Loneliness significantly predicted acute (OR:1.887;95%CI1.857-1.917) and chronic pain (OR:1.843;95%CI1.816–1.870). Each social exclusion factor alone and in combination significantly predicted pain with largest effects for individuals scoring high on all social exclusion factors, for acute (OR:2.087;95%CI2.026-2.150) and chronic (OR:2.314;95%CI2.249-2.380) pain. Coefficients remained statistically significant when models were adjusted for demographics and sleep. Social exclusion (as a multifaceted construct) and loneliness are associated with an increased prevalence of acute and chronic pain. Poor sleep has a potential mediating effect on these associations. Exploration of the incidence of pain in loneliness and social exclusion in the general population is warranted. From a public health perspective these findings could be used to design social interventions to prevent or manage pain and mitigate social exclusion.

Keywords: Social Exclusion; Public Health; Pain; UKBiobank; Loneliness; Sleep.

Introduction

Chronic pain affects almost 28 million adults in the UK (Fayaz et al., 2016) and presents a huge burden for individuals, particularly due to accompanying psychological problems (de Heer et al., 2018; Demyttenaere et al., 2007), in addition to societal challenges in offering appropriate support. (GBD, 2016) The relationship between pain and psychological symptoms is bi-directional, since persistent pain can both lead to psychological problems, and vice versa. (Cheatle et al., 2016; de Heer et al., 2018) Studies indicate that over half of patients with chronic pain report insomnia (Okifuji and Hare, 2011) and up to 85% present with a comorbid depression-anxiety disorder. (Tsang et al., 2008) Therefore research addressing chronic pain is a major public health priority.

Growing evidence suggests the psychosocial environment is associated with a higher likelihood of reporting pain. (Blyth et al., 2007) A number of longitudinal studies propose that some social factors can determine an individual's future risk of developing chronic musculoskeletal pain. (Nahit et al., 2003) Emerging evidence also suggests that painful feelings associated with social disconnection share some of the same neurobiological substrates that underpin experiences of physical pain. (Eisenberger, 2012) Further, brain-imaging research has demonstrated that experiences of social exclusion predominantly activate the brain regions known to play a role in physical distress. (Eisenberger et al., 2003) Pain is also socially realised. This explains an interest in using data to understand inequalities, which by connecting to broader debates about the social determinants of health (Godlee, 2019), could improve the disabling experience. (Dyson and Berghs, 2019) The prescription of opioids for chronic pain has developed into an epidemic whereas social interventions might be needed to prevent social exclusion. (Eisenberger, 2012) Mental health problems including insomnia, depression, anxiety and irritability are common symptoms of opioid withdrawal (Srisurapanont and Jarusuraisin, 1998) and poor sleep has been linked to both acute pain sensitivity (Okifuji and Hare, 2011) and chronic pain. (O'Brien et al., 2010)

The concept of social exclusion aligns with economic deprivation; social isolation; and the inability to fully participate in society, and incorporates a number of factors including social status, financial situation, community roles, disability, and access to services. (van Bergen et al., 2017) The Social Exclusion Index for Health Surveys (SEI-HS) was developed in a Dutch population and defines social exclusion as comprising of "limited social participation", "material deprivation", "inadequate access to social rights" and "lack of normative integration". (van Bergen et al., 2017) However, there is currently no such measure for the UK population.

Social exclusion is often associated with lower socio-economic status, which is consistently linked to increased morbidity, infant mortality and decreased life expectancy (Poleshuck and Green, 2008); and often attributable to reduced access to health services, non-optimal living conditions and poor health behaviours. Unsurprisingly, lower SES is regularly associated with increased risk for pain, potentially due to increased financial stress and vulnerability to economic hardship. (Rios and Zautra, 2011) Further, there are large social gradients in opioid prescriptions and a recent UK study found more opioids were prescribed in areas of greater social deprivation. (Mordecai et al., 2018)

Loneliness is defined in different ways. In this article, it is conceived as a subjective, negative feeling of disconnectedness or isolation. Loneliness has been found to be associated with chronic medical conditions such as cardiovascular disease, obesity, insomnia, anxiety and depression. (Petitte et al., 2015) Loneliness is also associated with a higher likelihood of experiencing pain (Blyth et al., 2007) and therefore may be involved in the development or exacerbation of chronic pain.

The UKBiobank is a large population-based study comprising biological data and mental health assessments of over 500,000 volunteers. The design has been described extensively elsewhere.(Sudlow et al., 2015) Approximately 9.2 million NHS patients aged over 40 were invited to participate, and 5.5% consenting adults took part in baseline assessments.(Fry et al., 2017) Previous UKBiobank studies have identified relationships between psychological problems and pain,(Nicholl et al., 2014) and others have examined loneliness and mortality.(Elovainio et al., 2017) However, the dimensions of social exclusion as well as the links between social exclusion loneliness, pain and the influence of sleep, have not yet been explored.

Objectives

Our aim was to examine the latent structure of social exclusion in the UKBiobank and explore associations between loneliness, social exclusion and the prevalence of acute and chronic pain via poor sleep. A diagrammatic representation of the hypothesised associations are shown in figure 1.

-Insert Figure 1-

Further, we aimed to specifically address the following research questions:

1. Can we construct and determine the dimensional structure of a composite measure of social exclusion based on the factors of the SEI-HS, in UKBiobank data?
2. How is social exclusion related to loneliness, poor sleep and the experience of acute and chronic pain?
3. Do socially excluded and lonely individuals have a higher likelihood of experiencing acute and chronic pain, and does poor sleep mediate these associations?

Methods

Study design

This was a cross-sectional analysis of a large population-based study comprising of participants enrolled in the UKBiobank.

Study setting and sample

The UKBiobank recruited 502,655 participants by postal invitation between March 13, 2006, and Oct 1, 2010. Participants attended one of 22 assessment centres across England, Scotland, and Wales, where they provided informed consent, completed touchscreen and nurse-led questionnaires, had physical measurements taken, and provided biological samples. All individuals registered with the NHS aged 40–69years who were living within 25 miles from an assessment centre were invited to participate; those who responded and had capacity to consent were included.

Participants for the current study were those who took part in the initial baseline assessment and answered questions on pain, sleep, social support, and loneliness (N=502,528). Sample size was therefore determined by the availability of data pertaining to our research questions.

Ethics statement

All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. UKBiobank received ethical approval from the NHS National Research Ethics

Service North West(11/NW/0382). Written informed consent was obtained from all participants throughout the project.

Variables

Predictor variables

The main predictors were loneliness and social exclusion. Loneliness was assessed by the question 'Do you feel lonely?' and answers classified as "yes" or "no".

A composite social exclusion score for each participant was calculated using relevant items from the UKBiobank data which were arranged into groups based on the four factors of the Social Exclusion Index for Health Surveys(SEI-HS)(van Bergen et al., 2017) as follows:

- *Social participation: Data included three questions regarding friends/family, and social activities. Higher scores indicated lower levels of social participation. "How often do you visit friends or family or have them visit you?" was scored as 1= "almost daily"; 2= "2-4 times a week"; 3 = "about once a week"; 4= "about once a month"; 5 = "once every few months"; 6 = "never or almost never" or "no friends/family outside of household". For "Which of the following do you attend once a week or more often? numerous activities could be selected. This was scored as 5="None of the above"; 3= one activity; and 1= multiple activities. Responses to "How often are you able to confide in someone close to you?" were scored as 5= "Never or almost never"; 4= "Once every few months; 3= "About once a month"; 2= "About once a week"; 1 = "2-4 times a week"; and 0= "Almost daily".*
- *Material deprivation: Household income was used as a proxy measure of material deprivation. Higher scores indicated lower standard of living, therefore 5 = "<£18,000 pa"; 4 = "£18,000 - £31,000" pa; 3 = "£31,000 - £52,000", pa; 2 = "£52,000 - £100,000" pa; and 1 = ">£100,000".*
- *Normative integration: Data representing normative integration included level of education and employment status. Higher scores indicated less integration. Qualifications were scored as: 1= "college or university degree"; 2= "A levels"; 3= "NVQ, CSEs or O levels" and 5= "none of the above". Employment status was scored as: 1= "employed"; 2 = "student"; 3= "volunteering"; 4= "at home or retired"; and 5 = "unemployed or unable to work"*
- *Access to social rights: Indices of multiple deprivation (IMD) data were used as a distal measure of access to social rights. IMD scores offer a detailed view of deprivation based on a participant's postcode at baseline assessment. As IMD scores are calculated in different ways between countries, scores were converted into quintiles and scored from the most 'deprived' = 5 and the least deprived = 1 (see appendix A). These provide four scores relating to participant's access to adequate housing, education, employment, and healthcare, respectively.*

The factor structure of the social exclusion measure was explored before being used in further analyses. The results of this are presented in the Results.

Outcome variables

Acute pain and chronic pain were dichotomous outcome variables.

Acute pain was determined by the question "In the last month have you experienced any of the following that interfered with your usual activities? with the following choices: "headache"; "facial pain"; "neck or shoulder pain"; "back pain"; "stomach or abdominal pain"; "hip pain"; "knee pain";

“pain all over the body” or “none of the above”. Indication of any pain = “yes” “none of the above” = “no”.

Chronic pain was determined by the question “have you had [... pain] for more than 3 months?” and was classified as ‘yes’ or ‘no’.

Other variables

Sleep was an aggregate continuous variable determined by five questions. Answers to “About how many hours sleep do you get in every 24 hours?” were scored as 0 = “7-9 hours”; 1 = “6 or 10 hours”; 2 = 5 or 11 hours; 3 = <5 or >11 hours. “On an average day, how easy do you find getting up in the morning?” was scored as; 0= “very easy”; 1= “fairly easy”; 2= “not very easy” and 3 = “not at all easy”. The three questions; “do you have a nap during the day?” “do you have trouble falling asleep at night or do you wake up in the middle of the night?” and “do you doze through the day?” were scored as 0 = “never/rarely”; 1 = “sometimes”; 2= “usually”. Scores were summed to give a total sleep score between 0 and 12, with higher scores indicating poorer sleep.

Age, gender and ethnicity were determined at initial assessment by self-report. Age was a continuous variable, whereas gender (male/female) and ethnicity were categorical (white/mixed/Asian or Asian British/black or black British/Chinese/other ethnic origin).

Missing data for each question is reported in appendix A.

Statistical methods

All analyses were conducted using SPSS v26.0.

Step 1: The factor structure of social exclusion

Principal components analysis (PCA) with Varimax rotation and Kaiser Normalisation was conducted on the composite measure of social exclusion. The Kaiser-Meyer-Olkin measure verified the sampling adequacy for the analysis (KMO=.737; excellent) and Bartlett’s test of Sphericity showed a significant result ($BS(45)=815874.677, p<.001$). Therefore, suggesting the suitability of the data for PCA. PCA was chosen as the most appropriate statistical method in order to achieve an accurate, low-dimensional representation of the data relating to social exclusion in the UKBiobank with minimal loss of information. We chose to determine the components of social exclusion using PCA in order to define the latent variables underpinning the concept in a similar manner used to construct the SEI-HS (van Bergen et al., 2017).

The 10 social exclusion items described in the methods were entered into the analysis and factor loadings greater than .35 were considered significant. Factors with eigenvalues above 1.00 were extracted in line with Kaiser’s criterion. Missing data was treated using pairwise deletion.

To produce dichotomous variables, a median split was performed on the total scores for each factor that emerged to distinguish high (more socially excluded/deprived) from low (less socially excluded/deprived) scoring individuals.

The interactions between the three factors were then computed to produce 8 categorical dummy variables as follows: “none”(low all factors); “social participation” (high factor 1 only); “individual deprivation”(high factor 2 only); “area deprivation”(high factor 3 only); “social participation + individual deprivation”(high factors 1+2); “social participation + area deprivation” (high factors 1+3);

“individual deprivation + area deprivation”(high factors 2+3) and “all aspects of social exclusion”(high all factors).

Step 2: Associations between social exclusion, loneliness, pain and sleep

Independent samples t-tests were conducted between ‘lonely’ and ‘not-lonely’ individuals and those experiencing and not experiencing i) acute and ii) chronic pain on each social exclusion factor. Pearson’s bivariate correlations were performed to assess the relationship between sleep and social exclusion. Missing data was treated using listwise deletion.

Step 3: Loneliness and social exclusion as predictors of acute and chronic pain

Binary logistic regression analyses (enter-method) were conducted with loneliness and social exclusion (each factor alone and in combination with “none” as the reference group) as predictors and acute pain and chronic pain as categorical outcomes. Odds likelihood ratios including confidence intervals are reported for each predictor in each model. The first models contained only predictors and dependent variables; the second models controlled for demographics; and the third controlled for demographics and sleep. Missing data was treated using listwise deletion.

Results

Descriptive characteristics of the sample are displayed in table 1.

-Table 1 here -

Main results

Step 1: The factor structure of social exclusion

In the PCA, three factors (instead of four in the SEI-HS) were extracted, accounting for 56.80% of the overall variance. The items grouped together as expected, with the exception of the housing IMD score which did not load on any factor. Factor loadings are presented in Table 2.

Factor 1: The questions relating to social support grouped together and were labelled “[limited] social participation”.

Factor 2: Household income, qualifications and employment status loaded onto the same factor, and this factor was named “individual deprivation”.

Factor 3: As expected the IMD scores for employment, education and health grouped together on one factor which was named “area deprivation”.

- Table 2 here -

Step 2: Associations between social exclusion, loneliness, pain and sleep

Independent samples t-tests showed that lonely individuals scored significantly higher on all three factors of social exclusion and the combined total, as compared to non-lonely individuals.

Individuals suffering acute pain and chronic pain also scored higher on each factor and the combined total. These differences were the same for poor sleep with individuals experiencing loneliness, acute pain and chronic pain reporting more sleep problems, respectively. Small but significant positive correlations were also observed between each factor and poor sleep. Results can be observed in table 3.

-Table 3 here-

Step 3: Loneliness and social exclusion as predictors of acute and chronic pain

Table 4 (model 1) shows that both acute pain and chronic pain are significantly predicted by loneliness and this does not change substantially when adjusted for demographics. Adjusting for sleep(model 3) reduces the odds for experiencing acute pain from 1.887(95%CI1.857-1.917) to 1.510(95%CI1.485-1.535), and for chronic pain from 1.843(95%CI1.816–1.870) to 1.479(95%CI1.457-1.502).

-Table 4 here-

Social exclusion significantly predicted experiencing acute pain as well as chronic pain. All models remained significant when adjusted for demographics and sleep. With “none” as the reference group, and singular component factors explored, the smallest effect was observed for “social participation”, with Odds Ratios approaching 1, and individual deprivation showing higher odds ratios than area deprivation. Odds ratios rise in case of two component factors and the largest effect was observed for all aspects of social exclusion taken together, with ORs ranging from 2.087(95%CI2.026-2.150) for acute pain to 2.314(95%CI2.249-2.380) for chronic pain (model 1).

Discussion

The aim of the current study was to explore the associations between loneliness, social exclusion and the prevalence of both acute and chronic pain in the UKBiobank. This is the first study to our knowledge to examine the relationships between pain and social exclusion in a general population.

The findings provide a proxy measure of social exclusion from the available UKBiobank data and have defined three factors; “[limited] social participation”, “area deprivation” and “individual deprivation”. However, it must be acknowledged that our measure is not as comprehensive as that of van Bergen,(van Bergen et al., 2017) as our items did not include aspects of the fourth factor identified by van Bergen, normative integration. This might be identified by items such as giving to charity or recycling. Other important aspects of normative integration may be being able to communicate in the language of your family, friends and social networks, in addition to how long a person has lived in a particular locality and their history of migration. Another difference is that the items in the Dutch questionnaire were all self-report, whereas ours included data based on area scores. In the current study we used individual IMD scores rather than the Townsend deprivation index as they provide a broader view of the status of an area based on multiple factors. This might be an advantage compared to the Dutch scale. Our factors were deemed adequate representations of social exclusion, appropriate to the intended analyses of this paper, and could be used in future UKBiobank studies to provide easily understandable and appropriate markers of social exclusion.

Lonely individuals scored higher on all measures of social exclusion. Self-reported loneliness has previously been associated with perceptions of relative economic and social deprivation(Demakakos et al., 2006), therefore this finding provides further support to evidence this interaction. As loneliness has also repeatedly been related to health and well-being(Pereira et al., 2013), it is likely that social exclusion and deprivation also play a role. This is further supported by our finding that individuals with acute pain, and chronic pain also scored higher on all aspects of social exclusion.

Poor sleep was related to all aspects of social exclusion and was higher in individuals who reported loneliness, which aligns with research indicating that social exclusion at work can contribute to poor sleep.(Pereira et al., 2013) Furthermore, this poor sleep trend was observed in individuals reporting acute pain and chronic pain which is commensurate with the well-documented bidirectional relationship between sleep and pain.(Cheatle et al., 2016)

The prevalence of loneliness in this sample of the UKBiobank(18.2%) is lower than half of that reported in a general UK population survey in a nationally representative, quota-controlled sample of 2,256 participants(45%).(Griffin, 2010) This lower prevalence could potentially be due to fewer socially isolated individuals choosing to take part. If present, loneliness was found to be significantly associated with an almost two-fold increased prevalence of both acute pain and chronic pain. The odds ratios were similar for both acute and chronic pain, and for both outcomes reduced when adjusted for age, sex and ethnicity (model 2) and reduced further when adjusted for sleep(model 3).

Social exclusion was also associated with an increased prevalence of acute and chronic pain, with odds ratios similar for both acute and chronic pain, and not changing greatly when adjusted for age, sex and ethnicity or for sleep for either outcome. Unsurprisingly the size of the effect was the smallest in the groups who experienced only one type of social exclusion, particularly “social participation”, and was largest for the groups experiencing all three types of social exclusion, exhibiting over two-fold risk of experiencing acute pain(OR:2.087) and chronic pain(OR:2.365) respectively. This indicates that levels of deprivation (on both an individual and area level) may play a larger role in the development of pain in comparison to the influence that limited social support and participation may have.

The prevalence of acute and chronic pain in the current sample of the UKBiobank was 60.6% and 43.7% respectively. Previous research suggests that chronic pain can affect between 13–50% of adults in the UK(Mills et al., 2019), therefore this is close to the upper limit, however this was an older-adult population. Nevertheless, it must be acknowledged that there is large variation in population estimates for the prevalence of chronic pain, mainly attributed to differences in definition, methods of assessment, and population. There has been a call for exploring the relationship between aging and the experience of pain(Gagliese, 2009), which would potentially raise questions about the causes of pain throughout the life course. Such an influence is not suggested in this study as the association between either loneliness or social exclusion and acute or chronic pain remains approximately the same after correction for age. While this does not rule out the possible impact of life course, it does raise interesting questions about the experience of pain and social exclusion.

The findings of this paper show an association between acute and chronic pain and highlights interesting issues surrounding the social determinants of health and the impact of inequalities in later life. It must be stressed that we do not propose that these issues lie solely within the individual, but rather that a complex interaction of intrinsic and extrinsic factors pertaining to social exclusion and loneliness can influence experiences of pain. We also acknowledge the possibility of bi-directionality, as it is plausible that experiences of pain may contribute to increases in social exclusion and loneliness (e.g. by hindering the ability to participate in social activities, maintain employment).This raises questions about causality, along with the broader impact of inequalities, that might be addressed in a longitudinal design.

The reduction of the odds ratios in each model with the addition of sleep, amounted to a difference of approximately 0.3, which indicates a small effect. Although this contrasts with the well-documented relationships between sleep and pain in previous literature on clinical samples, a relevant effect of sleep is still evident in this general population sample and warrants further exploration.

The United Nations Convention on rights of people with disability(Resolution, 2006) states that disability results from the interaction between persons with impairments and attitudinal and environmental barriers that hinders their full and effective participation in society on an equal basis with others. Our findings suggest that such an interaction may be the case for people who experience social isolation and pain. Currently, people with pain often seek medical treatment that involves mostly prescription of painkillers, if possible combined with Cognitive Behavioural Treatment. In view of the ongoing opioid crisis(Giraudon et al., 2013), and in view of our findings, research into preventive

public health interventions might be warranted that should facilitate environmental integration and improving quality of life for people, to increase their capability and resilience and to encourage them to flourish. For example, such an intervention might focus on prevention of social exclusion or bullying at the workplace.

Clinical studies could explore alternative strategies for pain management such as social prescribing. Also, further research would be warranted into quality of life questionnaires that explore loneliness as part of quality of life. The Recovering Quality of Life questionnaire (ReQoL)(Keetharuth et al., 2018) is a new quality of life questionnaire that explicitly assesses loneliness, contrary to the EQ-5D and the SF36, and hence this questionnaire would be especially suitable for conducting such research.

This study for the first time explores the association between loneliness, social exclusion and acute and chronic pain in a large general population sample, and explores the role of sleep as potential mediator, which is innovative and a strength of the study. Another, obvious strength is the large sample size of about 500,000 participants, which is much larger than most population studies examining associations between psychosocial factors and pain. Further, the use of a composite measure for social exclusion based upon the model of van Bergen(van Bergen et al., 2017), and the factor analysis exploring the composite factors, can be considered a methodological strength. Another strength of the study is that we avoid locating the problem solely within the individual, by looking at external aspects of social exclusion as well as individual ones.

The main limitation was the categorical assessment of both acute and chronic pain via yes or no responses. Pain is undoubtedly a dimensional concept which should be assessed as so, however such measures were unfortunately not available in the dataset. This simple categorical assessment method may also have contributed to the high rates of pain recorded within the current study. Other limitations include the obvious question of co-morbidities, which may connect to an identified painful physical condition. Future studies with the dataset should also explore the associations more thoroughly to assess for diagnosed pain and as previously mentioned, adjust for comorbid conditions. Furthermore, variables such as levels of disability, and rurality are likely to influence the associations examined in the current study, however this data was not available. Finally, the use of composite scores to assess sleep may also be regarded as a limitation, compared to using validated measures. However, this is a limitation of the dataset as a whole.

Further, the cross-sectional nature of the analyses means that direction of causality cannot be reliably inferred. Although, it is clear there are links between social exclusion and pain, we cannot absolutely conclude that social exclusion can lead to pain. In order to explore that, further studies aim to utilise follow-up data from the UK Biobank to conduct longitudinal analyses.

As participants were mainly white, and aged over 45 years, they are not entirely representative of the UK population. The recruitment of participants living only within 25 miles of an assessment centre may also mean that more isolated participants living out of this radius area might not be properly represented, however, this was not corroborated by the data on area deprivation in this study.

In summary, social exclusion is a multifaceted construct, which together with loneliness is associated with an increased prevalence of both acute and chronic pain in the general population as represented in the UK Biobank. Poor sleep appears to play a small but significant, potentially mediating role in this association. From a public health perspective these findings could be used to design novel interventions to prevent and manage pain (e.g. fostering social networks), or social interventions to mitigate social exclusion, and in clinical conditions by social prescribing. Further exploration of the incidence of chronic pain in loneliness and social exclusion in the general population to explore causal

relations is warranted. Sub-group analysis (e.g. exploring differences in experience between people born with an impairment and those who acquire impairment later in life) may also be useful.

Conflict of Interests

No conflicts to declare.

Author Contribution

Sarah Allen: Conceptualization; Data curation; Formal analysis; Funding acquisition; Project administration; Writing – original draft; Writing – review & editing

Simon Gilbody: Conceptualization; Funding acquisition; Writing – review & editing

Karl Atkin: Conceptualization; Writing – review & editing

Christina van der Feltz-Cornelis: Conceptualization; Data curation; Funding acquisition; Supervision; Writing – review & editing

References

- Blyth, F.M., Macfarlane, G.J., Nicholas, M.K., 2007. The contribution of psychosocial factors to the development of chronic pain: the key to better outcomes for patients? *Pain* 129(1), 8-11.
- Cheatle, M.D., Foster, S., Pinkett, A., Lesneski, M., Qu, D., Dhingra, L., 2016. Assessing and managing sleep disturbance in patients with chronic pain. *Anesthesiol Clin* 34(2), 379-393.
- de Heer, E., ten Have, M., van Marwijk, H.W., Dekker, J., de Graaf, R., Beekman, A.T., van der Feltz-Cornelis, C.M., 2018. Pain as a risk factor for common mental disorders. Results from the Netherlands Mental Health Survey and Incidence Study-2: a longitudinal, population-based study. *Pain* 159(4), 712-718.
- Demakakos, P., Nunn, S., Nazroo, J., 2006. Loneliness, relative deprivation and life satisfaction, in: *Studies, T.I.f.F. (Ed.) Retirement, Health and Relationships of the Older Population in England. Patersons Tunbridge Wells* pp. 297-318.
- Demyttenaere, K., Bruffaerts, R., Lee, S., Posada-Villa, J., Kovess, V., Angermeyer, M.C., Levinson, D., de Girolamo, G., Nakane, H., Mneimneh, Z., 2007. Mental disorders among persons with chronic back or neck pain: results from the World Mental Health Surveys. *Pain* 129(3), 332-342.
- Dyson, S., Berghs, M., 2019. Ethnicity, Disability and Chronic Illness, in: Chattoo, S., Atkin, K., Craig, G., Flynn, R. (Eds.), *Understanding Race and Ethnicity: Theory, history, policy and politics*. Policy Press, Bristol.
- Eisenberger, N.I., 2012. The pain of social disconnection: examining the shared neural underpinnings of physical and social pain. *Nat Rev Neurosci* 13(6), 421-434.
- Eisenberger, N.I., Lieberman, M.D., Williams, K.D., 2003. Does rejection hurt? An fMRI study of social exclusion. *Science* 302, 290-292.
- Elovainio, M., Hakulinen, C., Pulkki-Råback, L., Virtanen, M., Josefsson, K., Jokela, M., Vahtera, J., Kivimäki, M., 2017. Contribution of risk factors to excess mortality in isolated and lonely individuals: an analysis of data from the UK Biobank cohort study. *Lancet Public Health* 2(6), e260-e266.
- Fayaz, A., Croft, P., Langford, R., Donaldson, L., Jones, G., 2016. Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies. *BMJ Open* 6(6), e010364.
- Fry, A., Littlejohns, T., Sudlow, C., Doherty, N., Adamska, L., Sprosen, T., Collis, R., Allen, N., 2017. Comparison of Sociodemographic and Health-Related Characteristics of UK Biobank Participants with those of the General Population. *Am J Epidemiol* 186(9), 1026-1034.
- Gagliese, L., 2009. Pain and aging: the emergence of a new subfield of pain research. *J Pain* 10(4), 343-353.
- GBD, 2016. Disease and Injury Incidence and Prevalence Collaborators: Global, regional, and national incidence, prevalence and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*(388), 1545-1602.
- Giraudon, I., Lowitz, K., Dargan, P.I., Wood, D.M., Dart, R.C., 2013. Prescription opioid abuse in the UK. *Br J Clin Pharmacol* 76(5), 823-824.
- Godlee, F., 2019. Inequality matters. *BMJ*(367).
- Griffin, J., 2010. *The lonely society?* Mental Health Foundation.
- Keetharuth, A.D., Brazier, J., Connell, J., Bjorner, J.B., Carlton, J., Buck, E.T., Ricketts, T., McKendrick, K., Browne, J., Croudace, T., 2018. Recovering Quality of Life (ReQoL): a new generic self-reported outcome measure for use with people experiencing mental health difficulties. *BJPsych* 212(1), 42-49.
- Mills, S.E., Nicolson, K.P., Smith, B.H., 2019. Chronic pain: a review of its epidemiology and associated factors in population-based studies. *British journal of anaesthesia* 123(2), e273-e283.

- Mordecai, L., Reynolds, C., Donaldson, L.J., Williams, A.C., 2018. Patterns of regional variation of opioid prescribing in primary care in England: a retrospective observational study. *Br J Gen Pract* 68(668), e225-e233.
- Nahit, E., Hunt, I., Lunt, M., Dunn, G., Silman, A., MacFarlane, G.J., 2003. Effects of psychosocial and individual psychological factors on the onset of musculoskeletal pain: common and site-specific effects. *Ann Rheum Dis* 62(8), 755-760.
- Nicholl, B.I., Mackay, D., Cullen, B., Martin, D.J., Ul-Haq, Z., Mair, F.S., Evans, J., McIntosh, A.M., Gallagher, J., Roberts, B., 2014. Chronic multisite pain in major depression and bipolar disorder: cross-sectional study of 149,611 participants in UK Biobank. *BMC Psychiatry* 14(1), 350.
- O'Brien, E.M., Waxenberg, L.B., Atchison, J.W., Gremillion, H.A., Staud, R.M., McCrae, C.S., Robinson, M.E., 2010. Negative mood mediates the effect of poor sleep on pain among chronic pain patients. *Clin J Pain* 26(4), 310-319.
- Okifuji, A., Hare, B.D., 2011. Do sleep disorders contribute to pain sensitivity? *Curr Rheumatol Rep* 13(6), 528-534.
- Pereira, D., Meier, L.L., Elfering, A., 2013. Short-term effects of social exclusion at work and worries on sleep. *Stress and Health* 29(3), 240-252.
- Petitte, T., Mallow, J., Barnes, E., Petrone, A., Barr, T., Theeke, L., 2015. A systematic review of loneliness and common chronic physical conditions in adults. *Open Psychol J* 8(Suppl 2), 113.
- Poleshuck, E.L., Green, C.R., 2008. Socioeconomic disadvantage and pain. *Pain* 136(3), 235.
- Resolution, A., 2006. RES/61/106. Convention on the Rights of Persons with Disabilities. Sixty-first United Nations General Assembly, New York 13.
- Rios, R., Zautra, A.J., 2011. Socioeconomic disparities in pain: The role of economic hardship and daily financial worry. *Health Psychol* 30(1), 58.
- Srisurapanont, M., Jarusuraisin, N., 1998. Amitriptyline vs. lorazepam in the treatment of opiate-withdrawal insomnia: a randomized double-blind study. *Acta Psychiatr Scand* 97(3), 233-235.
- Sudlow, C., Gallacher, J., Allen, N., Beral, V., Burton, P., Danesh, J., Downey, P., Elliott, P., Green, J., Landray, M., 2015. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med* 12(3), e1001779.
- Tsang, A., Von Korff, M., Lee, S., Alonso, J., Karam, E., Angermeyer, M.C., Borges, G.L.G., Bromet, E.J., De Girolamo, G., De Graaf, R., 2008. Common chronic pain conditions in developed and developing countries: gender and age differences and comorbidity with depression-anxiety disorders. *J Pain* 9(10), 883-891.
- van Bergen, A.P., Hoff, S.J., Schreurs, H., van Loon, A., van Hemert, A.M., 2017. Social Exclusion Index-for Health Surveys (SEI-HS): a prospective nationwide study to extend and validate a multidimensional social exclusion questionnaire. *BMC Public Health* 17(1), 253.

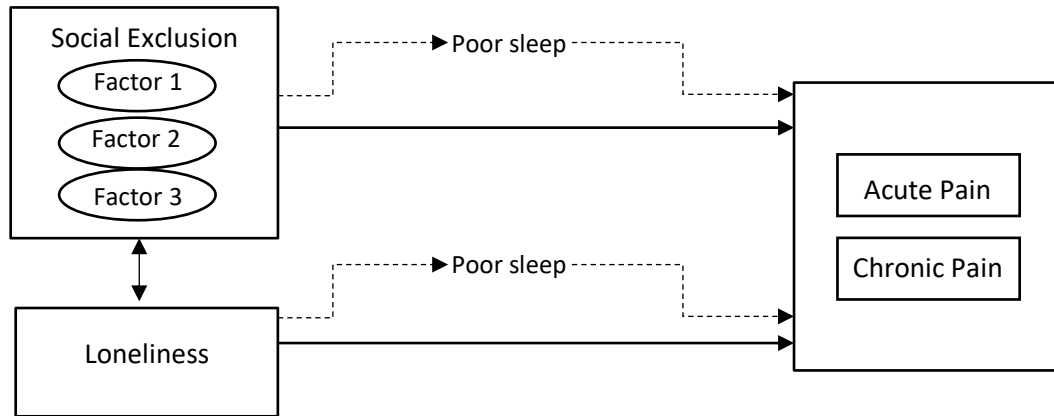


Figure 1. The hypothesised relationships between loneliness, social exclusion and both acute and chronic pain, via poor sleep, that will be examined in the current study.

Table 1. Description of the sample (N=502,528).

Variable		n (valid %)
<i>Age</i>	Mean [\pm SD]	56.63 [\pm 8.10]
<i>Sex</i>	Female	273397 (54.4%)
	Male	229131 (45.6%)
<i>Ethnic Background</i>	White	468755 (94.6%)
	Mixed	2930 (0.6%)
	Asian/Asian British	9800 (2.0%)
	Black/Black British	8014 (1.6%)
	Chinese	1553 (0.3%)
	Other	4522 (0.9%)
	Undeclared	2777 (0.6%)
<i>Loneliness</i>	Yes	91414 (18.2%)
	No	401241 (79.8%)
<i>Acute pain</i>	Yes	303227 (60.8%)
	No	197111(39.2%)
<i>Chronic pain</i>	Yes	216825 (43.7%)
	No	279326 (55.6%)
<i>Social participation</i> (range 3-15)	Mean [\pm SD]	6.96 [\pm 2.54]
<i>Individual deprivation</i> (range 3-15)	Mean [\pm SD]	8.03 [\pm 3.10]
<i>Area deprivation</i> (range 3-15)	Mean [\pm SD]	8.88 [\pm 3.89]
<i>Total Social Exclusion</i> (range 9-45)	Mean [\pm SD]	23.88 [\pm 6.57]
<i>Sleep</i> (range 0-13)	Mean [\pm SD]	3.19 [\pm 1.90]

Table 2. Factor loadings for each of the social exclusion items

	Rotation Factor loading		
	Factor 1: Social participation	Factor 2: Individual deprivation	Factor 3: Area deprivation
1. <i>Family/friends visits</i>	.521		
2. <i>Ability to confide</i>	.629		
3. <i>Leisure activities</i>	.705		
4. <i>Household income</i>		.775	
5. <i>Qualifications</i>		.758	
6. <i>Employment status</i>		.666	
7. <i>Education (IMD)</i>			.857
8. <i>Housing (IMD)</i>			.939
9. <i>Employment (IMD)</i>			.912
10. <i>Health (IMD)</i>	-	-	-
<i>Eigen values</i>	1.215	1.392	3.072

Factor loadings lower than .35 were suppressed.

Table 3. Differences in social exclusion scores in relation to loneliness, acute pain, chronic pain and levels of poor sleep.

		<i>Social participation</i> M [SD]	<i>Individual deprivation</i> M[SD]	<i>Area deprivation</i> M[SD]	<i>Total social exclusion</i> M[SD]	<i>Sleep</i> M[SD]
Loneliness	Yes	7.89 [2.76]	8.91 [3.06]	9.70 [3.95]	26.61 [6.66]	4.06 [2.10]
	No	6.74 [2.43]	7.80 [3.07]	8.68 [3.85]	23.19 [6.37]	2.98 [1.78]
	<i>p</i>	<.001**	<.001**	<.001**	<.001**	<.001**
Acute pain	Yes	7.05 [2.56]	8.32 [3.15]	9.17 [3.92]	24.58 [6.70]	3.50 [1.98]
	No	6.81 [2.50]	7.57 [2.96]	8.42 [3.80]	22.79 [6.22]	2.72 [1.67]
	<i>p</i>	<.001**	<.001**	<.001**	<.001**	<.001**
Chronic Pain	Yes	7.09 [2.57]	8.57 [3.16]	9.28 [3.93]	25.02 [6.74]	3.66 [2.03]
	No	6.85 [2.50]	7.60 [2.97]	8.55 [3.83]	22.97 [6.29]	2.83 [1.70]
	<i>p</i>	<.001**	<.001**	<.001**	<.001**	<.001**
Sleep	<i>r</i>	.099**	.178**	.113**	.198**	-
	<i>p</i>	<.001**	<.001**	<.001**	<.001**	-

*=p<.05, **=p<.001

Independent samples t-tests show differences in social exclusion scores between groups determined by loneliness, acute pain and chronic pain. (Means, [SD]). Pearson's correlations show the relationships between sleep quality and each social exclusion score.

Table 4. The association between loneliness and social exclusion and prevalence of pain, in odds ratios with 95% confidence intervals

Predictors			Acute Pain			Chronic Pain		
			Model 1 Unadj odds ratio	Model 2 Adj odds ratio	Model 3 Adj odds ratio	Model 1 Unadj odds ratio	Model 2 Adj odds ratio	Model 3 Adj odds ratio
Loneliness	No	81.8	1	1	1	1	1	1
	Yes	18.2	1.887* [1.857-1.917]	1.843* [1.814-1.873]	1.510* [1.485-1.535]	1.843* [1.816-1.870]	1.823* [1.796-1.850]	1.479* [1.457- 1.502]
Social Exclusion	None	24.4	1	1	1	1	1	1
	Social participation only	13.7	1.073* [1.046- 1.101]	1.075* [1.047-1.102]	1.033* [1.006-1.060]	1.088* [1.060 -1.117]	1.112* [1.084-1.142]	1.067* [1.039- 1.096]
	Individual deprivation only	11.1	1.235* [1.201-1.269]	1.369* [1.330-1.410]	1.292* [1.254-1.330]	1.436* [1.397-1.476]	1.432 * [1.392-1.474]	1.340* [1.301-1.380]
	Area deprivation only	12.4	1.211* [1.180- 1.244]	1.177* [1.146- 1.209]	1.146* [1.115-1.177]	1.189* [1.157-1.221]	1.182* [1.150-1.214]	1.149* [1.118-1.181]
	Social participation + individual deprivation	6.3	1.431* [1.383-1.481]	1.577* [1.522-1.633]	1.398* [1.348-1.449]	1.663* [1.608-1.720]	1.693* [1.635-1.752]	1.485* [1.433-1.539]
	Social participation + area deprivation	7.8	1.378* [1.335-1.422]	1.333* [1.291-1.376]	1.229* [1.189-1.269]	1.358* [1.316 - 1.401]	1.374* [1.331-1.418]	1.260* [1.220-1.301]
	Individual deprivation + area deprivation	14.1	1.762* [1.717-1.809]	1.897* [1.846-1.949]	1.692* [1.646-1.740]	1.958* [1.909-2.008]	1.959* [1.908- 2.012]	1.728* [1.682-1.776]
	Social participation+ individual deprivation + area deprivation	10.3	2.087* [2.026-2.150]	2.227* [2.160 2.296]	1.830* [1.774 1.889]	2.314* [2.249-2.380]	2.365* [2.298- 2.434]	1.913* [1.857-1.971]

*=p<.05 .Binary logistic regression analyses in which loneliness and social exclusion grouping are predictors, and acute pain and chronic pain are outcomes. Model 1: No adjustments. Model 2: Adjusted for age, sex and ethnicity. Model 3: Adjusted for ages, sex, ethnicity and poor sleep.

