Chronic pain and COVID-19 hospitalisation and mortality: a UK Biobank cohort study

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1. Introduction

Chronic pain significantly affects well-being, with chronic low back pain being the leading cause of disability globally. In the United Kingdom, the prevalence of chronic pain in adults is estimated to be between 35.0% and 51.3%. Globally, chronic pain affects 1 in 5 adults, although this is believed to be an underestimate. Chronic pain is a complex condition which is challenging to treat. The burden of disease due to chronic pain and demand for effective pain management is likely to increase during the COVID-19 pandemic, with joint and muscle pain being reported both in the acute phase and by those with long COVID. Chronic pain can be a result of SARS-CoV-2 infection, it remains unclear whether chronic pain may predispose to more severe SARS-CoV-2 infection or higher risk of adverse outcome.

To mitigate the impact of COVID-19 and target public health and clinical interventions, many hospital and community studies have tried to identify risk factors for COVID-19 outcomes. Socio-demographic characteristics such as older age, socioeconomic deprivation, male sex, and Black and South Asian ethnicity have consistently been associated with higher risk of SARS-CoV-2 infection and death in the United Kingdom. The association between ethnicity and COVID-19 has been shown to be modified by occupation, although other factors including overcrowded housing, poorer socioeconomic status, and structural racism are also important. Some individual long-term conditions (LTCs), for example, cardiac disease, diabetes, and obesity, have been associated with higher COVID-19 case fatality. Furthermore, multimorbidity (the presence of 2 or more LTCs) is also associated with increased risk of SARS-CoV-2 infection as is frailty.
Chronic pain is more likely to be reported by those of Asian and Black ethnicity and in those of low socioeconomic status. A study of multimorbidity in primary care found that pain was associated with all the 10 most prevalent multimorbidity clusters. Research into whether chronic pain is associated with SARS-CoV-2 infection or COVID-19 mortality is limited. A recent study observed that, in children and adults with sickle cell disease, those with frequent prior acute care visits for pain were more likely to be hospitalised during their COVID-19 illness than those without such a history. However, it is not known whether this relationship exists in the general population.

We explored whether UK Biobank participants with self-reported chronic pain had a higher risk of COVID-19 hospitalisation and mortality.

2. Methods

2.1. Participants

UK Biobank is a prospective cohort study. It recruited 502,624 participants aged 37 to 73 years across England, Scotland, and Wales between 2006 and 2010. At baseline, touch-screen questionnaires and nurse-administered interviews were used to collect demographic, health, environmental, and lifestyle data using standardised protocols and to record biological measurements. This study received ethical approval from the North West Multi-Centre Research Ethics Committee (REC reference: 16/NW/0274). All participants gave written informed consent for data collection, analysis, and record linkage.

2.2. Definitions

Baseline data from UK Biobank were linked, both prospectively and retrospectively, to hospital inpatient data, comprising Hospital Episode Statistics (HES) Admitted Patient Care data for England and Scottish Morbidity Record (SMR01) data for Scotland. Potential participants were excluded if their baseline assessment centre was in Wales because Welsh hospital inpatient data have not been updated to include the pandemic period.

Primary outcome was COVID-19 hospitalisation, defined as ICD code U071 (virus identified). Secondary outcome was COVID-19 mortality, defined as ICD code U071 or U072 (virus probable, suspected, or clinically epidemiologically diagnosed) recorded as the primary cause of death.

The hospital data included admission date and COVID-19 diagnosis. For those who had a COVID-19 diagnosis, admissions data were available between 15 of August 2019 and 26 of March 2021. Data were linked to Death Register Data for England and Scotland (available from 5 March 2020 to 17 March 2021). All COVID-19 deaths were included regardless of where they occurred: in the community and during or after admission to hospital. Chronic pain, self-reported at baseline (2006-2010), using a touch-screen questionnaire, was defined as having pain for at least 3 months in one or more of the following sites: head, face, neck/shoulder, back, abdomen, hip, and knee. A binary yes/no variable was constructed for chronic pain. The total number of sites of chronic pain was categorised as none (no chronic pain), 1, 2 to 3, or 4 to 7. Chronic widespread pain was defined as self-reported pain all over the body for at least 3 months. It was analysed as a separate exposure, comparing participants who reported chronic widespread pain with those without chronic pain.

Ethnicity was self-reported and categorised as White, Black, South Asian, Chinese, mixed, or other. Current age was calculated as age at assessment plus the number of years between assessment date and date of death or censor date. Current age was entered into all analyses as a continuous variable. Body mass index (BMI) was derived from weight (kg)/height (m$^2$) and categorised into underweight (<18.5 kg/m$^2$), normal weight (18.5-24.9 kg/m$^2$), overweight (≥25-29.9 kg/m$^2$), obese (≥30-34.9 kg/m$^2$), and morbidly obese (≥35 kg/m$^2$). Area-level socioeconomic deprivation was assessed using the Townsend deprivation index, which incorporates unemployment, car ownership, home ownership, and household overcrowding. Higher Townsend scores represent greater socioeconomic deprivation; scores were categorised into quintiles within the study sample. Smoking status, frequency of alcohol consumption, and physical activity were self-reported. Smoking status was categorised as never or current or previous smoker. Alcohol consumption was categorised into never or special occasions only, 1 to 3 times a month, 1 to 4 times a week, and daily or almost daily. Physical activity was categorised into none, low, medium, or high using Metabolic Equivalent Task (MET) scores based on the International Physical Activity Questionnaire (IPQA short form) scoring protocol.

Number of LTCs was defined as a count of 43 self-reported conditions which have previously been used in UK Biobank studies of multimorbidity (Supplementary Table 1, available at http://links.lww.com/PAIN/B629). This list of conditions is based on previously published literature on multimorbidity. For chronic pain as a binary and ordinal variable, the “painful conditions” grouping contained only trigeminal neuralgia, shingles, and headache. For chronic widespread pain, the “painful conditions” grouping also contained back pain/problems, sciatica/disc/nerve problems, plantar fasciitis, carpal tunnel syndrome, and joint osteo/spine arthritis/spondylitis/arthritis with no other symptoms. LTC count was entered into models categorised as 0, 1, 2 to 3, and ≥4 LTCs.

2.3. Statistical analyses

Univariable Poison regression analysis was performed for the association between chronic pain and COVID-19 diagnosis (in hospital). In multivariable analysis, the model was first adjusted for sociodemographic factors (current age, sex, Townsend deprivation quintile, ethnicity, and assessment centre location), then additionally adjusted for lifestyle factors (smoking status, alcohol frequency, BMI, and physical activity), and finally for number of LTCs. The adjustment for number of LTCs was performed last because LTCs can be considered as a confounder or a mediator or both in the relationship between chronic pain and COVID-19 diagnosis and mortality. Chronic pain was coded first as a binary variable, then as an ordinal variable derived from number of pain sites (none, 1, 2-3, and 4-7), and finally as chronic widespread pain vs no chronic pain.

Cox proportional hazards regression was performed for the association between chronic pain and COVID-19 mortality (deaths in the whole study sample), and for the association between chronic pain and COVID-19 case fatality (deaths among those hospitalised for COVID-19), both adjusted as above. Models included time to event (mortality or end of follow-up) from baseline assessment. The proportional hazards assumption was assessed through formal tests of Schoenfeld residuals. Analyses were undertaken using Stata v14.

3. Results

From an initial sample of 502,503 UK Biobank participants, 28,806 were excluded because they died before the first hospital
admission for COVID-19, and a further 19,438 were excluded because they attended a Welsh assessment centre (Supplementary Fig. 1, available at http://links.lww.com/PAIN/B629). Of the remainder, complete data on chronic pain and covariates were available for 441,403 participants. Of these, 3180 (0.7%) were admitted with a COVID-19 diagnosis and there were 1040 (0.2%) COVID-19–related deaths. 1724 (54%) of those hospitalised for COVID-19 had a history of chronic pain, as did 539 (52%) of those whose death was related to COVID-19.

Table 1 presents participant characteristics by COVID-19 hospitalisation. Among participants with a positive COVID-19 test in hospital, 54% had self-reported chronic pain in at least 1 site at baseline, compared with 43% of those without a positive test. Presence of chronic pain was associated with SARS-CoV-2 infection univariably (Table 2; IRR 1.57, 95% CI 1.46-1.68, $P < 0.001$); the association was attenuated after adjustment for potential confounders (adjusted IRR 1.25, 95% CI 1.17-1.35, $P < 0.001$) and further attenuated but remained significant after adjustment for LTCs (fully adjusted IRR 1.16, 95% CI 1.08-1.24, $P < 0.001$) and further attenuated but remained significant after adjustment for LTCs (fully adjusted IRR 1.68, 95% CI 1.36-2.08, $P < 0.001$); the association was attenuated after adjustment for potential confounders (adjusted IRR 1.25, 95% CI 1.17-1.35, $P < 0.001$) and further attenuated but remained significant after adjustment for LTCs (fully adjusted IRR 1.16, 95% CI 1.08-1.24, $P < 0.001$).

When chronic pain was treated as an ordinal variable, there was a positive association between number of pain sites and COVID-19 hospitalisation. Among participants with a positive COVID-19 test in hospital, 54% had self-reported chronic pain in at least 1 site at baseline, compared with 43% of those without a positive test. Presence of chronic pain was associated with SARS-CoV-2 infection univariably (Table 2; IRR 1.57, 95% CI 1.46-1.68, $P < 0.001$); the association was attenuated after adjustment for potential confounders (adjusted IRR 1.25, 95% CI 1.17-1.35, $P < 0.001$) and further attenuated but remained significant after adjustment for LTCs (fully adjusted IRR 1.16, 95% CI 1.08-1.24, $P < 0.001$).

Chronic widespread pain was associated with COVID-19 hospitalisation univariably (Table 4; IRR 3.07, 95% CI 2.50-3.77, $P < 0.001$); the association was attenuated after adjustment for potential confounders (adjusted IRR 1.68, 95% CI 1.36-2.08; $P < 0.001$) and further attenuated but remained significant after adjustment for LTCs (fully adjusted IRR 1.33, 95% CI 1.06-1.66; $P = 0.012$).

There was an association between pain and COVID-19 mortality univariably (Table 2; HR 1.40, 95% CI 1.24-1.59, $P < 0.001$), but this was fully attenuated after adjustment for confounders and LTCs (adjusted HR 1.01, 95% CI 0.89-1.15, $P = 0.834$). The pattern was similar when chronic pain was treated as an ordinal variable (Table 3; unadjusted compared with no pain, 1 site HR 1.15, 95% CI 0.99-1.34; 2-3 sites HR 1.45, 95% CI 1.23-1.70; 4–7 sites HR 2.40, 95% CI 1.84-3.13; global $P$-value < 0.001). The dose-response relationship remained and was still significant after adjustment for LTCs (global $P$-value = 0.834). Chronic widespread pain was associated with COVID-19 mortality univariably (Table 4; HR 3.14, 95% CI 2.24-4.41, $P < 0.001$). However, the association was attenuated after adjustment for confounders (HR 1.84, 95% CI 1.29-2.62, $P$-value = 0.001) and further attenuated after adjustment for LTCs (HR 1.50, 95% CI 1.04-2.16, $P$-value = 0.032). There was no evidence of violation of the proportional hazards assumption.

There was no clear association between chronic pain and COVID-19 case fatality. For the exposures, chronic pain status (Table 2) and number of pain sites (Table 3) hazard ratios were close to 1. For chronic widespread pain, there was a suggestion of increased case fatality but 95% confidence intervals were very wide (Table 4; fully adjusted HR 1.34, 95% CI 0.90-1.99, $P$-value=0.150). This may reflect the rarity of the outcome rather than there being no effect.

### 4. Discussion

To the best of our knowledge, this is the first study to explore the associations between chronic pain and COVID-19 hospitalisation and mortality in the general population. Chronic pain, both at

| Chronic pain | No | Yes | $\chi^2$ test | $P$ |
|--------------|----|-----|---------------|----|
|               | 249,090 (57.03) | 1456 (45.79) | <0.001 |
|               | 188,314 (42.97) | 1724 (54.21)  |           |

| Townsend deprivation quintile | No | Yes | $\chi^2$ test | $P$ |
|------------------------------|----|-----|---------------|----|
| 1 (least deprived)           | 89,252 (20.37) | 431 (13.55)   | <0.001 |
| 2                            | 88,709 (20.24) | 496 (15.57)   |           |
| 3                            | 87,787 (20.03) | 522 (16.42)   |           |
| 4                            | 87,641 (20.00) | 668 (21.01)   |           |
| 5 (most deprived)            | 84,834 (19.36) | 1064 (35.46)  |           |

**Table 1**

Characteristics of study population by hospitalisation for COVID-19.

| BMI category | No | Yes | $\chi^2$ test | $P$ |
|--------------|----|-----|---------------|----|
| Underweight  | 2179 (0.50) | 11 (0.35)   | <0.001 |
| Normal        | 141,324 (32.25) | 515 (16.19) |           |
| Overweight    | 188,632 (43.04) | 1280 (40.25) |           |
| Obese         | 76,777 (17.92) | 855 (26.89) |           |
| Morbidly obese| 29,311 (6.69) | 519 (16.32) |           |

| Smoking status | No | Yes | $\chi^2$ test | $P$ |
|----------------|----|-----|---------------|----|
| Never          | 244,872 (55.88) | 1361 (42.80) | <0.001 |
| Current/previous| 193,351 (44.12) | 1819 (57.20) |           |

| Alcohol consumption frequency | No | Yes | $\chi^2$ test | $P$ |
|-------------------------------|----|-----|---------------|----|
| Never/special occasions       | 82,979 (19.84) | 962 (30.25) | <0.001 |
| 1-3 times a month             | 49,270 (11.42) | 351 (11.04) |           |
| 1-4 times a week              | 216,820 (49.48) | 1328 (41.76) |           |
| Daily or almost daily         | 89,154 (20.34) | 539 (16.95) |           |

| Physical activity | No | Yes | $\chi^2$ test | $P$ |
|-------------------|----|-----|---------------|----|
| High              | 46,218 (10.55) | 180 (5.66) | <0.001 |
| Medium            | 349,605 (79.78) | 2411 (75.82) |           |
| Low               | 15,868 (3.62) | 180 (5.66) |           |
| None              | 26,532 (6.05) | 400 (12.58) |           |

| Number of long-term conditions | No | Yes | $\chi^2$ test | $P$ |
|--------------------------------|----|-----|---------------|----|
| 0                              | 175,807 (40.12) | 703 (22.11) | <0.001 |
| 1                              | 146,912 (33.52) | 956 (30.06) |           |
| 2-3                            | 101,907 (23.25) | 1230 (38.68) |           |
| ≥4                             | 101,907 (23.25) | 1230 (38.68) |           |

**Table 2**

Participant characteristics by COVID-19 hospitalisation.

| N (%) | N (%) | Hospitalisation for COVID-19 |
|-------|-------|-----------------------------|
| 62-75 | 73 (66-78) | Current age (years) |
| 0.001 | Current age (years) | Median (IQR) | Wilcoxon P |
individual sites and widespread, was associated with COVID-19 hospitalisation independent of potential confounders including presence of LTCs, and there was a clear dose-response relationship with the number of pain sites. Any association between pain and COVID-19 mortality was less clear, suggesting that pain increases the risk of serious illness but may not increase the risk of what happens thereafter. The effect sizes observed imply potentially small increases in the risk of COVID-19 hospitalisation at a population level. For example, the lower limit of the fully adjusted 95% confidence interval when chronic pain is treated as a binary variable may also make individuals susceptible to more severe COVID-19 infection, requiring hospitalisation, as may also be the case for other conditions where inflammation seems to be causally related, eg, cardiovascular disease. Furthermore, diminished physical functioning due to chronic pain may predispose to complications of COVID-19. For example, greater immobility due to chronic pain may potentiate thromboembolic complications and poorer preinfection cardiorespiratory function.

The strengths of UK Biobank include its large sample size and extensive phenotyping, which enabled us to adjust for a wide range of potential confounders including comorbidities and sociodemographic and lifestyle risk factors. Nonetheless, as with all observational studies, residual confounding because of unknown or unmeasured confounders is possible, for example, differential access to testing or hospitalisation. UK Biobank is not representative of the general population (response rate 5.5%).

### Table 2
Poison and Cox regression models of the associations between chronic pain status and COVID-19 hospitalisation, mortality, and case fatality.

| Chronic pain | Unvariable | Multivariable 1* | Multivariable 2† | Multivariable 3‡ |
|--------------|------------|------------------|------------------|------------------|
| COVID-19 hospitalisation, IRR (95% CI) | No (N = 251,365) | 1 | 1.57 (1.46-1.68) | 1.47 (1.37-1.58) | 1.25 (1.17-1.35) | 1.16 (1.08-1.24) |
| Yes (N = 190,038) | | | | | | |
| COVID-19 mortality, HR (95% CI) | No (N = 251,365) | 1 | 1.40 (1.24-1.59) | 1.32 (1.16-1.49) | 1.09 (0.96-1.23) | 1.01 (0.89-1.15) |
| Yes (N = 190,038) | | | | | | |
| COVID-19 case fatality, HR (95% CI) | No (N = 1456) | 1 | 0.94 (0.81-1.08) | 0.97 (0.84-1.12) | 0.92 (0.79-1.06) | 0.91 (0.79-1.06) |
| Yes (N = 1724) | | | | | | |

* Adjusted for age, sex, Townsend score, ethnicity, and assessment centre location.
† Additionally adjusted for smoking status, alcohol intake frequency, BMI, and physical activity.
‡ Additionally adjusted for number of long-term conditions.
CI, confidence interval; HR, hazard ratio; IRR, incidence rate ratio.

### Table 3
Poison and Cox regression models of the association between chronic pain category and COVID-19 hospitalisation, mortality, and case fatality.

| Number of chronic pain sites | Unvariable | Multivariable 1* | Multivariable 2† | Multivariable 3‡ |
|-----------------------------|------------|------------------|------------------|------------------|
| COVID-19 hospitalisation, IRR (95% CI) | 0 (N = 251,365) | 1 | 0.99 (0.83-1.18) | 0.96 (0.79-1.14) | 0.94 (0.78-1.12) |
| 1 (N = 101,609) | | | | | |
| 2-3 (N = 70,422) | | | | | |
| 4-7 (N = 12,495) | | | | | |
| Global test | | | | | |
| COVID-19 mortality, HR (95% CI) | 0 (N = 251,365) | 1 | 0.96 (0.79-1.14) | 0.91 (0.75-1.09) | 1.01 (0.75-1.37) |
| 1 (N = 101,609) | | | | | |
| 2-3 (N = 70,422) | | | | | |
| 4-7 (N = 12,495) | | | | | |
| Global test | | | | | |
| COVID-19 case fatality, HR (95% CI) | 0 (N = 1456) | 1 | 0.93 (0.70-1.24) | 1.16 (0.87-1.56) | 1.01 (0.75-1.37) |
| 1 (N = 710) | | | | | |
| 2-3 (N = 711) | | | | | |
| 4-7 (N = 209) | | | | | |
| Global test | | | | | |

* Adjusted for age, sex, Townsend score, ethnicity, and assessment centre location.
† Additionally adjusted for smoking status, alcohol intake frequency, BMI, and physical activity.
‡ Additionally adjusted for number of long-term conditions.
CI, confidence interval; HR, hazard ratio; IRR, incidence rate ratio.
because its participants are less socioeconomically deprived, have fewer self-reported health conditions, and are less ethnically diverse. Nonetheless, estimates of effect size are expected to be generalisable and comparable with those obtained from more representative general population studies. Although we were able to measure the number of LTCs, we did not have data on their severity. Adjustment for LTC severity could have produced different estimates to our final models (adjusted for a simple LTC count) if those with severe LTCs have higher risk of adverse COVID-19 outcomes compared with those with only mild LTCs.

Data on chronic pain were collected before the COVID-19 pandemic excluding the possibility of reverse causation. In this analysis, we assumed that most of the UK Biobank participants who reported chronic pain at baseline continued to experience persistent pain over the medium to long term albeit that it may fluctuate regarding intensity and interference. Although pain status may, in reality, have changed over the intervening period, this is unlikely to have introduced systematic error. Studies that measure duration of chronic pain show that it persists, at least in the medium term, for 5 to 7 years. Kamaleri and colleagues measure duration of chronic pain show that it persists, at least in status may, in reality, have changed over the intervening period, fluctuate regarding intensity and interference. Although pain persistent pain over the medium to long term albeit that it may who reported chronic pain at baseline continued to experience pandemic excluding the possibility of reverse causation. In this

COVID-19 outcomes compared with those with only mild LTCs. different estimates to our final models (adjusted for a simple LTC count) if those with severe LTCs have higher risk of adverse COVID-19 outcomes compared with those with only mild LTCs.

The availability of testing and the testing strategies used have changed over the course of the pandemic. Therefore, incomplete ascertainment of infections is possible. Our ascertainment method should be relatively robust against changes in test strategy because we limited outcomes to COVID-19 hospitalisations and mortality. This excludes people tested in the community who were likely to have had milder symptoms, were more likely to have been denied access to testing, and experienced more dramatic temporal changes in access to testing.

5. Conclusion
Our analyses of UK Biobank data demonstrated an association between chronic pain (at separate sites or all over the body) and COVID-19 hospitalisation, independent of known LTCs, and clear evidence of a dose-response relationship with number of pain sites. Pain may be a proxy measure of undiagnosed underlying physical or mental health disease processes. Future studies are needed to corroborate our novel findings, investigate the underlying mechanisms, and investigate whether pre-existing pain is also an independent risk factor for long COVID.

Conflict of interest statement
The authors have no conflicts of interest to declare.

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Appendix A. Supplemental digital content
Supplemental digital content associated with this article can be found online at http://links.lww.com/PAIN/B629.

Supplemental video content
A video abstract associated with this article can be found at http://links.lww.com/PAIN/B630.

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References
[1] Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet 2012;380:37–43.

[2] Batty GD, Gale CR, Kivimaki M, Deary IJ, Bell S. Comparison of risk factor associations in UK Biobank against representative, general population
based studies with conventional response rates: prospective cohort study and individual participant meta-analysis. BMJ 2020;368:m131.

[3] Carfi A, Bernabei R, Landi F, Gemelli Against C-P-ACSG. Persistent symptoms in patients after acute COVID-19. JAMA 2020;324: 603–5.

[4] Cassell A, Edwards D, Harshfield A, Kennedy MC, Woods AC. Managing patients with chronic pain during the COVID-19 outbreak: considerations for the rapid introduction of remotely supported (e)health pain management services. PAIN 2020; 161:889–93.

[5] Cazzola M, Atzeni F, Bocaccini L, Cassisi G, Sarzi-Puttini P. Physiopathology of pain in rheumatology. Reumatismo 2014;69:4–13.

[6] Collins R. What makes UK Biobank special? Lancet 2012;379:1173–4.

[7] Deer TR, Sayed D, Pope JE, Chakravarthy KV, Petersen E, Moeschler TM, Reid MC, Williams ACC. Managing patients with chronic pain during COVID-19: risk stratification for the interventionalist. Anesth Analg 2020;131:387–94.

[8] Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman RD, Morris CD, McDonald HI, Bates C, Bacon S, Walker AJ, Evans D, Inglesby P, Mehrkar A, Curtis HJ, DeVito NJ, Croker R, Drysdale H, Cockburn J, Parr J, Hester F, Harper S, Douglas I, Tomlinson L, Evans SJW, Greive R, Harrison D, Rowan K, Khunti K, Chaturvedi N, Smeeth L, Goldacre B, Open SC. Ethnic differences in SARS-CoV-2 infection and COVID-19 related hospitalisation, intensive care unit admission, and death in 17 million adults in England: an observational cohort study using the OpenSAFELY platform. Lancet 2020;396:2832–40.

[9] Fine PG. Long-term consequences of chronic pain: mounting evidence for pain as a neurological disease and parallels with other chronic disease states. Pain Med 2011;12:996–1004.

[10] Fry A, Littlejohns TJ, Sudlow C, Doherty N, Adamska L, Sprosen T, Collins R, Allen NE. Comparison of sociodemographic and health-related characteristics of UK biobank participants with those of the general population. Am J Epidemiol 2017;186:1026–34.

[11] GBD. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018;392:1789–858.

[12] Ghai B, Malhotra N, Bajwa SJS. Telemedicine for chronic pain management during COVID-19 pandemic. Indian J Anaesth 2020;64: 603–5.

[13] Ghele M, Stiles TC, Borchgrevink PC, Landmark T. The natural course of chronic pain in a general population: stability and change in an eight-wave longitudinal study over four years (the HUNT pain study). J Pain 2020;21: 689–99.

[14] Goldberg N, Pebley AR, Lee K, Andrasfay T, Pratt B. Racial and ethnic differentials in COVID-19-related job exposures by occupational standing. BMJ Open 2021;11:e045695.

[15] Harker J, Reid KJ, Bekkering GE, Petersen E, Bala MM, Riemsma R, Worthy J, Franko LM, Niedzwiedz CL, Sattar N, Pell JP, Ho FK, Niedzwiedz CL, Hastie CE, Anderson J, Mark PB, Sullivan M, O’Donnell CA, Mair FS, Nicholl BI. Multimorbidity, polypharmacy, and COVID-19 infection within the UK Biobank cohort. BMJ Open 2020;10:e028301.

[16] Milis SEE, Nicolson KF, Smith BMH. Chronic pain: a review of its epidemiology and associated factors in population-based studies. Br J Anaesth 2019;123:e273–83.

[17] Mukalo L, Brandow AM, Dasgupta M, Mason SF, Simpson PM, Singh A, Taylor BW, Woods JK, Yusuf FI, Panepinto JP. Comorbidities are risk factors for hospitalization and serious COVID-19 illness in children and adults with sickle cell disease. Blood Adv 2021;5:2717–24.

[18] Nam C, Macdonald M, Niedzwiedz CL, Hulme WJ, Pell JP, Niedzwiedz CL, Hastie CE, Anderson J, Mark PB, Sullivan M, O’Donnell CA, Mair FS, Nicholl BI. Multimorbidity and COVID-19: a large population-based study. Anesth Pain Med 2020;10:e95776.

[19] Nicholl BI, Mackay D, Cullen BI, Martin DJ, Uli-Han Z, Mair FS, Evans J, Mcintosh AM, Gallagher J, Roberts B, Dealy J, Pell JP, Smith DJ. Chronic multisite pain in major depression and bipolar disorder: cross-sectional study of 149,611 participants in UK Biobank. BMC Psychiatry 2014;14:350.

[20] Nicholl BI, Smith DJ, Cullen B, Evans J, Anderson J, Lyall DM, Nicholl BI, Mackay D, Cullen BI, Martin DJ, Uli-Han Z, Mair FS, Evans J, Mcintosh AM, Gallagher J, Roberts B, Dealy J, Pell JP, Smith DJ. Chronic multisite pain in major depression and bipolar disorder: cross-sectional study of 149,611 participants in UK Biobank. BMC Psychiatry 2014;14:350.

[21] Nicholl BI, Mackay D, Cullen BI, Martin DJ, Uli-Han Z, Mair FS, Evans J, Mcintosh AM, Gallagher J, Roberts B, Dealy J, Pell JP, Smith DJ. Chronic multisite pain in major depression and bipolar disorder: cross-sectional study of 149,611 participants in UK Biobank. BMC Psychiatry 2014;14:350.

[22] Nicholl BI, Mackay D, Cullen BI, Martin DJ, Uli-Han Z, Mair FS, Evans J, Mcintosh AM, Gallagher J, Roberts B, Dealy J, Pell JP, Smith DJ. Chronic multisite pain in major depression and bipolar disorder: cross-sectional study of 149,611 participants in UK Biobank. BMC Psychiatry 2014;14:350.

[23] Niedzwiedz CL, O’Donnell CA, Mair FS, Nicholl BI. Multimorbidity and COVID-19 infection: cross-sectional results from UK Biobank. BMC Fam Pract 2015;16:128.

[24] Niedzwiedz CL, O’Donnell CA, Mair FS, Nicholl BI. Multimorbidity and COVID-19 infection: cross-sectional results from UK Biobank. BMC Fam Pract 2015;16:128.

[25] Orandi A. Predicting factors of pain duration in patients with chronic pain: a population-based study. Anesth Pain Med 2020;10:e95776.

[26] Pell JP, Jani BD, Ho FK, Niedzwiedz CL, Hastie CE, Anderson J, Mark PB, Sullivan M, O’Donnell CA, Mair FS, Nicholl BI. Multimorbidity, polypharmacy, and COVID-19 infection within the UK Biobank cohort. BMJ Open 2020;10:e028301.

[27] Mills SEE, Nicolson KF, Smith BMH. Chronic pain: a review of its epidemiology and associated factors in population-based studies. Br J Anaesth 2019;123:e273–83.

[28] Krause SJ, Taal RC, Margolis RB. Pain distribution, intensity, and duration in patients with chronic pain. J Pain Symptom Manage 1989;4:67–71.

[29] Lu LW, Chew AMK, Gunasekaran DV. Digital health for patients with chronic pain during the COVID-19 pandemic. Br J Anaesth 2020;125:e567–70.

[30] Logue JK, Franko NM, McCulloch DJ, McDonald D, Magedson A, Wolf CR, Chu HY. Sequelae in adults at 6 months after COVID-19 infection. JAMA Netw Open 2021;4:e210830.

[31] Ghele M, Stiles TC, Borchgrevink PC, Landmark T. The natural course of chronic pain in a general population: stability and change in an eight-wave longitudinal study over four years (the HUNT pain study). J Pain 2020;21: 689–99.

[32] Goldman N, Pebley AR, Lee K, Andrasfay T, Pratt B. Racial and ethnic differentials in COVID-19-related job exposures by occupational standing. BMJ Open 2021;11:e045695.

[33] Harker J, Reid KJ, Bekkering GE, Kellers E, Balou MM, Romsma R, Worthy G, Misso K, Kleijnen J. Epidemiology of chronic pain in Denmark and Sweden. Pain Res Treat 2012;2012:271248.

[34] Hartvigsen J, Hancock MJ, Kongsted A, Louw Q, Ferreira ML, Genewy S, Hoy D, Karppinen J, Pransky G, Sieper J, Smeets R, Underwood M. Lancet Low Back Pain Series Working G. What low back pain is and why it matters: a 14-year prospective study. PAIN 2009;141:25–30.
mediation analysis in chronic pain patients. Pain Res Manag 2016;2016:3204914.

[44] Shanthanna H, Strand NH, Provenzano DA, Lobo CA, Eldabe S, Bhatia A, Wegener J, Curtis K, Cohen SP, Narouze S. Caring for patients with pain during the COVID-19 pandemic: consensus recommendations from an international expert panel. Anaesthesia 2020;75:395–44.

[45] Sudlow C, Gallacher J, Allen N, Beral V, Burton P, Danesh J, Downey P, Elliott P, Green J, Landray M, Liu B, Matthews P, Ong G, Peli J, Silman A, Young A, Sprosen T, Peakman T, Collins R. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. PLoS Med 2015;12:e1001779.

[46] Sylwander C, Larsson I, Andersson M, Bergman S. The impact of chronic widespread pain on health status and long-term health predictors: a general population cohort study. BMC Musculoskelet Disord 2020;21:36.

[47] Tauben DJ, Langford DJ, Sturgeon JA, Rundell SD, Towe C, Bockman C, Nicholas M. Optimizing telehealth pain care after COVID-19. PAIN 2020;161:2437–45.

[48] Townsend PP. Health and deprivation: Inequality and the North. In: Beattie A, ed. London: Croom Helm Ltd, 1987.

[49] van Hecke O, Hocking LJ, Torrance N, Campbell A, Padmanabhan S, Porteous DJ, McIntosh AM, Burrin AV, Tanaika H, Williams FM, Smith BH. Chronic pain, depression and cardiovascular disease linked through a shared genetic predisposition: analysis of a family-based cohort and twin study. PLoS One 2017;12:e0170533.

[50] WHO. Body mass index - BMI. Available at: https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi. Accessed August 19, 2021.

[51] Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, Curtis HJ, Mehkar A, Evans D, Inglesby P, Cockburn J, McDonald HI, MacKenna S, Tominson L, Douglas L, Rentsch CT, Mathur R, Wong AYS, Grieve R, Harrison D, Forbes H, Schultze A, Croker R, Parry J, Hester F, Harper S, Perera R, Evans SJW, Smeeth L, Goldacre B. Factors associated with COVID-19-related death using OpenSAFELY. Nature 2020;584:430–6.