



Clinical science

Pre-existing musculoskeletal pain and its association with mortality in newly diagnosed co-morbid conditions: an electronic health record cohort study

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Abstract

Objective: Musculoskeletal pain is a common risk factor for co-morbid conditions and might increase the risk of poor outcomes. The objective was to determine whether patients with pre-existing musculoskeletal pain have an increased risk for mortality following a new diagnosis of a co-morbid condition.

Methods: Patients aged ≥ 45 years with a new diagnosis of acute coronary syndrome (ACS), stroke, cancer, dementia or pneumonia recorded in a UK electronic primary care database linked to hospital and mortality records were examined. The association of mortality with musculoskeletal pain (inflammatory conditions, OA and regional pain) was determined.

Results: The sample size varied from 128 649 (stroke) to 406 289 (cancer) by cohort, with 22–31% having pre-existing musculoskeletal conditions. In the ACS cohort, there was a higher rate of mortality for all musculoskeletal types. There were also higher unadjusted mortality rates in patients with inflammatory arthritis compared with those without musculoskeletal pain in the stroke, cancer and dementia cohorts and for patients with OA in the stroke and cancer cohorts. After adjustment for the number of prescribed medications and age, the increased risk of mortality remained only for patients with inflammatory arthritis in the ACS cohort (adjusted hazard ratio = 1.07; 95% CI 1.03, 1.10).

Conclusion: Older adults with inflammatory arthritis and OA have increased risk of mortality when they develop a new condition, which seems to be related to the prescription of multiple medicines. Pre-existing musculoskeletal pain is an indicator of a complex patient who is at risk of poorer outcomes at the onset of new illnesses.

Lay Summary

What does this mean for patients?

Musculoskeletal pain (pain in the joints and muscles around them) is common, and those with pain often have other long-term conditions. We wanted to find out whether people with musculoskeletal pain have an increased risk of earlier death following diagnosis of a new serious illness. We studied anonymized health-care records of patients aged 45 years and over with a new diagnosis of heart attack, stroke, cancer, dementia or pneumonia. Approximately one-third of people with these new diagnoses had a musculoskeletal pain condition, such as inflammatory arthritis, osteoarthritis or regional (e.g. back, knee) pain. This group had an increased risk of earlier death compared with those without existing musculoskeletal pain, with the highest risk in those with inflammatory arthritis and osteoarthritis. However, this increased risk was explained by those with musculoskeletal pain being older and on many medications. Taking multiple medicines suggests that patients have more illnesses but increases the possibility of taking medicines with little benefit or that cause harm and the possibility of not taking medicines as instructed. Doctors need to consider all of a patient's current illnesses and medicines when treating a new illness. Improving musculoskeletal pain recognition and management, and regular medicine reviews, might help to improve the outcomes of other illnesses.

Keywords: musculoskeletal pain, mortality, co-morbidity, epidemiology, primary care.

Key messages

- Adults with musculoskeletal pain are at increased risk of mortality from a new co-morbid condition.
- Increased mortality was largely explained by them being older and being prescribed more medications.
- This study has highlighted the complexity of patients with severe musculoskeletal pain and new-onset conditions.

Introduction

Musculoskeletal pain is common, with up to one in five adults consulting primary care in the UK for a painful musculoskeletal condition each year, and it has a major impact on everyday activity and is a major burden on health-care systems [1, 2]. Musculoskeletal pain commonly co-exists with other conditions and can increase the risk of developing new illnesses. For example, OA [3–5], RA [6–8] and low back pain [9, 10] have been shown to be associated with an increased risk of developing heart disease and stroke. Regional pain, such as back pain, PsA and PMR, have been linked to the onset of cancer [11–13], OA with dementia [14] and inflammatory musculoskeletal conditions with hospitalization for community-acquired pneumonia [15]. However, it is less clear whether musculoskeletal pain impacts the outcomes of these other conditions. For example, in cardiovascular disease, studies have shown increased in-hospital mortality after acute myocardial infarction, intracranial haemorrhage and ischaemic stroke in patients with RA or SLE [16], but other studies have shown no association [17, 18] or even reduced mortality in patients with RA [19]. Knowledge of the impact of musculoskeletal pain on the prognosis of other conditions would be important in the management of these conditions and of the musculoskeletal pain. The aim of this study was therefore to determine whether pre-existing painful musculoskeletal conditions are associated with long-term mortality in those with other newly diagnosed conditions and whether this varies by type of musculoskeletal pain. The study focused on five conditions with evidence of links to musculoskeletal pain that are among the most common reasons for hospitalization globally. These index conditions were acute coronary syndrome (ACS), stroke, cancer, dementia and community-acquired pneumonia.

Methods**Study design and setting**

This was a cohort study using the UK Clinical Practice Research Datalink (CPRD) Aurum database. CPRD Aurum contains anonymized primary care electronic health records for >40 million patients from >1000 general practices using EMIS Web® software [20]. These data were linked to hospital inpatient admission data from Hospital Episode Statistics (HES) and to Office for National Statistics (ONS) Death Registration Data. Given that the study used anonymized patient electronic health records from CPRD, it did not require consent from individual participants. The study was approved by the CPRD Independent Scientific Advisory Committee/Research Data Governance {references 20_000105 ACS/stroke and 20_000147 cancer (October 2020 build); 21_000504 dementia (June 2021 build) [21]; and 21_000689 pneumonia (November 2021 build) [22]}. The approved protocols were made available to reviewers.

Study population

The study population consisted of patients aged ≥ 45 years with a first ever record of one of our index illnesses and with ≥ 24 months prior registration at their practice to obtain consultation records for musculoskeletal pain and covariates. For ACS and stroke, we included patients with first myocardial infarction or unstable angina, or first stroke or transient ischaemic attack in their primary care record between 2000 and 2019 and a matching hospital inpatient record with admission date within 1 month of the primary care recorded date. For cancer, we included patients with a first diagnosis of breast, colon, lung or prostate cancer in primary care between 2000 and 2019. We also included patients with a first ever recorded diagnosis of dementia in primary care between 2005 and 2019. Finally, we included patients with a first ever recorded diagnosis of bacterial pneumonia in primary care, or as the reason for admission to hospital, between 2014 and 2018. Patients recorded with a diagnosis of pneumonia within 2 weeks after a hospital stay were excluded to ensure that the pneumonia was not acquired in hospital. Patients were also excluded if they had a previous record of viral pneumonia.

Diagnoses are recorded in UK primary care using the Read code system up to 2018 and SNOMED CT codes from 2018. Within hospital admissions, illnesses are recorded using International Classification of Diseases (ICD-10) codes. Derivation of code lists was based on those previously developed through a rigorous consensus approach in research studies by health-care practitioners, epidemiologists and statisticians with expertise in electronic health record research at Keele University [11, 23, 24] and code lists based on those from external studies using electronic health records. The code lists used for each index condition can be found at <https://eprints.keele.ac.uk/id/eprint/11580/> [25]. The date of first diagnosis of the index condition was defined as the index date for that patient.

Outcome

The outcome was all-cause mortality. Patients were followed from their index date until the earliest of end of their registration at the practice (including death) or last date of collected data. For the ACS and stroke cohorts, those with a death record, end of registration or last data collection date before 30 days after the index date were excluded. For pneumonia, given that it is an acute morbidity, mortality was measured from the index date for a maximum of 12 months.

Exposure

Exposure was defined as presence or absence of a painful musculoskeletal condition identified from primary care records in the 24 months before the index date. The types of musculoskeletal pain examined were diagnosed inflammatory conditions (RA, gout, AS, GCA or PsA); diagnosed OA; and

the most common non-specific regional pains recorded in primary care (low back pain/backache, knee pain, hip pain or hand/wrist pain).

In a secondary analysis, patients with musculoskeletal pain were subgrouped by severity and the recency of pain as an alternative to type. Primary care electronic health records do not contain direct evidence of pain severity; therefore, we used proxy measures based on the following factors: a coded referral to a pain management clinic, rheumatology, orthopaedics or physiotherapy specialists; or prescription of a strong analgesic medicine (i.e. a strong opioid, such as tramadol, morphine or oxycodone) [26], on the assumption that a referral or stronger analgesic would normally indicate more severe pain. Current musculoskeletal pain was defined as a recorded consultation for musculoskeletal pain in the 6 months before the index date. Patients were subgrouped as follows: current and severe (recorded consultation within the 6 months before the index date and either a referral or a prescription of strong analgesia); current and non-severe; or recent (recorded consultation between 6 and 24 months before the index date).

Covariates

Covariates included in the analyses for all cohorts were as follows: age at index date, sex, geographical location, race, neighbourhood-level deprivation (index of multiple deprivation), year of index consultation, recorded co-morbidity in the 24 months before the index date (depression, anxiety or stress; diabetes; other musculoskeletal conditions), general multi-morbidity based on prescription count (number of different medications prescribed, excluding analgesia), BMI, and smoking status recorded in the 60 months prior to the index date. Cohort-specific covariates were as follows: peripheral vascular disease and statin medicine for ACS and stroke; chronic kidney disease for cancer; stroke for dementia; and chronic obstructive pulmonary disease (COPD), dementia, renal disease, stroke and type of antibiotic for pneumonia.

Analysis

Binary/categorical patient characteristics were summarized as the number and percentage within each category, and continuous characteristics (index year, age at index date, and number of prescriptions in the 24 months before the index date) were presented using the median and interquartile range (IQR).

Analysis of the association of prior musculoskeletal consultation with mortality used flexible parametric survival models, with three (ACS and stroke) or four (cancer, dementia and pneumonia) degrees of freedom. Each model was run with only musculoskeletal pain [categorized as none (reference), regional pain, OA or inflammatory] in the model, progressing to inclusion of all covariates. Musculoskeletal pain was included as a time-dependent effect in the fully adjusted models for cancer, dementia and pneumonia, with four degrees of freedom for time-dependent effects. All models included robust standard errors clustered at the practice level. Adjusted hazard ratios (HR; with 95% CI) are presented, and for the ACS, stroke, cancer and dementia cohorts, also determined at 2, 5 and 10 years of follow-up to assess the consistency of association over time.

In the secondary analysis, associations of mortality with recency and severity of musculoskeletal pain (none; recent; current, non-severe; or current, severe) were assessed.

Sensitivity analyses

In the main analysis, missing data for race, BMI, smoking status and alcohol status were recorded as the reference category [White, normal BMI (18.0–24.9 kg/m²), never smoked and does not drink, respectively], with sensitivity analyses also undertaken and estimates compared for the complete case analysis and where missing data were coded as missing categories. All analyses were performed using Stata/MP v.17.0 (StataCorp LLC, USA).

Results

Patient characteristics

Baseline characteristics of each of the cohorts are shown in Table 1, and subgrouped by type of musculoskeletal pain within each cohort in Supplementary Tables S1–S5, available at *Rheumatology Advances in Practice* online. The size of the population ranged from 128 649 (stroke) to 406 289 (cancer). Between 22 and 31% of patients had a consultation for one of the painful musculoskeletal conditions in the 24 months before the index date. Regional pain was the most common (12–17%), followed by OA (6–10%) and inflammatory arthritis (4–5%).

In all cohorts apart from dementia, those with OA (median 74–81 years) or inflammatory arthritis (75–80 years) were older than those with regional pain (69–77 years) or no musculoskeletal pain (69–77 years; Supplementary Tables S1–S5, available at *Rheumatology Advances in Practice* online). Prevalence of co-morbidities and counts of prescribed medications were also generally higher for those with musculoskeletal pain compared with those without musculoskeletal pain. Those with musculoskeletal pain were more commonly ex-smokers and recorded as overweight or obese than those without musculoskeletal pain, and there were fewer men recorded with regional pain or OA in all cohorts apart from ACS (Supplementary Tables S1–S5, available at *Rheumatology Advances in Practice* online).

In the ACS cohort, there was a higher rate of mortality for all three musculoskeletal types. Patients with pre-existing inflammatory arthritis had the highest rate [92 per 1000 person-years (py); unadjusted HR *vs* no pre-existing musculoskeletal pain = 1.51; 95% CI 1.47, 1.56], followed by OA (77/1000 py; unadjusted HR = 1.27; 95% CI 1.23, 1.30). In those without musculoskeletal pain, the rate of mortality was 61/1000 py, and with regional pain it was 59/1000 py (Table 2). There were also higher unadjusted rates of mortality in patients with pre-existing inflammatory arthritis compared with those without pre-existing musculoskeletal pain in the stroke (114 *vs* 95/1000 py), cancer (186 *vs* 145/1000 py) and dementia (241 *vs* 222/1000 py) cohorts and for patients with OA in the stroke (106 *vs* 95/1000 py) and cancer (164 *vs* 145/1000 py) cohorts. Patients newly diagnosed with cancer with regional pain (160/1000 py) had higher unadjusted rates of mortality than those with no musculoskeletal pain. There was no evidence of increased mortality in those with musculoskeletal pain in the pneumonia cohort.

Most covariates did not change the associations found in the unadjusted analyses. However, the number of prescribed medications and, to a lesser extent, age did impact the associations, and the increased risk of mortality remained only for patients with inflammatory arthritis in the ACS cohort (adjusted HR = 1.07; 95% CI 1.03, 1.10) after adjusting for these covariates (Table 2). Table 3 shows the number of

Table 1. Patient characteristics by cohort

Characteristic	ACS 165 350	Stroke 128 649	Cancer 406 289	Dementia 199 961	Pneumonia 192 587
Total, <i>n</i>					
Type of MSK pain, <i>n</i> (%)					
No MSK pain	116 231 (70)	89 949 (70)	291 256 (72)	137 042 (69)	149 871 (78)
Regional pain	27 344 (17)	20 799 (16)	68 339 (17)	33 783 (17)	23 352 (12)
OA	12 863 (8)	10 966 (9)	30 451 (7)	19 941 (10)	10 989 (6)
Inflammatory	8912 (5)	6935 (5)	16 243 (4)	9195 (5)	8375 (4)
Recency and severity of MSK pain, <i>n</i> (%)					
No MSK pain	116 231 (70)	89 949 (70)	291 256 (72)	137 042 (69)	149 871 (78)
Recent	29 198 (18)	23 065 (18)	66 327 (16)	38 294 (19)	25 756 (13)
Current, non-severe	10 960 (7)	8829 (7)	25 599 (6)	14 864 (7)	8794 (5)
Current, severe	8961 (5)	6806 (5)	23 107 (6)	9761 (5)	8166 (4)
Follow-up, median (IQR), years	4.9 (2.0, 9.3)	3.6 (1.5, 7.1)	3.3 (1.1, 7.7)	4.6 (2.5, 7.9)	4.6 (3.4, 6.0)
Age, median (IQR), years	70 (60, 79)	75 (66, 83)	70 (62, 78)	83 (77, 87)	77 (65, 86)
Males, <i>n</i> (%)	106 500 (64)	66 639 (52)	202 451 (50)	77 253 (39)	94 318 (49)
Smoking status, <i>n</i> (%) ^b					
Current smoker	44 548 (27)	28 216 (22)	89 114 (22)	28 972 (14)	33 000 (17)
Ex-smoker	42 438 (26)	32 928 (26)	110 048 (27)	57 646 (29)	46 930 (24)
Never smoked/not recorded	78 364 (47)	67 505 (52)	207 127 (51)	113 343 (57)	112 657 (59)
BMI, <i>n</i> (%) ^b					
Underweight (10.0–18.0 kg/m ²)	2157 (1)	2461 (2)	7153 (2)	9052 (5)	7069 (4)
Normal/not recorded (18.0 to <25.0 kg/m ²)	86 554 (52)	69 684 (54)	203 223 (50)	107 742 (53)	116 502 (61)
Overweight (25.0 to <30.0 kg/m ²)	47 670 (29)	35 129 (27)	135 295 (33)	61 901 (31)	43 143 (22)
Obese (30.0–79.9 kg/m ²)	28 969 (18)	21 375 (17)	60 618 (15)	21 266 (11)	25 873 (13)
Index of multiple deprivation quintiles, <i>n</i> (%) ^a					
Least deprived/not recorded	34 116 (21)	27 574 (21)	100 377 (25)	44 371 (22)	36 421 (19)
Second-least deprived	34 193 (21)	27 205 (21)	91 009 (22)	43 364 (22)	36 082 (19)
Mid-deprived	32 913 (20)	26 306 (20)	80 674 (20)	39 971 (20)	37 354 (19)
Second-most deprived	32 048 (19)	24 078 (19)	70 508 (17)	37 052 (19)	38 935 (20)
Most deprived	32 080 (19)	23 486 (18)	63 721 (16)	35 203 (18)	43 795 (23)
White/not recorded race, <i>n</i> (%) ^b	154 740 (94)	121 323 (94)	389 089 (96)	189 647 (95)	179 253 (93)
Specific co-morbid conditions, <i>n</i> (%) ^a					
Diabetes	30 557 (18)	23 491 (18)	43 940 (11)	33 266 (17)	21 578 (11)
Peripheral vascular disease	5183 (3)	3622 (3)	N/A	N/A	N/A
Depression, anxiety or stress	12 937 (8)	10 258 (8)	52 341 (13)	26 095 (13)	12 955 (7)
Other MSK consultation	46 224 (28)	36 140 (28)	24 487 (6)	61 287 (31)	42 678 (22)
Renal disease	N/A	N/A	14 353 (4)	N/A	6394 (3)
Stroke	N/A	N/A	N/A	15 501 (8)	5154 (3)
COPD/asthma	N/A	N/A	N/A	N/A	27 637 (14)
Dementia	N/A	N/A	N/A	N/A	11 131 (6)
Number of prescriptions, median (IQR) ^a	9 (4, 16)	11 (6, 18)	9 (5, 16)	12 (7, 19)	9 (0, 18)
Prescribed statins, <i>n</i> (%) ^a	61 787 (37)	47 122 (37)	N/A	N/A	N/A
Prescribed antibiotic, <i>n</i> (%)	N/A	N/A	N/A	N/A	20 044 (10)

^a Recorded in 24 months before the index date.^b Recorded in 60 months before the index date.

ACS: acute coronary syndrome; COPD: chronic obstructive pulmonary disease; IQR: interquartile range; MSK: musculoskeletal; N/A: not applicable.

different medications prescribed during the baseline period, with the highest counts in those with inflammatory arthritis. Associations of musculoskeletal pain with mortality were generally consistent at 2, 5 and 10 years of follow-up.

In the secondary analysis, when assessing the association of mortality with recency and severity of musculoskeletal condition, the patients with current, severe musculoskeletal pain had the highest rates of mortality for the ACS, cancer and dementia cohorts and the lowest for pneumonia (Table 4). As with the primary analysis, adjustment for the number of prescribed medications had the greatest impact on observed associations, and current, severe pain was associated with an increased adjusted risk of mortality only in patients with cancer (adjusted HR *vs* no musculoskeletal pain = 1.25; 95% CI 1.21, 1.29).

Sensitivity analyses

Similar estimates were obtained using the different approaches to account for missing data and did not change the study findings (data not shown).

Discussion

To our knowledge, this is the first study to explore whether pre-existing musculoskeletal pain impacts the prognosis following incident ACS, stroke, cancer, dementia or community-acquired pneumonia through increased rates of mortality. This study has shown increased rates of mortality across four common chronic conditions (ACS, stroke, cancer and dementia) for people with pre-existing musculoskeletal pain. This is particularly evident for those with inflammatory arthritis. However, after adjustment for the number of prescribed medications and age, the majority of these associations were not maintained. These findings persisted in the secondary analysis, which focused on the recency of consultation and severity of pain rather than the type of musculoskeletal condition.

Musculoskeletal pain is highly prevalent, as evidenced by up to one-third of people newly diagnosed with ACS, stroke, cancer, dementia and pneumonia having consulted for such a problem in the previous 2 years. It is also disabling and can

Table 2. Association of mortality with type of musculoskeletal pain by cohort

Cohort	Rate per 1000 py	Unadjusted HR (95% CI)	Adjusted HR ^a (95% CI)	Adjusted HR ^b (95% CI)	Adjusted HR ^c (95% CI)
ACS					
No MSK pain	61 (61, 62)	1	1	1	1
Regional pain	59 (58, 60)	0.98 (0.95, 1.00)	0.95 (0.93, 0.97)	0.81 (0.79, 0.83)	0.90 (0.88, 0.92)
OA	77 (75, 79)	1.27 (1.23, 1.30)	0.90 (0.87, 0.92)	0.98 (0.95, 1.01)	0.85 (0.83, 0.88)
Inflammatory pain	92 (89, 95)	1.51 (1.47, 1.56)	1.18 (1.14, 1.21)	1.12 (1.08, 1.16)	1.07 (1.03, 1.10)
Stroke					
No MSK pain	95 (94, 96)	1	1	1	1
Regional pain	88 (86, 90)	0.93 (0.91, 0.95)	0.92 (0.90, 0.95)	0.81 (0.79, 0.83)	0.90 (0.88, 0.92)
OA	106 (103, 109)	1.12 (1.09, 1.15)	0.90 (0.88, 0.92)	0.94 (0.91, 0.97)	0.86 (0.84, 0.89)
Inflammatory pain	114 (110, 118)	1.21 (1.17, 1.25)	1.08 (1.05, 1.12)	0.98 (0.95, 1.02)	1.00 (0.97, 1.04)
Cancer					
No MSK pain	145 (144, 146)	1	1	1	1
Regional pain	160 (158, 162)	1.09 (1.07, 1.10)	1.09 (1.07, 1.10)	0.98 (0.96, 1.00)	1.00 (0.98, 1.01)
OA	164 (161, 167)	1.10 (1.07, 1.13)	0.98 (0.95, 1.00)	0.94 (0.92, 0.97)	0.91 (0.89, 0.93)
Inflammatory pain	186 (182, 190)	1.24 (1.20, 1.28)	1.11 (1.07, 1.14)	1.00 (0.97, 1.03)	0.97 (0.94, 1.00)
Dementia					
No MSK pain	222 (221, 224)	1	1	1	1
Regional pain	218 (216, 221)	1.01 (0.99, 1.03)	1.02 (1.00, 1.04)	0.93 (0.91, 0.95)	0.95 (0.93, 0.97)
OA	216 (212, 219)	0.98 (0.95, 1.01)	0.96 (0.93, 0.99)	0.89 (0.86, 0.91)	0.92 (0.89, 0.95)
Inflammatory pain	241 (235, 247)	1.16 (1.11, 1.21)	1.16 (1.11, 1.21)	1.01 (0.96, 1.05)	1.01 (0.97, 1.06)
Pneumonia ^d					
No MSK pain	127 (126, 128)	1	1	1	1
Regional pain	105 (103, 108)	0.87 (0.85, 0.89)	0.86 (0.84, 0.88)	0.72 (0.71, 0.74)	0.86 (0.83, 0.88)
OA	107 (104, 111)	0.86 (0.83, 0.89)	0.73 (0.70, 0.75)	0.70 (0.67, 0.72)	0.75 (0.73, 0.78)
Inflammatory pain	125 (120, 130)	0.97 (0.93, 1.01)	0.86 (0.83, 0.90)	0.76 (0.73, 0.80)	0.83 (0.80, 0.87)

^a Adjusted for age.^b Adjusted for number of medications, excluding analgesia.^c Adjusted for all covariates.^d Mortality measured from index date to 12 months.

ACS: acute coronary syndrome; HR: hazard ratio; MSK: musculoskeletal; 1000 py: 1000 person-years.

Table 3. Median (interquartile range) number of different medications prescribed at baseline, excluding analgesia

Cohort	No MSK pain	Regional pain	OA	Inflammatory pain
ACS	8 (3, 14)	11 (6, 18)	12 (7, 20)	14 (8, 22)
Stroke	8 (4, 14)	12 (7, 18)	13 (8, 19)	14 (9, 21)
Cancer	8 (4, 14)	12 (7, 18)	14 (8, 20)	15 (10, 22)
Dementia	11 (7, 17)	14 (9, 21)	15 (9, 21)	17 (11, 24)
Pneumonia	5 (0, 15)	17 (10, 25)	18 (12, 26)	19 (13, 27)

ACS: acute coronary syndrome; MSK: musculoskeletal.

have a major impact on everyday life, reducing the ability to perform everyday tasks and impacting on sleep, mental health and work. Musculoskeletal pain is often neglected when a patient has co-occurring conditions, and its presence can be unrecognized or addressed inadequately [27, 28], with the non-musculoskeletal conditions prioritized owing to a perception of greater influence on mortality, morbidity and health-care use. For example, research has highlighted that people living with dementia are less likely to have recorded primary care consultation or prescription of analgesics for musculoskeletal conditions compared with those without dementia [29]. Despite previously observed associations of musculoskeletal pain with onset of clinical conditions [3–12], there is little prior evidence of its impact on the outcomes of these conditions. The limited number of previous studies assessing the impact of musculoskeletal conditions on mortality have given mixed findings and tended to be small and/or based outside the UK. To our knowledge, this is the first study to explore whether pre-existing musculoskeletal pain impacts the long-term prognosis following incident ACS,

stroke, cancer, dementia or community-acquired pneumonia through increased rates of mortality. Studies have shown inconsistent associations of inflammatory arthritis with in-hospital mortality in patients with ACS and stroke [16–18, 30]. Impairment of mobility was associated with mortality in pneumonia in a study in Portugal [31].

Patients with musculoskeletal pain, particularly inflammatory arthritis and OA, do have an increased risk of earlier mortality. This is explained, in part, by being older, but in addition the observed associations seemed also to be explained by increased polypharmacy in patients with musculoskeletal pain. This is consistent with our previous study looking at short-term (30-day) outcomes in patients with a new ACS or stroke [32]. In the present study, we found that patients with musculoskeletal pain were being prescribed an average of 13–19 different medicines over 2 years. This excluded prescribed painkillers and over-the-counter medicines, hence the overall number of medicines is likely to be higher. Although we also adjusted for specific co-morbidities, this might reflect a higher multimorbidity load and increased frequency of consultation in such patients. Taking a high number of medicines has been associated with poor adherence, especially when more than nine medications were prescribed, and might in itself affect disease outcomes and disease progression [33]. A further concern is the possibility of inappropriate prescribing, with specific medicines increasing the risk of poor outcome, for example increasing risks of falls, episodes of delirium and hospital admissions because of adverse drug reactions. Further research is needed to understand more about the impact of multiple medications across common conditions.

Although this study suggests that musculoskeletal pain does not directly cause poorer outcomes, it highlights that

Table 4. Association of mortality with recency and severity of musculoskeletal pain by cohort

Cohort	Rate per 1000 py	Unadjusted HR (95% CI)	Adjusted HR ^a (95% CI)
ACS			
No MSK pain	61 (61, 62)	1	1
Recent	66 (65, 68)	1.09 (1.07, 1.12)	0.91 (0.89, 0.93)
Current, non-severe	72 (70, 74)	1.18 (1.14, 1.22)	0.91 (0.89, 0.94)
Current, severe	76 (73, 78)	1.26 (1.22, 1.30)	0.97 (0.94, 1.01)
Stroke			
No MSK pain	95 (94, 96)	1	1
Recent	96 (94, 98)	1.01 (0.99, 1.03)	0.91 (0.89, 0.93)
Current, non-severe	101 (98, 104)	1.06 (1.03, 1.10)	0.91 (0.88, 0.93)
Current, severe	96 (93, 100)	1.02 (0.98, 1.06)	0.90 (0.87, 0.93)
Cancer			
No MSK pain	145 (144, 146)	1	1
Recent	157 (155, 159)	1.09 (1.08, 1.11)	0.96 (0.94, 0.97)
Current, non-severe	151 (148, 153)	1.07 (1.04, 1.09)	0.96 (0.93, 0.98)
Current, severe	216 (212, 220)	1.53 (1.48, 1.58)	1.25 (1.21, 1.29)
Dementia			
No MSK pain	222 (221, 224)	1	1
Recent	219 (217, 222)	1.02 (1.00, 1.04)	0.96 (0.94, 0.98)
Current, non-severe	222 (218, 226)	1.02 (0.98, 1.05)	0.97 (0.93, 1.00)
Current, severe	224 (219, 230)	1.07 (1.02, 1.12)	0.97 (0.92, 1.01)
Pneumonia ^b			
No MSK pain	127 (126, 128)	1	1
Recent	111 (109, 114)	0.90 (0.88, 0.92)	0.83 (0.81, 0.85)
Current, non-severe	130 (126, 135)	1.02 (0.98, 1.06)	0.86 (0.83, 0.89)
Current, severe	85 (81, 88)	0.71 (0.67, 0.74)	0.73 (0.70, 0.77)

^a Adjusted for all covariates.^b Mortality measured from index date to 12 months.

ACS: acute coronary syndrome; HR: hazard ratio; MSK: musculoskeletal; 1000 py: 1000 person-years.

musculoskeletal pain might be an indicator that patients might be more complex, being more likely to be older and have more co-morbidities and medications. There is potential for pain and restricted functioning and mobility resulting from a musculoskeletal condition to affect the delivery and effectiveness of treatment and rehabilitation. Improving recognition and management of musculoskeletal pain, including integration within rehabilitation, might help to improve its impact on everyday life in people across co-occurring conditions and their outcomes. Clinicians need to think about the patient as a whole when treating individual illnesses, including consideration of all their illnesses and current medicines, and this study highlights the importance of regular medicine reviews.

Strengths and limitations

The study was set in a database of routinely recorded primary care data currently including 20% of the population of England, which is nationally representative and was linked to secondary care and mortality information. Recorded morbidities in UK databases, such as CPRD, have shown high validity [34, 35].

Some patients might not have had pain at time of the onset of the new condition. Therefore, in secondary analysis we also examined those with a more recent (last 6 months) consultation to reflect increased likelihood of a current episode of pain. As expected, those with a more recent consultation necessitating onward referral or prescription of a strong analgesic had increased risk of mortality, but again that association tended to disappear when adjusting for the number of medications. Defining musculoskeletal pain by consultation to primary care suggests that the musculoskeletal pain was of a severity that prompted the need to seek health care;

however, there will be patients in the non-musculoskeletal comparison group who have musculoskeletal pain without recently seeking health care. This is a limitation of research using such databases, and future research could evaluate the impact of self-reported musculoskeletal pain on mortality. However, the subgroup of patients with musculoskeletal pain who have not consulted for 2 years are likely to have less severe or less chronic pain. We restricted analysis to the most common painful conditions and those previously shown to be associated with the onset of our index conditions, and we adjusted for consultation for other musculoskeletal conditions. The severity of pain is not recorded in electronic health records, and we therefore used surrogates for this, including onward referral to relevant specialists or prescription of a strong opioid analgesic (which cannot be bought over the counter). There might also be unmeasured confounding.

Conclusion

Musculoskeletal pain is common and a frequent reason for seeking health care within primary care. Older adults with inflammatory arthritis and OA often have co-existing illnesses and are on multiple medicines. As a consequence, when they have a new illness, they might be more likely to have poorer outcomes, such as mortality, compared with those without musculoskeletal pain. Pre-existing musculoskeletal pain might be an indicator of a complex patient who is at risk of poorer outcomes at the onset of a new illnesses.

Supplementary material

Supplementary material is available at *Rheumatology Advances in Practice* online.

Data availability

Data may be obtained from a third party and are not publicly available. The data were obtained from the Clinical Practice Research Datalink. Clinical Practice Research Datalink data governance does not allow us to distribute patient data to other parties. Researchers may apply for data access at <http://www.CPRD.com/>.

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ONS Data: The interpretation and conclusions contained in this study are those of the authors alone.

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ISAC reference: The study was approved by the CPRD Independent Scientific Advisory Committee (refs 20_000105; 20_000147; 21_000504; 21_000689). The approved protocols were made available to reviewers.

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