

The impact of
musculoskeletal conditions
on outcomes of other illnesses
(the MSKCOM study): a
linked electronic health
record study





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Executive summary

Overview

The MSKCOM study set out to assess whether people with an existing musculoskeletal painful condition (pain in the joints and the muscles around them) have worse outcomes following a diagnosis of another serious illness. The illnesses the study focused on were heart attack, stroke, cancer, dementia, and pneumonia. The study used information from patient medical records contained within a large national anonymised general practice database that also had linkage to hospital and death records. This executive summary summarises why the study was important, how it was carried out, the findings, and key recommendations arising from the study.

Background and importance

Musculoskeletal painful conditions, including pain at specific sites such as the back and knee, osteoarthritis, and inflammatory conditions, are common with estimates of nearly 20 million people in the UK currently having such pain ^(Keavy et al. 2022). Lots of people with pain seek help with one in five adults consulting primary care for a musculoskeletal condition each year, and these consultation rates increase in older aged adults ^(Jordan et al., 2014).

Musculoskeletal conditions are a major cause of disability worldwide and are the second most common reason for having to take time off work ^(Versus Arthritis 2021). They are also a major burden on healthcare systems; in the UK alone, they account for the third largest use of NHS healthcare costs. Having musculoskeletal pain has been shown to increase the risk of developing new illnesses. Osteoarthritis, inflammatory conditions (e.g., rheumatoid arthritis), and regional pain (e.g., low back pain) have all been shown to be associated with an increased risk of illnesses such as heart disease and stroke. A number of reasons for this have been suggested including that the presence of musculoskeletal pain leads to the development of common risk factors such as being obese or doing less exercise, or that they share common disease mechanisms, or even that the medicines taken for the musculoskeletal pain increase risk.

Another important consideration is when people have musculoskeletal pain in combination with other illnesses. As highlighted in discussion with our Patient and Public Involvement and Engagement (PPIE) Research Users Group, management of musculoskeletal pain is often not made a priority or considered important by health care professionals when a patient has another long-term or serious illness. These other illnesses are often prioritised due to a perception of greater influence on early death, quality of life, and healthcare use. Additionally, treatment guidelines for these other illnesses often focus on that illness alone, and do not address any other condition such as musculoskeletal pain that a patient may have. Yet musculoskeletal pain may also impact on the effectiveness of management of the other illness and influence the outcomes. This could be through severe pain, which can lead to poor mobility, poor mental health, and sleep interference, all of which can reduce the effectiveness of treatments and rehabilitation. People with a new illness and musculoskeletal pain may be more likely to be admitted to hospital as they cannot manage the combined burden of their illnesses or their treatments at home. For these reasons, we wanted to examine whether having a painful musculoskeletal condition worsens outcomes from other serious illnesses including increasing the risk of hospitalisation and longer length of stay in hospital if admitted, worse long-term outcomes such as faster progression or severity of the illness, earlier death, and also if there are increased health care costs.

The study focused on five illnesses (Box 1), which are amongst the most common reasons for hospitalisation and death and are of high priority for the NHS. The effect of painful musculoskeletal conditions on each of these illnesses was assessed.

Box 1. Illnesses explored for impact of musculoskeletal pain



Methodology

Study design & setting

The study used electronic primary care health care medical records from the UK Clinical Practice Research Datalink (CPRD) Aurum database containing information recorded electronically when a patient goes to their general practice to see their doctor or nurse. CPRD Aurum is an electronic health record (EHR) database containing routinely recorded information from consultations in over 1,000 contributing UK general practices, this data is anonymised (i.e., all identifiable information about patients is removed) before it can be used for research ^(CPRD 2021). CPRD Aurum contains patient data from approximately 20% of the UK population and these patients are similar to the whole UK population on age, sex, and ethnicity.

CPRD data is linked to hospital inpatient data including admission and discharge dates, diagnoses and procedures performed during the hospital stay. It is also linked to the Office for National Statistics (ONS) Death Registration Data which includes details of cause of death, and to the Index of Multiple Deprivation (IMD) which provides information on the level of deprivation within a given neighbourhood-level area in England.

The proposed analysis of data for each illness group was approved by the CPRD Independent Scientific Advisory Committee/Research Data Governance process; protocol refs: 20_000105 (heart attack and stroke); 20_000147 (cancer); 21_000504 (dementia); 21_000689 (pneumonia).

Study population

Included were patients aged 45 years or over with a first ever recorded heart attack, stroke, cancer, dementia, or community-acquired pneumonia. All included patients were also required to have at least 24 months prior registration at their practice.

These illnesses were identified based on recorded Read or SNOMED codes or hospital codes which are entered electronically when a patient consults or is treated. The date of first diagnosis of the illness was defined as that patient's starting point, called the "index date". Patients were followed

over time from their index date until either the end of their registration at the practice (including death) or last collected date of data, whichever was earliest.

Musculoskeletal pain

Patients were defined as having musculoskeletal pain if they had recently consulted their GP for a painful musculoskeletal condition, as identified by relevant Read or SNOMED codes. Those who had seen a primary care clinician recently about their musculoskeletal pain were compared to those that had not seen anyone recently about any musculoskeletal pain for a range of different outcomes. Painful musculoskeletal conditions, as described in Box 2, were identified from primary care healthcare records in the 24 months prior to index date.

Box 2. Defined types of musculoskeletal pain

- i) diagnosed inflammatory musculoskeletal condition (defined as rheumatoid arthritis, gout, ankylosing spondylitis, giant cell arteritis, psoriatic arthritis);
- ii) diagnosed osteoarthritis (OA);
- iii) the most common non-specific regional pains recorded in primary care; these are low back pain/backache, knee pain, hip pain, hand/wrist pain.

The analysis within each illness cohort compared the outcomes of that illness over time in those with to those without the presence of musculoskeletal pain. Within the analysis of patients with a musculoskeletal condition, the study also carried out further analysis to consider the “severity” of a patient’s pain. This was done by looking at how close the musculoskeletal pain consultation was to time of diagnosis of illness, and whether the patients were prescribed strong analgesic medicines or referred to secondary care for their pain.

Outcomes

Table 1. The outcomes examined in each of the illness cohorts

	Heart	Stroke	Cancer	Dementia	Pneumonia
Hospital admission*	-	-	✓	✓	✓
Length of hospital stay	✓	✓	✓	✓	✓
Readmission within 30 days of discharge	✓	✓	✓	✓	✓
Management of index condition	✓	✓	✓	✓	-
Disease progression	✓	✓	✓	✓	-
Mortality	✓	✓	✓	✓	✓
Healthcare costs	✓	✓	✓	✓	✓

*All patients with heart attack and stroke had to have a recorded hospital stay to be included in the analysis

Covariates

As well as looking at the whether the presence of musculoskeletal pain influenced outcomes of each illness, we also looked at other factors (covariates) that might influence this relationship. We examined six potential moderators including: age, sex, ethnicity, geographical region, neighbourhood deprivation, and mental health. Within the analysis we also took account (adjusted) for other factors such as the number of different medicines prescribed in the previous 24 months, the presence of other illnesses and conditions (comorbidities) including other musculoskeletal conditions, any relevant prescribed preventative medicine for the illness, the patient's body mass index, their smoking status, and year of the start of their illness. When looking

at the healthcare costs analysis, we adjusted for the costs incurred in the three months before index date.

Statistical analysis

To examine whether people with musculoskeletal pain have poorer outcomes we used appropriate regression models. Each model was initially run with only type of musculoskeletal pain in the model (none, regional pain, osteoarthritis, inflammatory condition), progressing to including all covariates. We also undertook analyses to see if how recently a person had seen a primary care clinician about their musculoskeletal pain before diagnosis of their illness or how severe their musculoskeletal pain was (based on the type of analgesia prescription or whether a referral was made) affected the outcomes.

Health economics

An economic analysis was undertaken to estimate the additional healthcare resource use and costs needed for people who had a musculoskeletal pain condition in the 5-year period following index date (12 months for pneumonia). Primary care consultations and prescriptions and hospital-based services were valued by applying current standardised UK unit costs for health and social care services to the data on services used in the electronic records.

Results

Characteristics

The number and characteristics of each of the cohorts are given in Table 2. Across the five illness cohorts, between 22% and 31% of patients had a recorded musculoskeletal pain consultation in the two years prior to their index date. Between 4%-6% had current and severe musculoskeletal pain.

Table 2. The number of patients and characteristics of each index condition cohort

	Heart attack	Stroke	Cancer	Dementia	Pneumonia
Number of patients	171,670	138,512	428,866	207,812	211,594
Mean age	70 years	76 years	70 years	83 years	77 years
% Male	64%	51%	50%	39%	49%
% with MSK pain	30%	30%	28%	31%	22%
No MSK pain	70%	70%	72%	69%	78%
Regional Pain	17%	16%	17%	17%	12%
Osteoarthritis	8%	9%	7%	10%	6%
Inflammatory	5%	5%	4%	4%	4%
No MSK pain	70%	70%	72%	69%	78%
Recent pain	18%	18%	16%	19%	13%
Current-non-severe	7%	7%	6%	7%	5%
Current-severe	5%	5%	6%	5%	4%

Abbreviation: MSK, Musculoskeletal.

Main findings

The main findings are summarised in Table 3. Across each illness cohort, patients with all 3 types of musculoskeletal pain had generally higher rates of readmission to hospital within 30 days of discharge and long-term mortality. Time to first hospitalization and to needing end of life care (cancer and dementia cohorts) were also generally quicker in those with musculoskeletal pain compared to those without musculoskeletal pain. Those with osteoarthritis or inflammatory arthritis had higher rates of a further heart attack (heart attack cohort) and stroke (stroke cohort). The inflammatory group tended to have the worse outcomes overall across the illnesses.

Table 3. A summary of the main study findings indicating where there were increased rates of outcomes for the musculoskeletal types, **BOLD CAPITALS** indicates increased risk remained after adjustment for the covariates.

	Heart Attack	Stroke	Cancer	Dementia	Pneumonia
Hospital admission	N/A	N/A	Regional Osteoarthritis	Regional OSTEOARTHRITIS Inflammatory	None
Length of first hospital stay	Osteoarthritis Inflammatory	None	Osteoarthritis Inflammatory	None	None
Readmission within 30 days of discharge	REGIONAL Osteoarthritis Inflammatory	Regional Osteoarthritis Inflammatory	REGIONAL Osteoarthritis INFLAMMATORY (for non-cancer readmission)	Regional Inflammatory	Regional Osteoarthritis Inflammatory
Disease progression – Palliative care	N/A	N/A	REGIONAL Osteoarthritis Inflammatory	Regional Osteoarthritis Inflammatory	N/A
Increase in markers of progression	N/A	N/A	N/A	REGIONAL OSTEOARTHRITIS INFLAMMATORY	N/A
Mortality (within 30 days)	Osteoarthritis Inflammatory	None	N/A	N/A	N/A
Mortality (long-term)	Osteoarthritis INFLAMMATORY	Osteoarthritis Inflammatory	Regional Osteoarthritis Inflammatory	Inflammatory	None
Further heart attack or stroke	Regional Osteoarthritis INFLAMMATORY	Regional Osteoarthritis Inflammatory	N/A	N/A	N/A

Most covariates we adjusted for did not affect the associations between musculoskeletal pain and the outcomes of the illnesses identified in the unadjusted analyses. However, two covariates did have an impact:

- AGE – older age explained some of the differences in outcomes between those with and without musculoskeletal pain.
- PRESCRIBED MEDICATION - patients with musculoskeletal pain had been prescribed more types of medicine and this also explained some of the differences in outcomes.

We found that there were some differences in how the serious illnesses were managed and treated. For example, patients with musculoskeletal pain were slightly more likely to have dual anti-platelet medicine prescribed in the heart attack cohort. The strongest association was seen in patients with inflammatory arthritis with an increased likelihood of being prescribed anti-coagulant medicine.

In the secondary analysis, with musculoskeletal pain categorised by how recently the person had seen a primary care clinician about musculoskeletal pain and how severe their pain was based on the patient being prescribed strong analgesics or a referral rather than by type, it was found that those with more recent and severe pain had the highest rates of most outcomes. Associations with outcomes compared to the no musculoskeletal pain group generally disappeared or were reduced after adjustment for age and medicine count.

We did not find strong evidence for any factors (moderators) that affected the strength of the relationship between musculoskeletal pain and outcomes. The relationships did not vary by age, sex, ethnicity, geographical region, neighbourhood deprivation, or mental health.

Health Economics

Patients with musculoskeletal pain had a higher total health care cost than those without musculoskeletal pain. Patients with musculoskeletal pain in the heart attack cohort had 4%-12% higher cost (depending on type of musculoskeletal pain) than those without musculoskeletal pain over five years. Increased costs for those with musculoskeletal pain were 6%-13% in stroke, 3%-

30% in cancer, 8%-12% in dementia, and 2%-7% in pneumonia. This meant that patients with musculoskeletal pain were incurring around £339 to £1,250 more for their consultations, prescriptions, and hospital admissions than those without musculoskeletal pain over five years for the heart attack, stroke, cancer, and the dementia cohorts; and around £167 to £785 over one year for the pneumonia cohort.

Research perspectives

The study used a large database of primary care records linked to hospital data that is reflective of the population within the UK. There was a robust approach to study design and in developing definitions of musculoskeletal pain and the illnesses examined from the EHR. A novelty of this study is its assessment of whether different types of musculoskeletal pain (e.g., regional pain, osteoarthritis, and inflammatory) impact on outcomes following new diagnosis of five different serious illnesses. This current work expands on previous studies which show that musculoskeletal painful conditions are risk factors for developing other chronic conditions including the index conditions we examined (heart attack, stroke, cancer, dementia, and pneumonia) and this study shows that musculoskeletal pain also has a role on how people progress once they have another illness.

The study defined musculoskeletal pain as a recorded consultation to general practice. There will be people with such pain who have not sought healthcare in the previous 2 years or for whom the musculoskeletal pain was not recorded in the GP records. These patients are likely to have less severe pain. We did not examine all types of musculoskeletal conditions but restricted to the most common painful conditions previously shown to be associated with the other morbidity. We adjusted in our models for consultation for other musculoskeletal conditions, but further research could broaden our study to include all types of musculoskeletal condition.

Key findings, messages, and implications

Up to a third of people newly diagnosed with heart attack, stroke, cancer, dementia, and pneumonia have consulted for a common musculoskeletal painful problem in the previous 2 years. A consultation for musculoskeletal pain appears to be an indicator of complex patients in that they often have multiple other illnesses and higher rates of risk factors for other conditions such as heart problems and stroke, and incur increased health care costs compared to patients with no musculoskeletal pain. Patients with musculoskeletal painful conditions such as inflammatory arthritis and osteoarthritis are at more risk of worse outcomes from other illnesses than patients without musculoskeletal pain. However, after taking into account characteristics such as age and number of medicines prescribed to the patient, musculoskeletal pain was not generally independently associated with poor outcomes. There were some indications from the secondary analyses in our study that having severe pain may independently increase the risk of worse outcomes and further research should explore this further. Severe pain may worsen quality of sleep and reduce exercise levels and the ability to take part in everyday activities and hence impact on rehabilitation following occurrence of a new illness.

RECOMMENDATIONS 1

- Clinicians need to be aware that in patients with serious illnesses, a substantial proportion will also have musculoskeletal pain and they are at risk of poorer outcomes from other illnesses and ensure appropriate management of the musculoskeletal pain and targeting of common risk factors.
- Improving recognition and appropriate management of musculoskeletal pain and disability in people across co-occurring conditions, including integration within rehabilitation, may help improve their outcomes. This includes improved surveillance of those patients presenting with new heart attack or stroke who may be at increased risk of further heart problems or another stroke.

Patients with musculoskeletal pain have a high number of prescribed medicines (polypharmacy) that appears to be associated with an increased risk of poor outcomes from other conditions.

Whilst this will relate to increased multimorbidity, there also is an increased risk of inappropriate prescribing given this high number of medicines.

RECOMMENDATIONS 2

- Clinicians need to think about the patient as a whole including all the illnesses and current medicines they may have when treating individual illnesses.
- Improved medicine reviews are needed in patients with musculoskeletal pain to assess appropriateness of prescribed medicine.
- Further research should explore the reasons for a relationship between prescriptions of multiple medicines and outcomes of illness in people with musculoskeletal pain.

We used data from healthcare use before the COVID-19 virus pandemic. There have been changes in health care use since the start of the pandemic including delays in referral and treatment.

RECOMMENDATIONS 3

- Future research is needed to assess whether the COVID-19 pandemic has increased the impact of musculoskeletal pain on outcomes of other conditions and altered how patients with musculoskeletal pain are treated.

Conclusions

Musculoskeletal pain is common and a frequent reason for going to see a clinician. It can have a major impact on everyday life, reducing the ability to perform everyday tasks and impacting on sleep and work. Clinicians should be aware that consulting for musculoskeletal pain also appears to be an indicator of a complex patient who is at risk of poorer outcomes from a range of different illnesses. Their costs of care will also be higher. People with musculoskeletal pain have many co-existing illnesses and are more likely to be prescribed multiple medicines, as a consequence when they have a new serious illness, they are more likely to have poorer outcomes compared to those without musculoskeletal pain.

Project information

The research team

The research team are listed below in Box 3.

Box 3. The Research Team

Kelvin Jordan (Chief Investigator): Professor of Biostatistics, Primary Care Centre Versus Arthritis, School of Medicine, Keele University, UK;

Michelle Marshall (Principal Investigator): Senior Research Fellow in Clinical Epidemiology & Imaging, Primary Care Centre Versus Arthritis, School of Medicine, Keele University, UK;

Kayleigh Mason: Research Associate in Epidemiology/Biostatistics, Primary Care Centre Versus Arthritis, School of Medicine, Keele University, UK;

James Bailey: Data Manager, Primary Care Centre Versus Arthritis, School of Medicine, Keele University, UK;

Neil Heron: Clinical Lecturer, Primary Care Centre Versus Arthritis, School of Medicine, Keele University, UK & Centre for Public Health, Queen's University Belfast, UK;

John Edwards: Honorary Senior Lecturer in General Practice, Primary Care Centre Versus Arthritis, School of Medicine, Keele University, UK;

Felix Achana: Senior Researcher in Health Economics, Nuffield Department of Primary Care Health Sciences, Oxford University, UK;

Ying Chen: Honorary Research Fellow: Biostatistics, Primary Care Centre Versus Arthritis, School of Medicine, Keele University, UK & Associate Professor (Biostatistics and Epidemiology), Academy of Pharmacy, Xi'an Jiaotong - Liverpool University, Suzhou, China;

Martin Frisher: Reader in Health Services Research, School of Pharmacy and Bioengineering, Keele University, UK;

Alyson Huntley: Senior Research Fellow in Evidence Synthesis, Centre for Academic Primary Care, Bristol Medical School, Bristol University, UK;

Christian Mallen: NIHR Professor of General Practice, Primary Care Centre Versus Arthritis, School of Medicine, Keele University, UK;

Mamas Mamas: Professor of Cardiology and Consultant Cardiologist, Keele Cardiovascular Research Group, Centre for Prognosis Research, Keele University, UK;

May Ee Png: Senior Lecturer in Health Economics, Nuffield Department of Primary Care Health Sciences, Oxford University, UK;

Stephen Tatton: PPIE member, Primary Care Centre Versus Arthritis, School of Medicine, Keele University, UK;

Simon White: Reader in Pharmacy Practice, School of Pharmacy and Bioengineering, Keele University, UK.

Advisory group

We established a steering committee consisting of an independent expert in electronic health records (EHR) research, a GP researcher, experts in the five index conditions, a statistician, and PPIE representation. The steering committee met twice during the project (at 10 and 22 months) and there was further correspondence by email/telephone in between. Their role was to monitor and supervise progress of the study towards its objectives including timelines and adherence to the protocol; ensure the project was conducted in accordance with Research Governance guidelines and the rigorous standards of Good Clinical Practice; and to advise the project team on dissemination strategy and its implementation.

The project advisory group consisted of:

Dr John Bedson: Senior Lecturer in General Practice, Primary Care Centre Versus Arthritis, School of Medicine, Keele University, UK;

Dr Paul Campbell: Senior Research Associate, Midlands Partnership NHS Foundation Trust, St George's Hospital, Stafford, UK;

Professor Carol Coupland: Professor of Medical Statistics in Primary Care, Faculty of Medicine & Health Sciences, University of Nottingham, UK;

Professor Deborah Symmons, Professor of Rheumatology and Musculoskeletal Epidemiologist, Division of Musculoskeletal and Dermatological Sciences, University of Manchester, UK.

Patient and Public Involvement and Engagement group

The Primary Care Centre Versus Arthritis at Keele University has a strong Patient and Public Involvement and Engagement (PPIE) infrastructure, including a Research Users' Group (RUG) who are involved throughout all stages of research. For the MSKCOM study five members of the RUG group who have musculoskeletal pain were recruited. They contributed to the development of the research proposal and application in particular highlighting that the five health conditions of heart attack, stroke, pneumonia, cancer, and dementia were important to study. One of the RUG members (Stephen Tatton) with long-term experience of musculoskeletal pain was a co-applicant. The study team met with the RUG members at three time points throughout the study to finalise the methods we used, assist on the interpretation of our findings, and contribute to our dissemination plans. These meetings were supported and overseen by experienced PPIE staff within our Centre.

Introduction

Background and importance

Musculoskeletal pain is common and is often present in people diagnosed with other illnesses. Its impact on everyday life may also reduce how well treatment for other illnesses works. The MSKCOM study set out to assess whether having an existing musculoskeletal pain condition led to worse outcomes from other serious illnesses. These illnesses were heart attack, stroke, cancer, dementia, and pneumonia. In this section we set out the reasons for doing this study.

Musculoskeletal pain

Musculoskeletal pain is common, with an estimated 18.8 million people in the UK affected by the condition ^(Keavy et al. 2022). It is a major cause of morbidity and one in five adults consult primary care for a musculoskeletal painful condition each year, with consultation rates highest in older adults ^(Jordan et al. 2014, Kassebaum et al. 2016). The number of people with musculoskeletal pain is expected to rise in the future due to a UK population that is getting older, becoming more obese, and doing less exercise. Common musculoskeletal conditions include regional (site-specific) pain such as back and knee pain, osteoarthritis, and inflammatory conditions. In the UK approximately 8.5 million people have painful joints that is attributed to osteoarthritis ^(NICE 2021). It is the most common musculoskeletal condition in older people and can develop in any joint in the body, but frequently affects the knees, hips, hands, and feet. Inflammatory conditions include rheumatoid arthritis (the most common), psoriatic arthritis, ankylosing spondylitis, and gout, with an estimated 8.5 million people in the UK suffering from rheumatoid arthritis ^(Versus Arthritis 2021). These painful problems can have a significant impact on individuals in terms of disability and their ability to work, and also are a major burden on healthcare systems. Musculoskeletal disorders are the main contributor to disability from non-communicable diseases worldwide. In England, they account for an estimated 21% of total years lived with disability (YLD) with low back pain the biggest contributor ^(Kassebaum et al. 2016) and are the second most common reason for having to take days off work ^(Versus Arthritis 2021). They also account for the third largest cause of NHS healthcare expenditure.

Multimorbidity

A large proportion of people with painful musculoskeletal conditions also have other long-term conditions (Barnett et al. 2012, Kadam et al, 2004, Kuo et al. 2016). Individuals with multiple health conditions, particularly those that are long-term, are often referred to as having multimorbidity. A systematic review identified three common types of condition that are often present in multimorbidity: a painful condition, a mental health condition, and a cardio-metabolic one (Violan et al., 2014). Common pairings included a painful condition with vascular disease (up to a third of people with coronary heart disease live with a painful condition (Barnett et al., 2012)), or cancer (Violan et al. 2014), and musculoskeletal pain is also common in dementia (Hunt et al. 2015, Scherder et al. 2009). 12-29% of people with cancer live with a painful condition, making this the commonest comorbidity for people living with cancer (Barnett et al. 2012).

General Practitioners (GPs) report problems managing patients with multimorbidity, including disorganised and fragmented care, and having to use treatment guidelines for individual diseases which do not address multimorbidity (Sinnott et al. 2013). Multimorbidity also impacts on hospital services. As the population gets older, more people require hospital care, and hospitals are increasingly struggling to supply enough beds. Use of hospital services by older people, who are more likely to suffer from multimorbidity, is rising. Episodes of care under a hospital consultant in people aged over 45 years between 2005-06 and 2015-16 increased by a third. In 2014-15, 62% of days spent in a hospital bed were used by people aged over 65 years, and delayed transfers to other care facilities in older people cost £820 million (National Audit Office 2016). Patients who have to be admitted to hospital are often the most frail and in need. They tend to be older and have many illnesses including musculoskeletal problems.

Impact of musculoskeletal pain on other illnesses

As well as being present alongside other illnesses, having musculoskeletal pain has been shown to increase the risk of developing new illnesses, including the index conditions used in the MSKCOM study. For example, having osteoarthritis (Wang et al. 2016, Hsu et al. 2017, Williams et al. 2018, Cox et al. 2021), an inflammatory condition such as rheumatoid arthritis (Holmqvist et al 2017, Nikiphorou et al 2020, Jamnitski et al. 2013) or regional pain such as low back pain (Fernandez et al. 2016, Wang et al. 2020) has been shown to be

associated with an increased risk of developing heart disease and stroke. This might be for a number of reasons and those suggested include there being common risk factors for musculoskeletal and heart disease such as being obese or doing less exercise, common pathogenic mechanisms, or being related to the medicine used for the musculoskeletal pain (Fernandes et al. 2015, Atiquzzaman et al. 2019). Musculoskeletal pain has also been linked to cancer, dementia, and pneumonia. For example, one study showed associations of existing back, hip and neck pain with new diagnosed prostate cancer, hip pain with breast cancer, and back pain with breast and lung cancer (Jordan et al. 2013). There are also links between inflammatory conditions such as psoriatic arthritis and polymyalgia rheumatica and onset of cancer (Hagberg et al. 2016, Muller et al 2014). A review of all the relevant literature concluded there was an increased risk of dementia in people with osteoarthritis (Weber et al. 2019). There is evidence of an association of inflammatory musculoskeletal conditions with hospitalisation for community-acquired pneumonia (Chung et al. 2020). Patients with rheumatoid arthritis have also been shown to have higher risk of serious infections (Mehta et al. 2019) and incidence of pneumonia increased after total knee replacement (Jauregui et al. 2016). The incidence of hospitalisation for pneumonia has increased in recent years in people with osteoarthritis in the USA (Singh et al. 2021).

It is likely that musculoskeletal pain may be unrecognised or inadequately addressed when a person has other serious illnesses (Barnet et al. 2012, Wang et al. 2016). Non-musculoskeletal conditions are often prioritised due to a perception of greater influence on early mortality, morbidity, and healthcare use. A review of the literature suggested musculoskeletal problems are not appropriately recognised when considering management of people with multiple illnesses (Smith et al. 2016). For example, people living with dementia are less likely to have a recorded primary care consultation or an analgesics prescription for their musculoskeletal condition compared to those without dementia suggesting musculoskeletal pain is often neglected in dementia (Bullock 2021). Pathways to support patients with comorbid musculoskeletal conditions are not clearly established. Yet is it realistic to hypothesise that musculoskeletal pain may impact other outcomes. First, it may impact on management of the other illness and therefore its outcomes through severe pain leading to poor mobility, worse mental health, and sleep interference and stopping delivery or reducing the effectiveness of treatment and rehabilitation, leading to reduced quality of life of people with musculoskeletal pain and other conditions. Second, people with a

new illness and musculoskeletal pain may be more likely to be admitted to hospital as they cannot manage the total morbidity and treatment burden at home. Third, there may be concerns about interactions between existing treatments and planned treatments. It is possible musculoskeletal pain may stop delivery of recommended treatments; for example, following a heart attack some medicines (dual antiplatelet agents and ACE inhibitors) may not be prescribed to patients on non-steroidal anti-inflammatory drugs (NSAIDs) if there are concerns around adverse events. In people living with dementia, musculoskeletal pain may reduce timely use of appropriate medicine, for example anti-dementia drugs such as donepezil, due to concerns over musculoskeletal side effects, and lead to increased use of drugs for behavioural and psychological symptoms of dementia, such as anti-psychotics, which in turn increase the risk of adverse outcomes.

There is some evidence from the USA that musculoskeletal problems play a significant role in multimorbidity of inpatients with a major impact on their care (Nguyen-Oghalai et al. 2005, Nguyen-Oghalai et al. 2008). The potential impact of musculoskeletal related disability is shown by one study estimating 11.5% of pneumonia cases requiring hospitalisation is attributable to limitations in mobility (Juthani-Mehta et al 2013), and mobility impairment has also been associated with mortality in pneumonia (Hespanhol & Barbara 2020). However, international studies have shown contradictory results; for example, in cardiovascular disease studies have mainly focussed on inflammatory arthritis and shown worse (Lai et al., 2020, Nguyen-Oghalai et al. 2005), similar (Mccoy et al. 2013; Isogai et al., 2017; Kang et al., 2018) and better (Francis et al., 2010) outcomes for patients with inflammatory arthritis. There is a lack of studies from the UK. This lack of research was reflected in our pre-study Patient and Public Involvement and Engagement (PPIE) Research Users Group meeting (see Box 4) where discussion highlighted that management of musculoskeletal pain is often not made a priority or considered important by health care professionals when a patient has another long-term or serious illness. The PPIE group considered that musculoskeletal pain may be an important driver of poor prognosis including prolonged hospital stay for other illnesses.

PPIE Research Users Group

We discussed the ideas for this study at a meeting with five RUG members who have musculoskeletal pain. They highlighted a number of things about having musculoskeletal pain

alongside having other health conditions that we felt were important for this study, these are listed in Box 4.

Box 4. Concerns raised by our RUG members about having musculoskeletal pain along with other health conditions

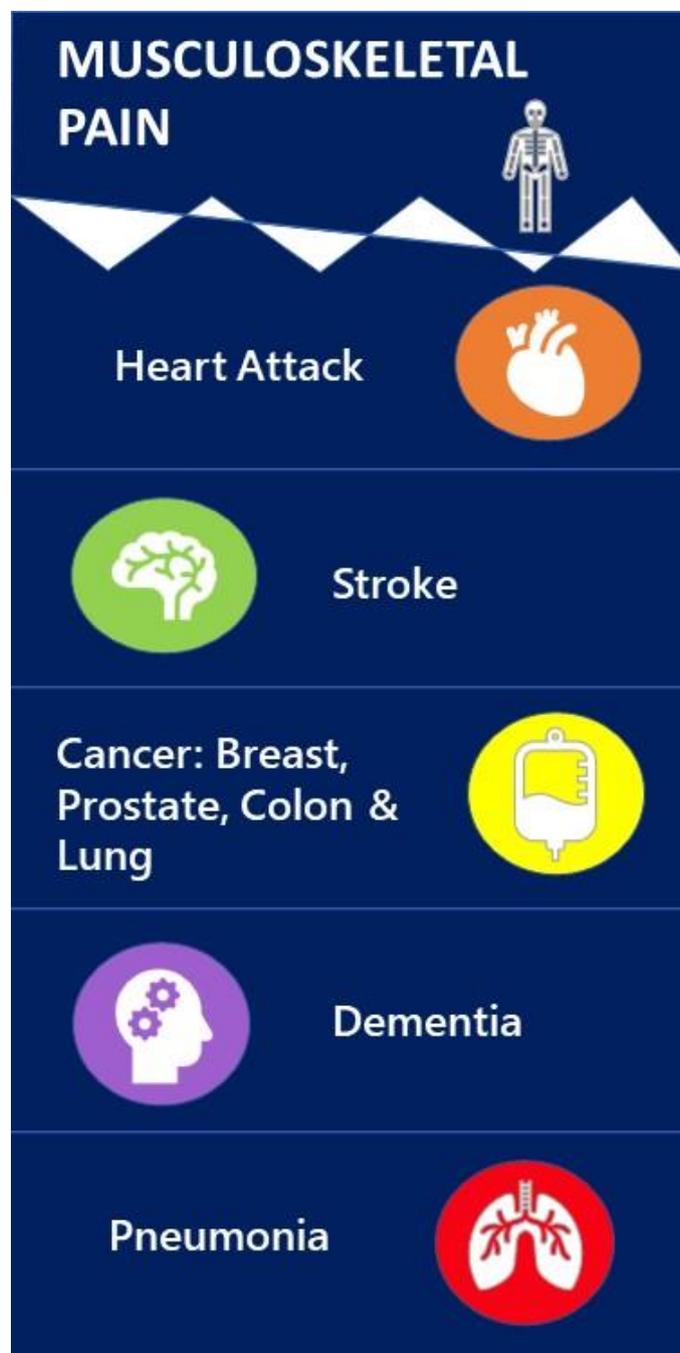
- When they have been in hospital for another illness, they had rarely been asked about co-existing musculoskeletal conditions, or how they managed them
- Their belief that musculoskeletal pain may delay discharge because it restricts the ability to self-care. For example, restricted mobility may stop someone being able to get up and go to the toilet
- Some musculoskeletal conditions may impact on hospitalisation more than others
- Poor mental health (for example, anxiety) alongside musculoskeletal pain may further worsen outcomes
- The possibility of a 'vicious circle': not only might musculoskeletal pain worsen outcomes of other conditions, but a stay in hospital may worsen musculoskeletal pain due to inactivity and being unable to exercise, self-manage, and use normal analgesia for musculoskeletal pain
- The importance of a holistic approach to care and rehabilitation covering co-existing musculoskeletal pain
- The health conditions of heart attack, stroke, pneumonia, cancer, and dementia were important to study.

The MSKCOM study novelly examined how musculoskeletal pain affects other common and serious medical conditions. The impact of musculoskeletal pain on key outcomes of these other illnesses and its effect on the management of these comorbidities was investigated. We also assessed social inequalities in the relationship of musculoskeletal pain with these outcomes. We hypothesized that that having a painful musculoskeletal condition worsens outcomes from other conditions including increasing the risk of hospitalisation and longer length of stay in hospital if admitted, worse long-term outcomes such as earlier mortality and progression of disease, and increased health care costs.

The study focused on five serious illnesses that we will refer to as index conditions. These were selected as they are amongst the most common reasons for hospitalisation and of high priority for the NHS (NHS Digital, 2016). These conditions also have evidence of links with musculoskeletal pain. These conditions (Box 5) are:

- i) heart attack
- ii) stroke
- iii) the most common forms of cancer
- iv) dementia
- v) community-acquired pneumonia.

Box 5. The five index conditions examined in the study



The effect of painful musculoskeletal conditions on each of these index conditions was assessed. Also, we examined whether any of the relationships identified varied by socioeconomic characteristics. For example, whether any relationship between musculoskeletal pain and

outcomes were stronger for people living in more deprived areas than those living in more affluent areas.

Study aims

To determine whether pre-existing painful musculoskeletal conditions lead to:

- increased likelihood of (earlier) admission to hospital for other conditions
- extended length of stay or early readmission in those admitted to hospital
- worse long-term outcomes of other conditions including earlier mortality and increased disease progression
- variation in recommended management of other conditions, which may explain any difference in outcomes
- increased healthcare resource use and costs in patients with other conditions

We also determined if:

- inequalities exist in these relationships by socioeconomic characteristics (age, ethnicity, deprivation, rurality, geographical region)
- relationships differ by type of painful musculoskeletal condition.

Methodology

This section sets out the methods we used for the study.

Study design & setting

The study used electronic primary health care medical records that are contained within the UK Clinical Practice Research Datalink (CPRD) Aurum database. CPRD Aurum is an electronic health record (EHR) database containing anonymised routinely, high-quality data recorded in consultations with over 40 million patients in over 1,000 contributing UK general practices ^(CPRD 2021, Wolf et al. 2019). Approximately 98% of the England and Wales population are registered with general practitioners (GPs), and in the UK general practice (primary care) is typically the first point of care for patients with new symptoms and the place where most chronic illnesses are managed.

The CPRD Aurum contains patient data from approximately 20% of the UK population and these patients are similar to the whole UK population on age, sex, and ethnicity. Data included in the records include patient symptoms and diagnoses, prescribed medicines, information on referrals (for example, to rheumatology, physiotherapy) and tests and investigations such as x-rays and blood tests. Validation studies have generally shown high levels of positive predictive values of diagnoses within primary care EHR, including cardiovascular, respiratory, cancer, dementia, and musculoskeletal conditions ^(Herrett et al. 2010).

CPRD data is linked to hospital inpatient data through NHS Digital Hospital Episode Statistics (HES) database which includes admission and discharge dates and all clinically recorded data including diagnoses and procedures performed during the hospital stay. It is also linked to the Office for National Statistics (ONS) Death Registration Data which includes details of cause of death and to the Index of Multiple Deprivation (IMD) which provides neighbourhood-level deprivation data in England.

Each of our cohort analyses were approved by the CPRD Independent Scientific Advisory Committee/Research Data Governance process; protocol refs: 20_000105 (heart attack and stroke); 20_000147 (cancer); 21_000504 (dementia); 21_000689 (pneumonia).

Study population

Incident (i.e., patients with a first ever record of the illness) cohorts were assembled for each of the index conditions. Included were patients aged 45 years or over with a first recorded heart attack, (cohort A), stroke (cohort B), cancer (cohort C), dementia (cohort D), or community-acquired pneumonia (cohort E), as defined below, and with at least 24 months prior registration at their practice.

Cohorts A and B (heart attack & stroke): Patients with a first ever recorded myocardial infarction or unstable angina, or with a first ever recorded stroke or transient ischaemic attack between 2000 and 2019 in CPRD Aurum, and a matching record in the linked hospital inpatient data with admission date within 1 month of the first CPRD recorded date.

Cohort C (cancer): Patients with a first ever recorded diagnosis of breast, colon, lung, or prostate cancer in CPRD Aurum between 2000 and 2019.

Cohort D (dementia): Patients with a first ever recorded diagnosis of dementia in CPRD Aurum between 2005 and 2019.

Cohort E (pneumonia): Patients with a first ever recorded bacterial pneumonia diagnosis in primary care in CPRD Aurum, or as the reason for admission to hospital between 2014 and 2018. Patients recorded with a pneumonia diagnosis within 2 weeks after a hospital stay were excluded to ensure pneumonia was not acquired in hospital. Patients were also excluded if they had a previous record of a viral pneumonia.

Index conditions

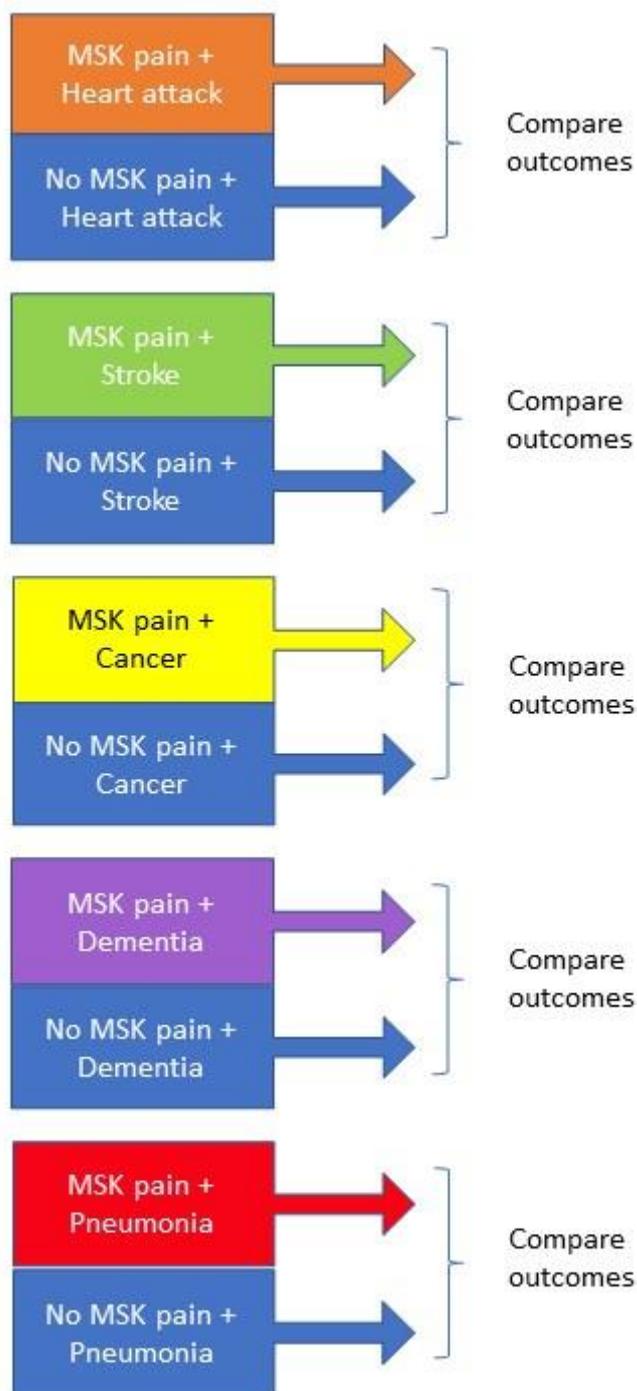
Diagnoses, symptoms, and processes of care (for example, referrals, tests) are recorded in UK primary care using a coding system. This system was the Read code system up to 2018 and SNOMED CT codes from 2018. Within hospital admissions illnesses are recorded using International Classification of Diseases (ICD-10) codes.

Definitions of the index conditions including derivation of appropriate Read and ICD code lists were based on those previously developed through a rigorous consensus approach in research studies by experts in electronic health record research at Keele University (Burton et al. 2013, Jordan et al. 2013, Jordan et al. 2017) 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://doi.org/10.21252/878s-x990>.

The date of first diagnosis of the index condition was defined as that patient's index date. Patients were followed from index date until either the end of their registration at the practice (including death) or last collected date of data in CPRD or HES, whichever was earliest.

Within each cohort patients with a recent consultation for a painful musculoskeletal condition (see the exposure section) were compared to patients without a recent consultation for musculoskeletal pain on the different outcomes as shown in Box 6.

Box 6. Patients with musculoskeletal pain were compared to those without for five index conditions for the outcomes of interest



Abbreviation: MSK, Musculoskeletal

Exposure: musculoskeletal pain

Primary analysis

Patients with a recent history of musculoskeletal healthcare use were compared to those without recent musculoskeletal healthcare use on the different outcomes. Painful musculoskeletal conditions were identified from primary care records in the 24 months prior to index date as described in Box 7.

Box 7. The types of musculoskeletal pain that was examined in the study

Three types of musculoskeletal pain were included:

- i) diagnosed inflammatory musculoskeletal condition (these were rheumatoid arthritis, gout, ankylosing spondylitis, giant cell arteritis, psoriatic arthritis);
- ii) diagnosed osteoarthritis (OA);
- iii) the most common non-specific regional pains recorded in primary care (these were low back pain/backache, knee pain, hip pain, hand/wrist pain).

Secondary analysis

In a secondary analysis, severity and “recency” of musculoskeletal pain were also examined. Primary care EHR do not contain reliable direct evidence of musculoskeletal pain severity, so we used proxy measures that most likely indicated more severe pain:

- i) A coded referral for a musculoskeletal condition (to a pain management clinic, rheumatology or orthopaedics specialty, or physiotherapy). The NICE guidelines for osteoarthritis, for example, suggest that core interventions (such as exercise, weight loss if appropriate, and education) should be used in primary care before referral is considered, implying that only people with more severe symptoms should be referred (NICE 2014).
- ii) Prescription of a strong analgesic (painkiller) medicine (i.e., a strong opioid) (Bedson et al. 2013) on the assumption a stronger painkiller would normally indicate more severe pain.

Recent musculoskeletal pain was defined as a recorded consultation for musculoskeletal pain in the six months before index date. In this secondary analysis, patients within each cohort were therefore classified as:

- Current and severe musculoskeletal pain (recorded consultation for musculoskeletal pain within the six months before index date and either a referral or a prescription of strong analgesia recorded)
- Current and non-severe musculoskeletal pain (recorded consultation for musculoskeletal pain within the six months before index date but no referral and no prescription of strong analgesia recorded)
- Recent musculoskeletal pain (recorded consultation for musculoskeletal pain between seven and twenty-four months before index date)
- No musculoskeletal pain (no recorded consultation for musculoskeletal pain in the twenty-four months before index date)

Outcomes

A number of outcomes were examined for each index condition. These are indicated in table 4.

Table 4. The outcomes examined in each cohort

	Heart Attack	Stroke	Cancer	Dementia	Pneumonia
Hospital admission*	-	-	✓	✓	✓
Length of hospital stay	✓	✓	✓	✓	✓
Readmission within 30 days of discharge	✓	✓	✓	✓	✓
Management of index condition	✓	✓	✓	✓	-
Disease progression	✓	✓	✓	✓	-
Mortality	✓	✓	✓	✓	✓
Healthcare costs	✓	✓	✓	✓	✓

*All patients with heart attack and stroke had to have a recorded hospital stay to be included in the analysis

Hospital admission. As all patients in the heart attack and stroke cohort had to have an inpatient hospital record (that is, they had been admitted into hospital) at index date, we did not examine hospital admission as an outcome for this cohort. For the cancer and dementia cohorts, the outcome was time to first hospitalisation after diagnosis. For the pneumonia outcome, the hospital admission outcome referred to whether they went into hospital for their pneumonia or not.

Length of hospital stay was length in days of the hospital stay related to the index event (heart attack; stroke; pneumonia) or for the first hospital stay after diagnosis (cancer; dementia) in those who were discharged from hospital.

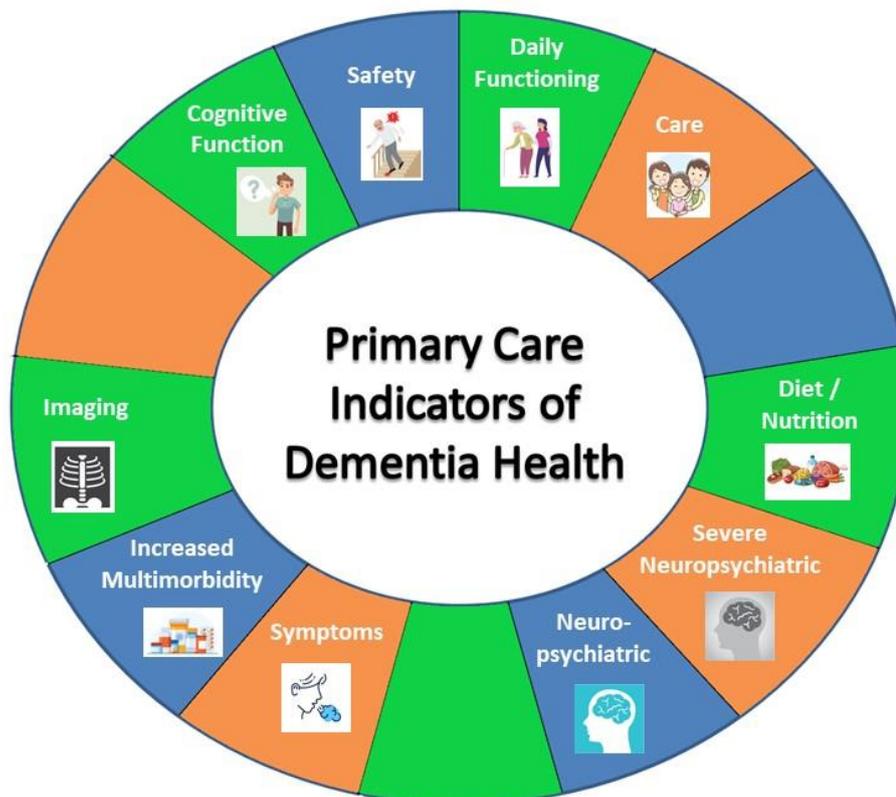
Readmission to hospital had to be within 30 days of discharge of their first hospital stay.

Disease progression was defined as end-of-life care for cancer and dementia, a further heart attack or stroke for the heart attack and stroke cohorts, and an increase in the recorded number of markers of progression recorded in the first 24 months after diagnosis for those patients with dementia. The markers of progression were a subset of those developed from another study shown in Figure 1.

Mortality (death) was assessed in the short term for heart attack and stroke (during hospitalisation and up to 30 days after discharge from initial hospital stay) and long term for all cohorts.

Health care costs in primary and secondary care were determined for the five years (12 months for pneumonia) after diagnosis of index condition. These included the costs related to consulting a primary care clinician, prescriptions, referrals, procedures, and surgery.

Figure 1. Markers of progression of dementia that were examined



Covariates

It is possible that the relationship between musculoskeletal pain and the outcomes may vary depending upon a characteristic of the patient (for example, the relationship may be stronger in older people than younger people). These characteristics are called moderators and we examined six potential moderators (age, sex, ethnicity, geographical region, neighbourhood deprivation, index year, and mental health) (Table 5).

Neighbourhood deprivation was measured using the Index of Multiple Deprivation, which is determined for local geographical areas in England with a mean population of 1500 and is a weighted combination of seven domains reflecting the local area: income; employment; health deprivation and disability; education, skills, and training; barriers to housing and services; living environment; and crime.

Mental health has a strong association with musculoskeletal pain and so we included as a potential moderator an existing record of depression, anxiety, or stress.

Table 5. Covariates that were adjusted for in each of the cohorts

	Heart Attack	Stroke	Cancer	Dementia	Pneumonia
Common	Age, sex, ethnicity, geographical region, neighbourhood deprivation, index year, mental health, diabetes, other MSK conditions, smoking status, BMI, number of different medicines prescribed				
Condition-specific	Peripheral vascular disease, Statins	Peripheral vascular disease, Statins	Renal disease	Stroke	COPD, Dementia, Renal disease, Stroke, Antibiotic type

Abbreviations: MSK, Musculoskeletal; COPD, Chronic Obstructive Pulmonary Disease.

It is also possible that other characteristics (confounders) may “explain” any relationship between musculoskeletal pain and outcomes of other illnesses. In particular, having other health conditions (comorbidities) may explain this relationship. Therefore, we adjusted for other health conditions, including other musculoskeletal conditions, patients had in order to be able to estimate the impact of the musculoskeletal pain beyond that of other comorbidities. As a general measure of comorbidity, we included in the analysis the number of different medicines prescribed in primary care in the previous 24 months (Perkins et al. 2004).

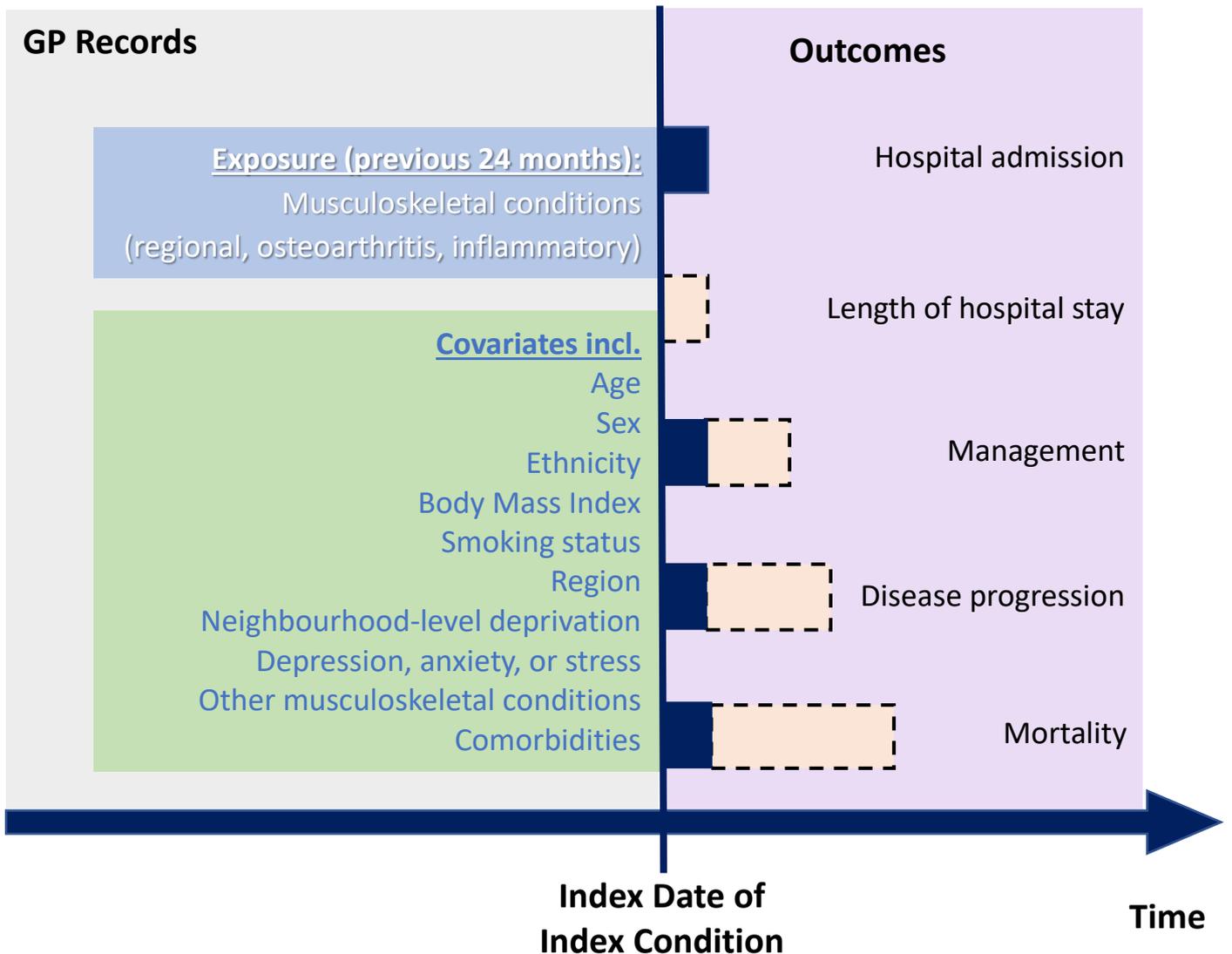
We also examined comorbidities and prescribed preventative medicine specific to each index disease. These were decided on following a review of the literature and consensus of academic clinicians within our research centre and included diabetes (linked to impact on all five index conditions), peripheral vascular disease and statin medicine for heart attacks and strokes, renal (chronic kidney) disease for cancer, having a stroke in people living with dementia, and chronic obstructive pulmonary disease (COPD), dementia, renal disease, stroke, and type of antibiotic for pneumonia. Comorbidity was defined based on a relevant primary care record in the 24 months prior to diagnosis of the index condition.

Body mass index, a known risk factor for osteoarthritis for example, may confound the relationship between musculoskeletal pain and outcomes and was also included, as were smoking status shown to be confounders of health outcomes from musculoskeletal pain in previous studies (Skillgate et al. 2009). As there may be temporal trends in health care use and clinical practice, we also included year of index date as potential confounder.

Figure 2 shows an outline of the analysis undertaken in the study for each index condition including the adjustment of moderators and confounders.

It was likely that patients with musculoskeletal pain would have higher healthcare use and costs prior to index date than patients without musculoskeletal pain. Thus, it was important for the cost-analyses to account for these baseline differences in costs. We included the costs incurred in the twelve months before index date as a covariate in the cost-analyses.

Figure 2. An outline of the analysis that was undertaken in the study



Statistical analysis

Analysis of the association of prior musculoskeletal consultation with outcomes used appropriate statistical regression models as listed in Table 6. Each model was run with only musculoskeletal pain (categorised as none, regional pain, osteoarthritis, inflammatory) in the model, progressing to including all covariates. We also accounted for clustering by practice (i.e., that patients within the same practice are likely to be more similar to each other in the way they are managed and, in their outcomes, than to patients in another practice) in the models.

Table 6. The regression models used for each outcome

Outcome	Cohort	Regression Model
Time to hospital admission	Cancer, Dementia	Flexible parametric survival
Hospital admission for pneumonia	Pneumonia	Robust Poisson
Length of initial hospital admission	Heart attack, Stroke	Negative binomial
Length of first hospital stay	Cancer, Dementia, Pneumonia	Negative binomial
Readmission to hospital within 30 days	All	Robust Poisson
Time to further Heart attack or Stroke	Heart attack, Stroke	Flexible parametric survival
Management	Heart attack, Stroke, Cancer, Dementia	Robust Poisson
Disease progression (time to palliative care)	Cancer, Dementia	Flexible parametric survival
Mortality within 30 days	Heart attack, Stroke	Robust Poisson
Mortality (long term)	All	Flexible parametric survival

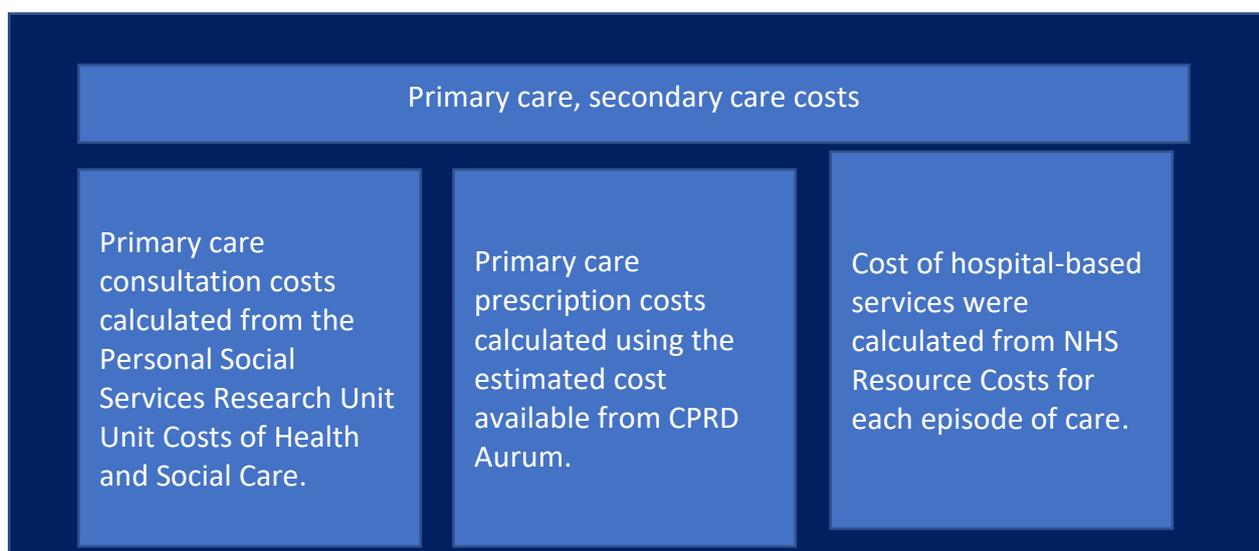
Further models used the proxies for musculoskeletal pain severity based on any relevant referral and type of analgesia prescription as described earlier. The outcomes were then compared between these subgroups to assess if recency and severity of an MSK condition further impacts on outcomes.

Interactions of musculoskeletal pain consultation with the moderators were also included to assess whether the effect of painful musculoskeletal conditions on outcomes varies depending on these factors.

Health economics

An economic analysis was conducted to estimate the additional healthcare resource use and costs attributable to each musculoskeletal comorbidity in the 5-year period (1-year for the pneumonia cohort) following index date. Primary and secondary care utilisation in the 1-year period prior to index date to 5-years after index date was extracted and valued by applying current UK unit costs of health and social care services to the resource use data extracted from the electronic records as shown in Figure 3.

Figure 3. How costs were calculated for healthcare service use



A two-parts model, which can account for the skewed distribution of economic costs due to a high frequency of patients who incurred low costs and a few patients who incurred extremely high costs, was used to model trends in healthcare resource use and costs over time. This model had two parts as its name suggests: 1) a logistic regression, in which the dependent variable (total cost) indicated presence of zero costs (yes/no); 2) followed by a generalised linear model with a gamma distribution and log-link function for economic costs relating to patients with positive values. The model included pre-existing musculoskeletal pain condition as the exposure of interest and accounted for the baseline costs and other covariates.

Results

Summary

The number and characteristics of each of the cohorts and a summary of the main findings are given in tables 7 and 8. Fuller details of the results are then presented by index condition cohort.

Table 7. The number of patients and characteristics of each index condition cohort

	Heart Attack	Stroke	Cancer	Dementia	Pneumonia
Number of patients	171,670	138,512	428,866	207,812	211,594
Median age	70 years	76 years	70 years	83 years	77 years
% Male	64%	51%	50%	39%	49%
% with MSK pain	30%	30%	28%	31%	22%
No MSK pain	70%	70%	72%	69%	78%
Regional Pain	17%	16%	17%	17%	12%
Osteoarthritis	8%	9%	7%	10%	6%
Inflammatory	5%	5%	4%	4%	4%
No MSK pain	70%	70%	72%	69%	78%
Recent pain	18%	18%	16%	19%	13%
Current-non-severe	7%	7%	6%	7%	5%
Current-severe	5%	5%	6%	5%	4%

Abbreviation: MSK, Musculoskeletal.

The cohort of patients with dementia was the oldest (average (median) age 83 years). There were more men in the heart attack cohort and more women in the dementia cohort.

The proportion of patients with musculoskeletal pain was similar across five of the cohorts; just under one in three people had seen their GP for musculoskeletal pain in the 2 years before the diagnosis of a new illness. The exception was the pneumonia cohort where there the proportion with musculoskeletal pain was slightly lower (22%; about one in five people). In terms of types of

musculoskeletal pain, the proportion with inflammatory arthritis was similar across the cohorts, but the proportion with diagnosed osteoarthritis varied ranging between 6% and 10% of the cohorts. The frequency of regional pain consultation was lower for pneumonia.

One in twenty (4-6%) of each cohort had consulted for musculoskeletal pain within the six months prior to their new diagnosis and had been prescribed a strong analgesic or been referred onwards and were classed as the current–severe group.

Table 8. A summary of the main study findings indicating where there were increased rates of outcomes for the musculoskeletal types **BOLD CAPITALS** indicates increased risk remained after adjustment

	Heart Attack	Stroke	Cancer	Dementia	Pneumonia
Hospital admission	N/A	N/A	Regional Osteoarthritis	Regional OSTEOARTHRITIS Inflammatory	None
Length of first hospital stay	Osteoarthritis Inflammatory	None	Osteoarthritis Inflammatory	None	None
Readmission within 30 days of discharge	REGIONAL Osteoarthritis Inflammatory	Regional Osteoarthritis Inflammatory	REGIONAL Osteoarthritis INFLAMMATORY (for non-cancer readmission)	Regional Inflammatory	Regional Osteoarthritis Inflammatory
Disease progression – Palliative care	N/A	N/A	REGIONAL Osteoarthritis Inflammatory	Regional Osteoarthritis Inflammatory	N/A
Increase in markers of progression	N/A	N/A	N/A	REGIONAL OSTEOARTHRITIS INFLAMMATORY	N/A
Mortality (within 30 days)	Osteoarthritis Inflammatory	None	N/A	N/A	N/A
Mortality (long-term)	Osteoarthritis INFLAMMATORY	Osteoarthritis Inflammatory	Regional Osteoarthritis Inflammatory	Inflammatory	None
Further heart attack or stroke	Regional Osteoarthritis INFLAMMATORY	Regional Osteoarthritis Inflammatory	N/A	N/A	N/A

What the evidence tells us about musculoskeletal pain and heart attack

Figure 4. Summary of characteristics of patients in the heart attack cohort

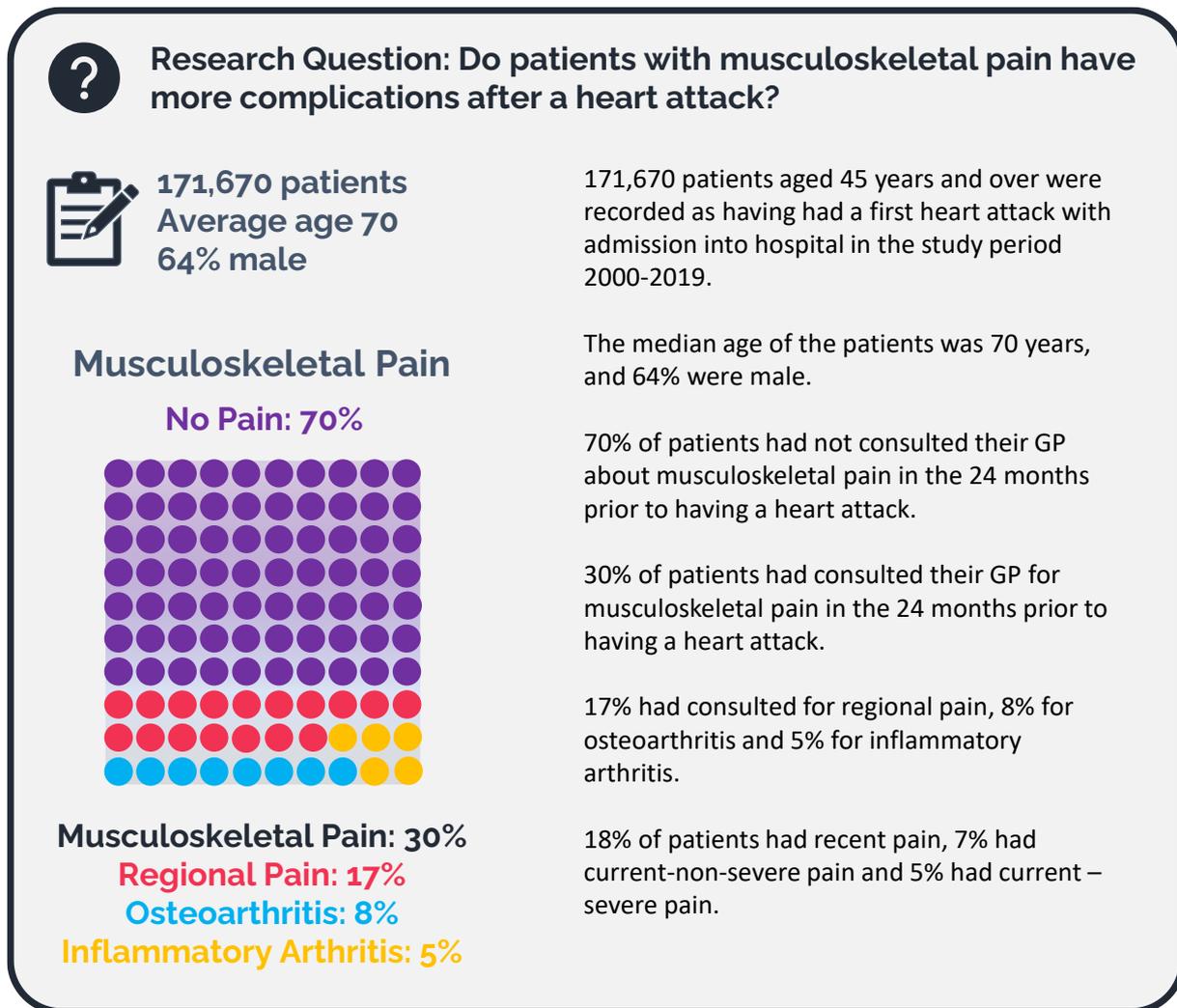
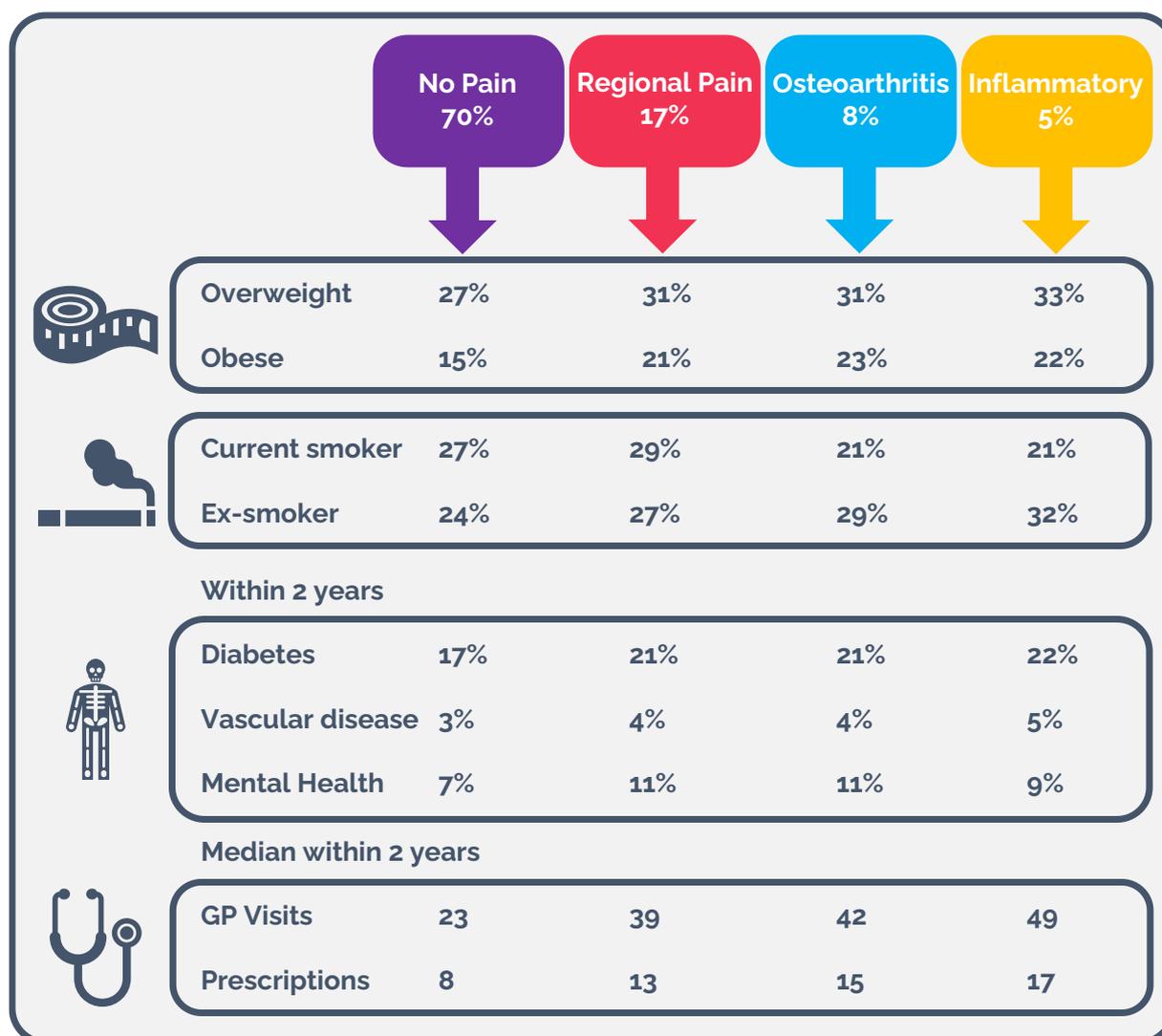


Figure 5. Lifestyle characteristics and frequency of other illnesses in heart attack patients by presence of musculoskeletal pain

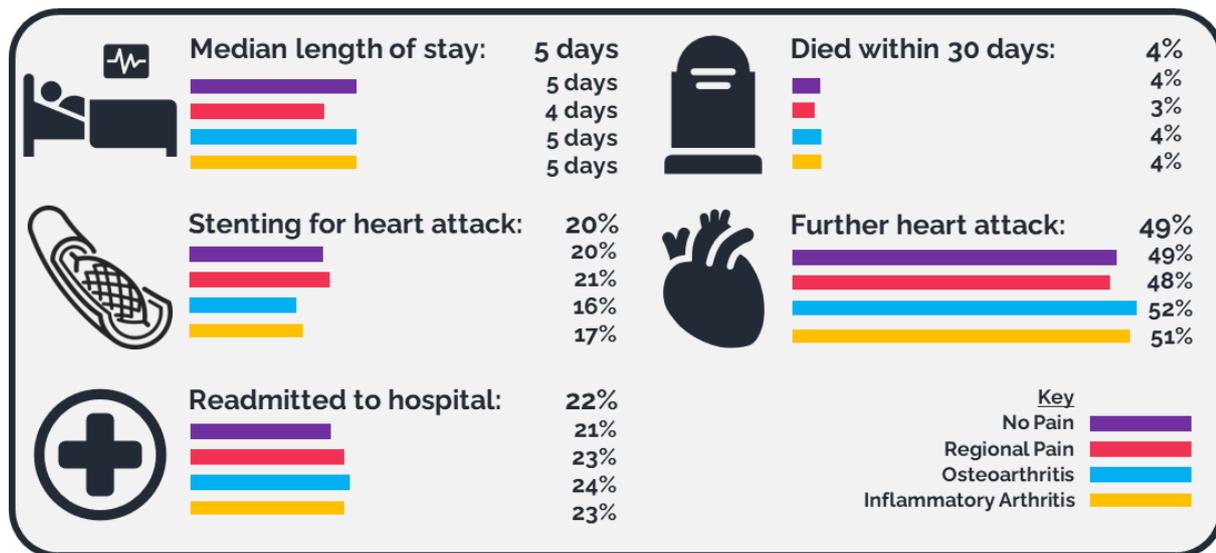


Patients consulting with musculoskeletal pain were more likely to be overweight or obese compared to patients that had had not consulted their GP about musculoskeletal pain in the 24 months prior to having a heart attack as shown in Figure 5.

There were differences in smoking status between those with and without musculoskeletal pain with a higher proportion of patients with inflammatory arthritis being ex-smokers and a higher proportion of those with regional pain recorded as current smokers.

Patients consulting with musculoskeletal pain were more likely to have had other health problems, including diabetes and mental health conditions, and had a much higher average (median) number of GP visits and different medicines prescribed in the 24 months before their heart attack than those with no musculoskeletal pain.

Figure 6. Summary of outcomes for the heart attack patients grouped by the presence of musculoskeletal pain



Unadjusted results

- Patients were followed in their records for a median of 4.6 years.
- The average (median) length of stay in hospital after a heart attack was 5 days. Patients with inflammatory arthritis and osteoarthritis had slightly longer stays compared to those with no musculoskeletal pain.
- The proportion of people having to go back into hospital within 30 days of the initial stay for the heart attack were slightly higher for all musculoskeletal pain groups compared to those without musculoskeletal pain (Figure 6).

- Patients in all musculoskeletal pain groups had an increased risk of having a further heart attack, highest for those with inflammatory arthritis (rate 146 per 1,000 person years), compared to those without musculoskeletal pain (rate 113 per 1,000 person years).
- A slightly higher proportion of patients with inflammatory arthritis died within 30 days (4.3%) compared to those without musculoskeletal pain (3.7%).
- Future (long-term) rates of dying from any cause was higher for patients with musculoskeletal pain with the highest rates for osteoarthritis (incidence rate 77 per 1,000 person years) and particularly inflammatory arthritis (incidence rate 92 per 1,000 person years) compared to those without musculoskeletal pain (incidence rate 61 per 1,000 person years).

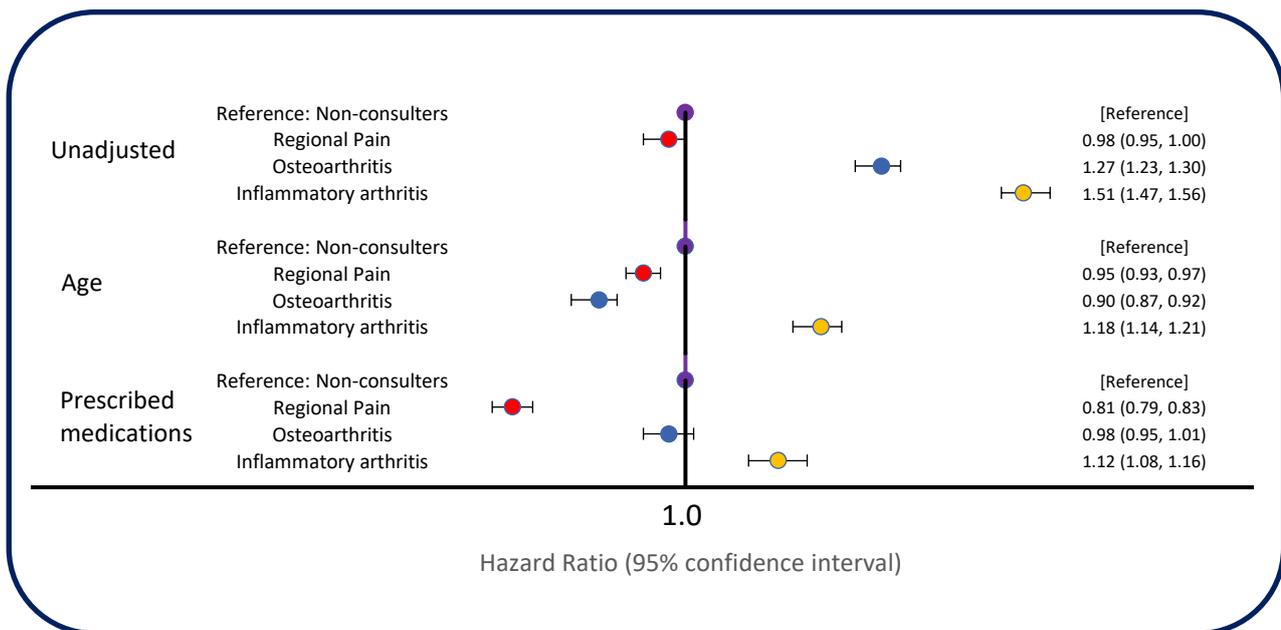
Adjusting for covariates

- When we adjusted for the patients' other characteristics, most of these characteristics had no impact on the association of muscle and joint pain with outcomes i.e., the relationships described above remained even after taking these other characteristics into account.
- However, two characteristics did have an impact:
 - AGE – patients with musculoskeletal pain were older and this explained some of the differences in outcomes between those with and without musculoskeletal pain.
 - PRESCRIBED MEDICATIONS - patients with musculoskeletal pain had been prescribed more medicine and this also explained some of the differences in outcomes.
- After adjustment there was an increased risk of readmission within 30 days of discharge for patients with regional pain, and an increased risk of further heart attack and of death in the long-term for patients with inflammatory conditions when compared to patients who did not consult for musculoskeletal pain.

- There were no increased risks for other patient outcomes (death in the short-term or length of hospital stay) for any type of musculoskeletal pain compared to those with no musculoskeletal pain.

An example of the impact of adjusting for age and prescribed medications on risk of long-term death for those with musculoskeletal pain compared to those without musculoskeletal pain is shown in Figure 7.

Figure 7. A plot showing the long-term risk of death in patients that had had a heart attack by groups of musculoskeletal pain unadjusted and after adjustment for i) age and ii) number of prescribed medications



Management outcomes

- A lower percentage of those with osteoarthritis or inflammatory arthritis underwent stenting than those without musculoskeletal pain (Figure 6), however patients who had regional musculoskeletal pain were slightly more likely to have stenting even after adjustment for other factors.
- The strongest associations with medicine were patients with regional pain having an increased likelihood of receiving dual anti-platelet or beta-blocker medicine, and those with inflammatory arthritis having an increased likelihood of being prescribed anti-coagulant medicine.

Secondary analysis

- When we examined musculoskeletal pain by how recent and severe it was rather than by type, patients with current-severe pain had increased risk of going back into hospital. They also had the highest rate of further heart attack and long-term mortality
- However, there were no increased risks of any patient outcome with musculoskeletal pain (by recency/severity) after adjustment for other factors
- Patients in all three musculoskeletal pain groups had an increased adjusted likelihood of receiving dual anti-platelet or beta-blocker medicine.

What the evidence tells us about musculoskeletal pain and stroke

Figure 8. Summary of characteristics of patients in the stroke cohort

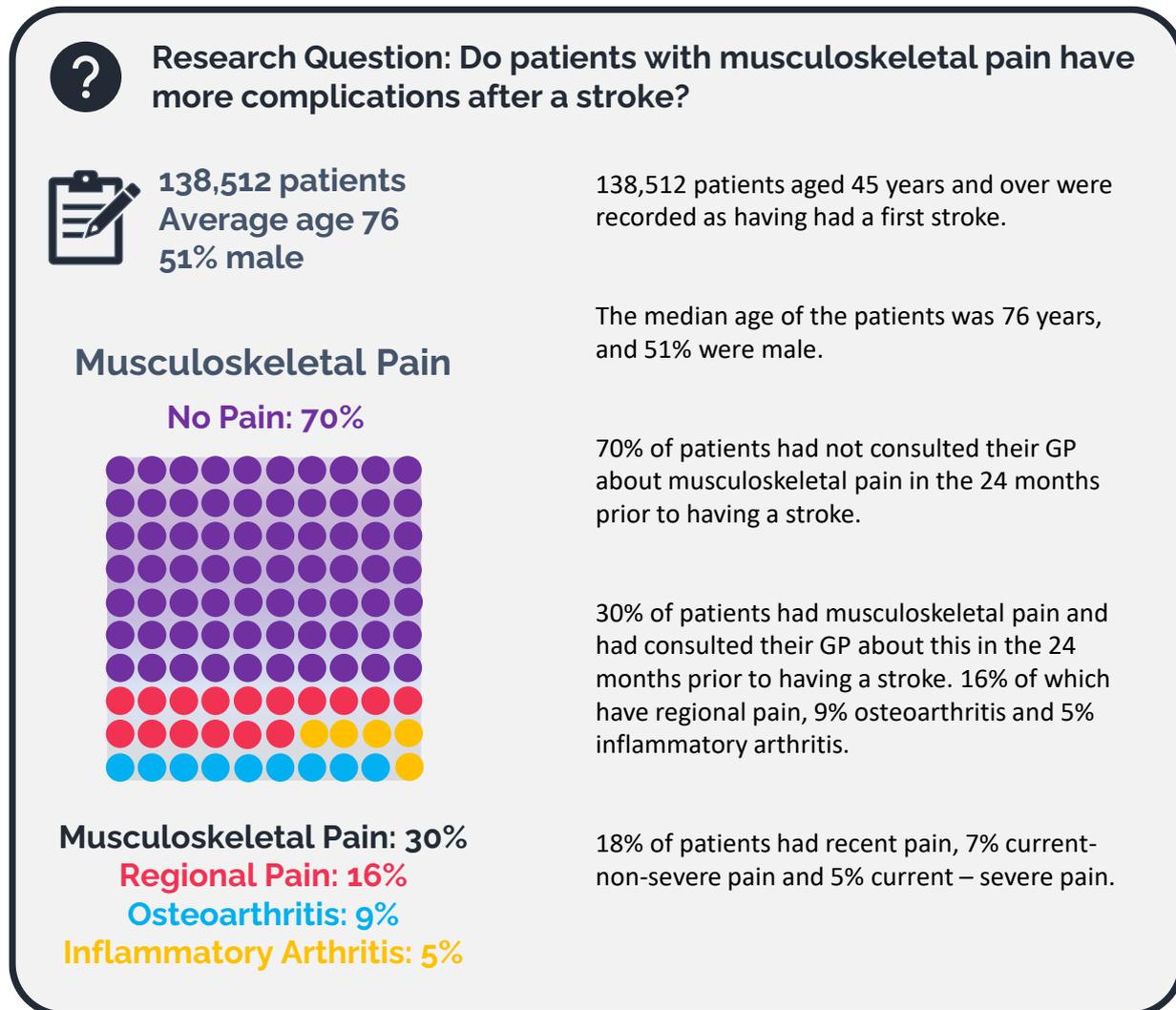
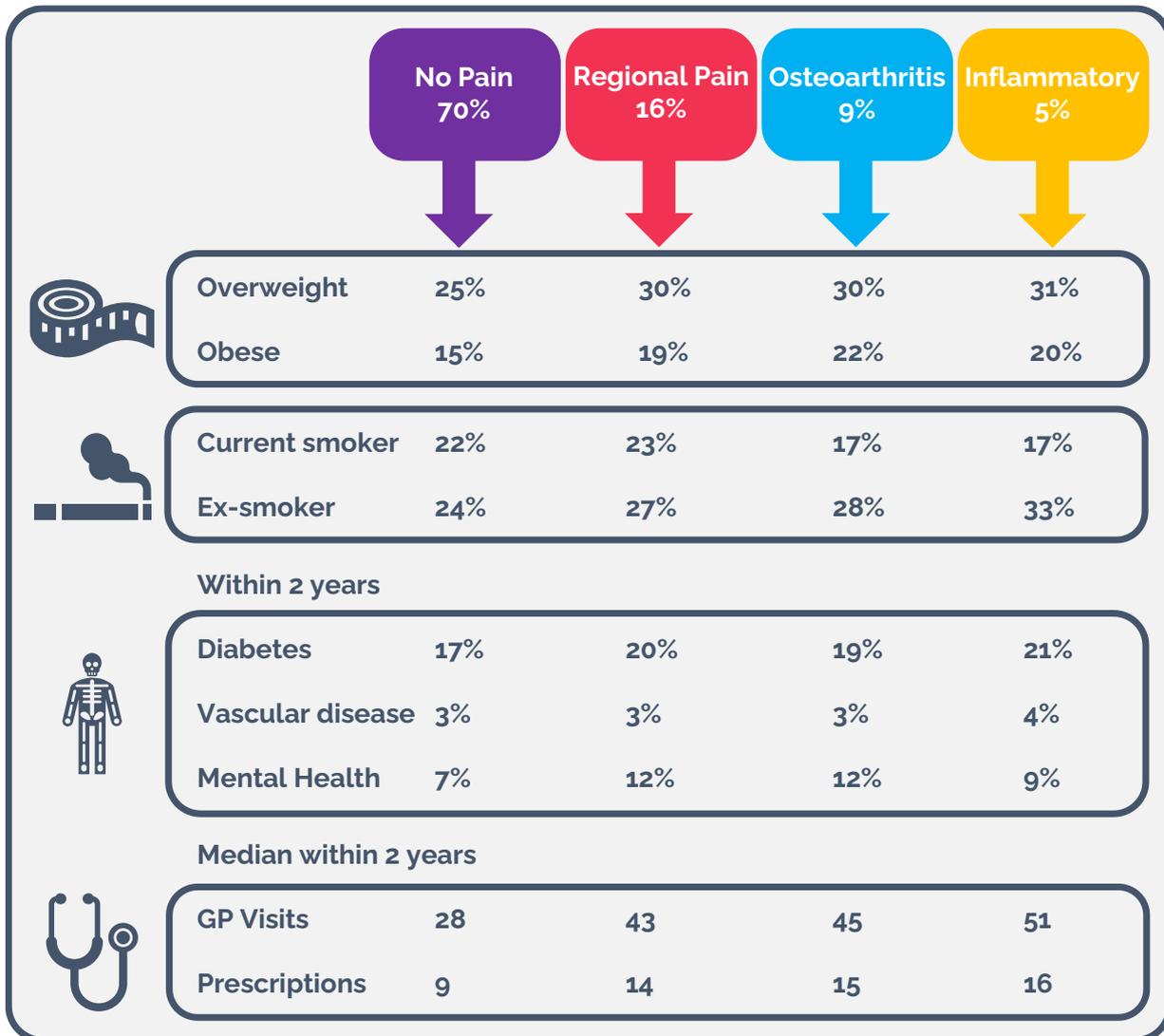
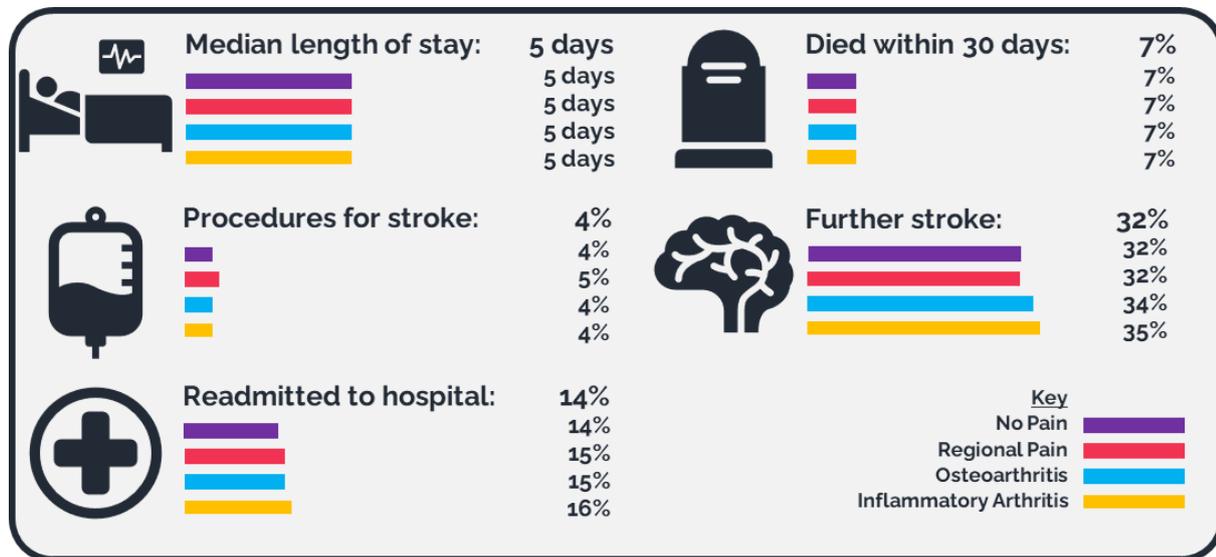


Figure 9. Lifestyle characteristics and frequency of other illnesses in stroke patients by presence of musculoskeletal pain



Lifestyle and other illnesses followed the same pattern as for heart attack. Patients consulting with musculoskeletal pain were more likely to be overweight or obese, were more likely to have diabetes or mental health conditions and had a higher median numbers of GP visits and prescriptions as shown in Figure 9.

Figure 10. Summary of outcomes for the stroke patients grouped by the presence of musculoskeletal pain



Unadjusted results

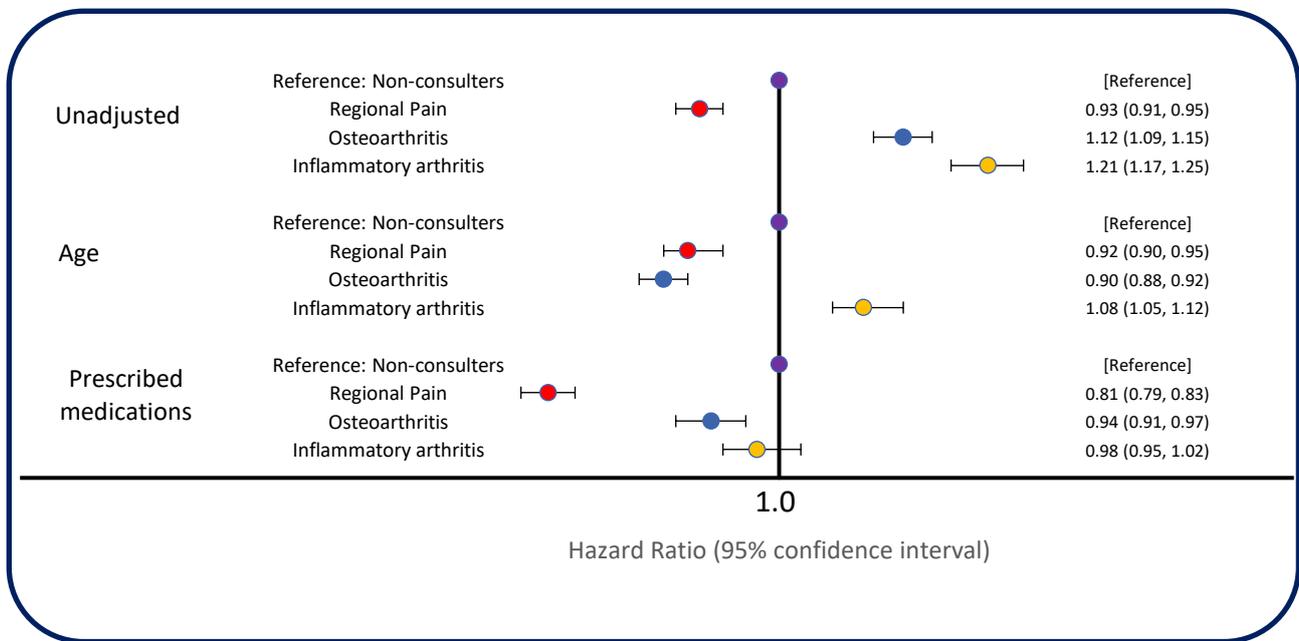
- Patients were followed in their records for a median of 3.2 years.
- The average (median) length of stay in hospital after a stroke was 5 days and this was similar in those with and without musculoskeletal pain.
- In patients that had a stroke, the risk of readmission into hospital were higher in all three groups with musculoskeletal pain compared to those that did not have musculoskeletal pain (Figure 10).
- Patients with musculoskeletal pain had higher rates of a further stroke and were highest for those with osteoarthritis (incidence rate 84 per 1,000 person years) and inflammatory arthritis (incidence rate 91 per 1,000 person years), compared to patients with no musculoskeletal pain (incidence rate 72 per 1,000 person years).

- In total, 7% of patients died after a stroke while in hospital or within 30 days of leaving hospital, and this was similar in those with and without musculoskeletal pain (Figure 10).
- However, there was an increased risk of longer-term mortality in patients with musculoskeletal pain for osteoarthritis (incidence rate 106 per 1,000 person years) and inflammatory arthritis (incidence rate 114 per 1,000 person years) compared to patients without musculoskeletal pain (incidence rate 95 per 1,000 person years).

Adjusting for covariates

- When we adjusted for the patients' other characteristics, most of these characteristics had no impact on the association of muscle and joint pain with outcomes i.e., the relationships described above remained even after taking these other characteristics into account.
- However, two characteristics had an impact:
 - AGE – patients with musculoskeletal pain were older and this explained some of the differences in outcomes between those with and without musculoskeletal pain.
 - PRESCRIBED MEDICATION - patients with musculoskeletal pain had been prescribed more medicine and this also explained some of the differences in outcomes.
- Rates of outcomes also improved for patients with musculoskeletal pain in more recent index years.
- The higher risk of readmission to hospital for patients with musculoskeletal pain was no longer evident after adjusting for number of prescribed medicines.
- The increased longer-term risk of further stroke or mortality for patients with musculoskeletal pain was also reduced after adjusting for age and number of prescribed medicines. This is shown for mortality in Figure 11.

Figure 11. A plot showing the risk of long-term death in patients that had had a stroke by groups of musculoskeletal pain unadjusted and after adjustment for i) age and ii) number of prescribed medications



Management outcomes

- There was an increased likelihood of having a procedure for stroke in patients with regional pain compared to those with no musculoskeletal pain.
- Patients with inflammatory conditions were more likely to be prescribed anti-coagulant medicine and those with regional pain and osteoarthritis were more likely to be prescribed anti-platelet medicines when compared to those without musculoskeletal pain after adjustment for other factors.

Secondary analysis

- When we examined musculoskeletal pain by how recent and severe it was rather than by type, patients with current-severe pain had an increased adjusted risk of going back into hospital.
- When we examined musculoskeletal pain by how recent and severe it was, rather than by type, patients with current pain that was severe had higher rates of anti-platelet medicines that remained after adjustment for other factors.

What the evidence tells us about musculoskeletal pain and cancer

Figure 12. Summary of characteristics of patients in the cancer cohort

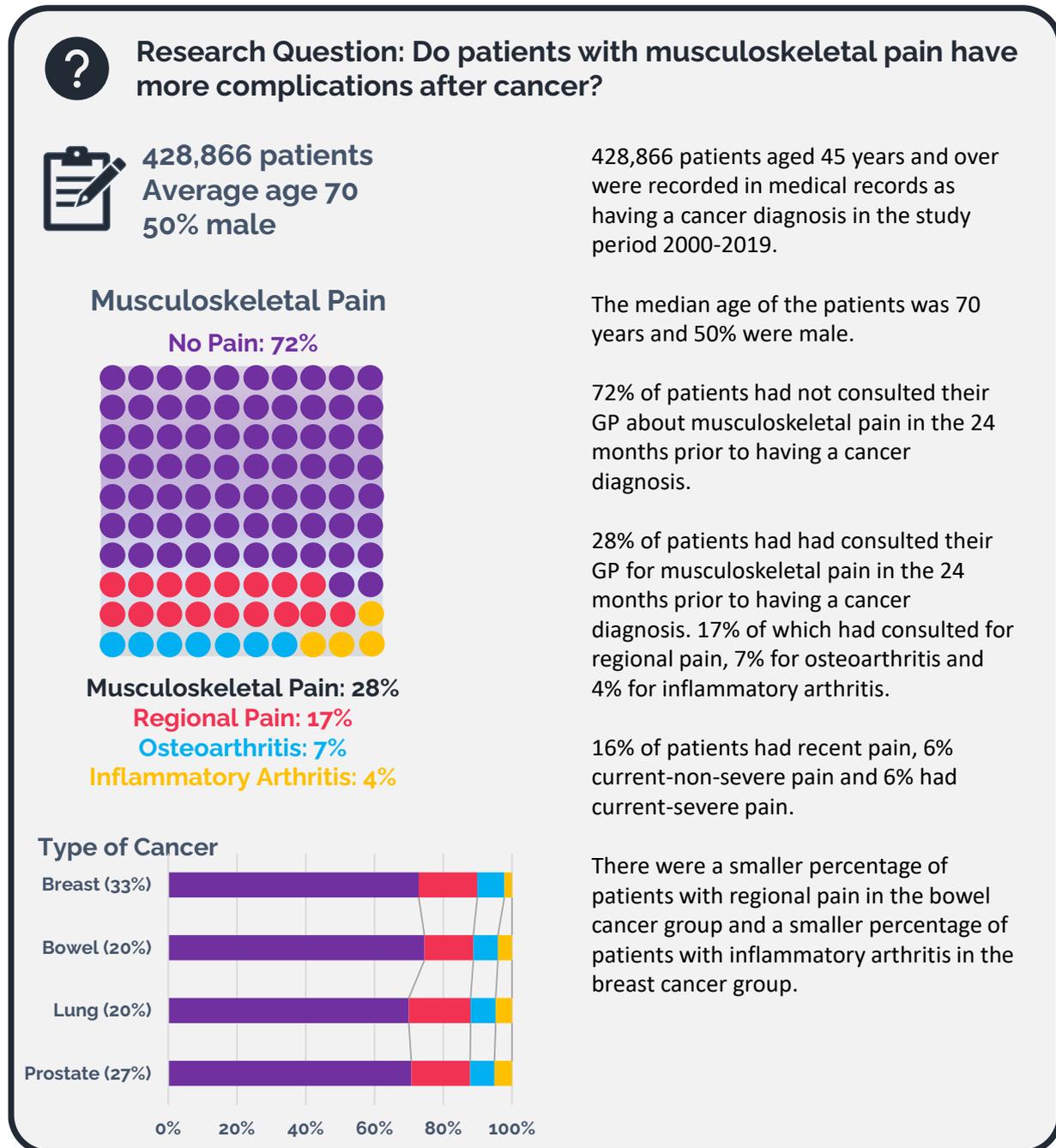
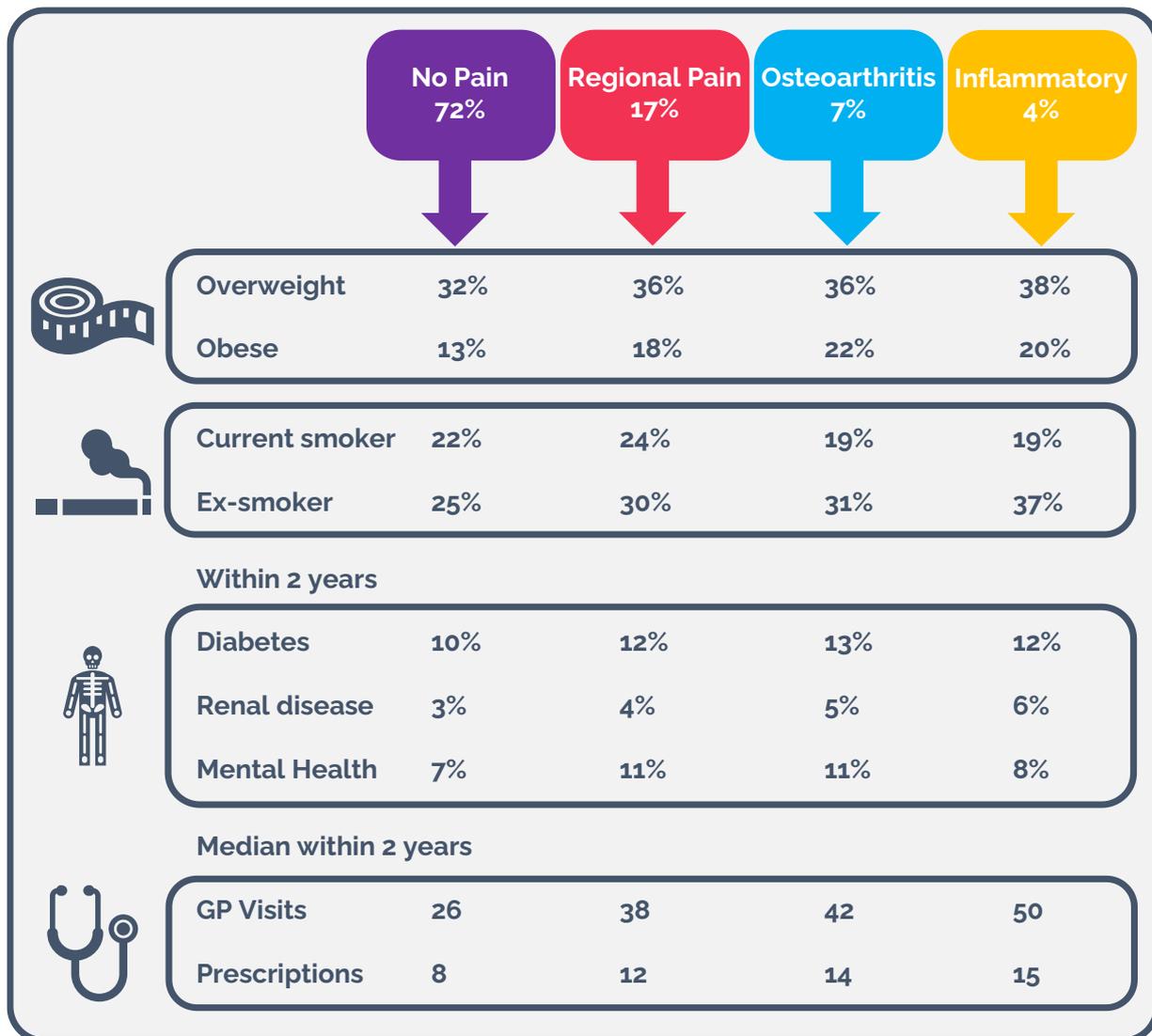


Figure 13. Lifestyle characteristics and frequency of other illnesses in cancer patients by presence of musculoskeletal pain

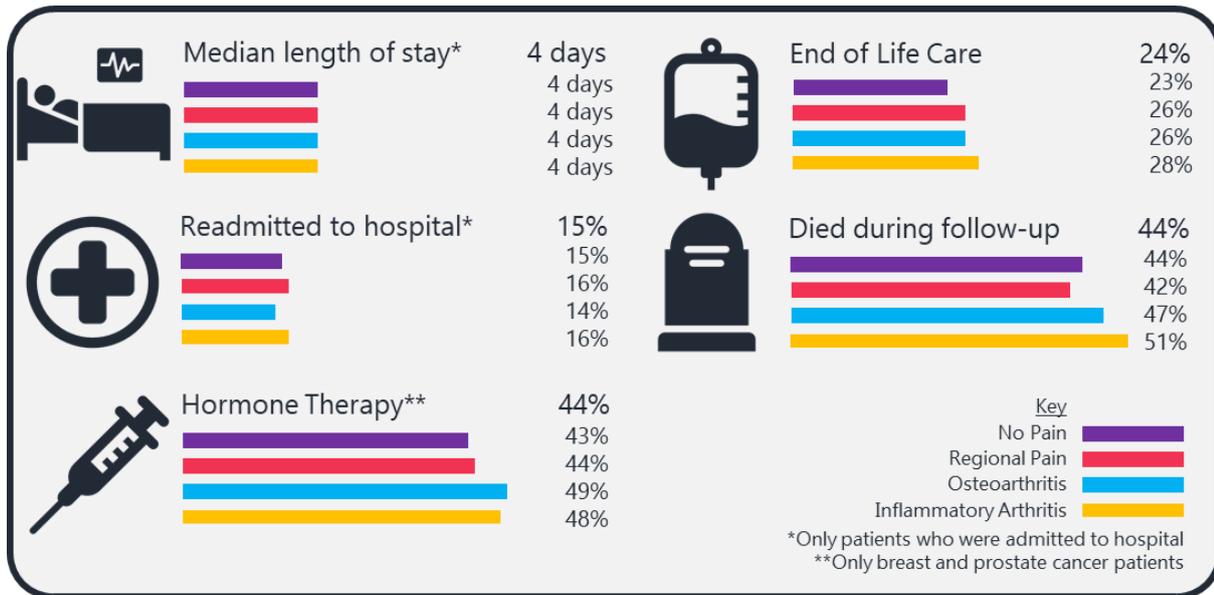


Similar to patients with heart attack and stroke, patients with newly diagnosed cancer who had consulted with musculoskeletal pain were more likely to be overweight or obese compared to patients that had had not consulted their GP about musculoskeletal pain in the 24 months prior to being diagnosed with cancer as shown in Figure 13.

By contrast to the patients with heart attack or stroke, there were smaller differences in having other health conditions between those with and without musculoskeletal pain in patients with cancer.

However, patients consulting with musculoskeletal pain had a much higher number of GP visits and prescriptions than those with no musculoskeletal pain.

Figure 14. The key findings for the cancer patients grouped by the presence of musculoskeletal pain



Unadjusted results

- Patients were followed in their records for a median of 3.3 years.
- Patients with musculoskeletal pain were more likely to be admitted into hospital sooner compared to those with no musculoskeletal pain during the follow-up period.
- Individuals with osteoarthritis and inflammatory pain had longer length of stay in hospital for first hospitalisation, and likelihood of readmission in the 30 days after discharge was higher for patients with musculoskeletal pain

- Patients with all three types of musculoskeletal pain were more likely to receive earlier end of life care compared to those with no musculoskeletal pain during the follow-up period (Figure 14). We also found this was the case across all types of cancer.
- Patients with inflammatory arthritis (rates 186 per 1,000 person years), osteoarthritis (rates 164 per 1,000) or regional pain (160 per 1,000 person years) had increased rates of mortality compared to those without musculoskeletal pain (145 per 1,000 person years).

Adjusting for covariates

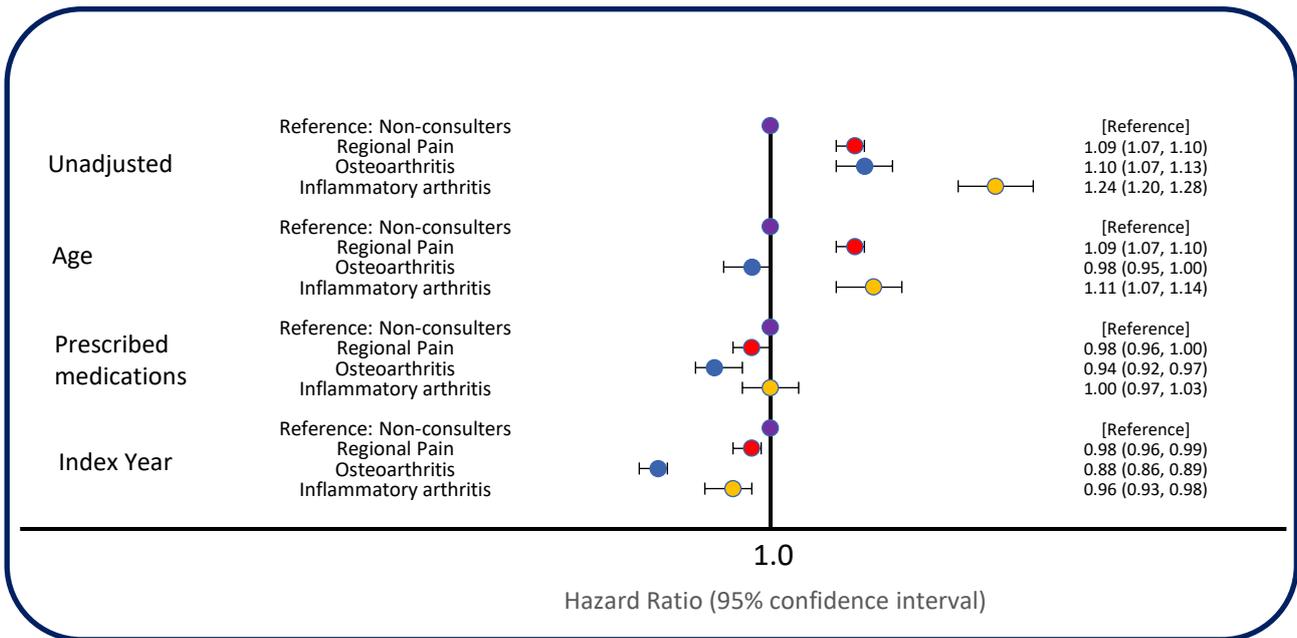
- After adjustment for other factors, patients with regional pain were more likely to receive end of life care.
- After adjustment for age, the number of medications prescribed, or year of diagnosis there no increased risk of mortality for any musculoskeletal group compared to those with no musculoskeletal pain (Figure 15). The only exception to this was for lung and prostate cancer where patients with regional pain were slightly more likely to die compared to those with no musculoskeletal pain.
- Increased rates of hospitalisation were not seen after adjustment for number of medicines, but an increased risk of readmission was observed for those with regional pain and inflammatory arthritis.

Management outcomes

- Patients with breast cancer and osteoarthritis or inflammatory arthritis were more likely to be prescribed hormone modulation therapy, although the increased likelihood did not persist after adjustment for other factors.

- There was an increased likelihood of having hormone modulation therapy for prostate cancer in patients with musculoskeletal pain compared to those with no musculoskeletal pain, which remained for patients with regional pain after adjustment for age and other covariates.

Figure 15. A plot showing the risk of death in patients that had had cancer by groups of musculoskeletal pain unadjusted and after adjustment for year of diagnosis



Secondary analysis

- When looking by recency and severity of pain rather than type, those with current and severe pain had increased rates of hospitalisation, readmission, palliative care, and death, which remained after adjusting for covariates
- Patients with current and severe pain were more likely to receive hormone modulation therapy for breast and prostate cancer, with the increased risk persisting after adjustment for those with prostate cancer.

What the evidence tells us about musculoskeletal pain and dementia

Figure 16. Summary of characteristics of patients in the dementia cohort

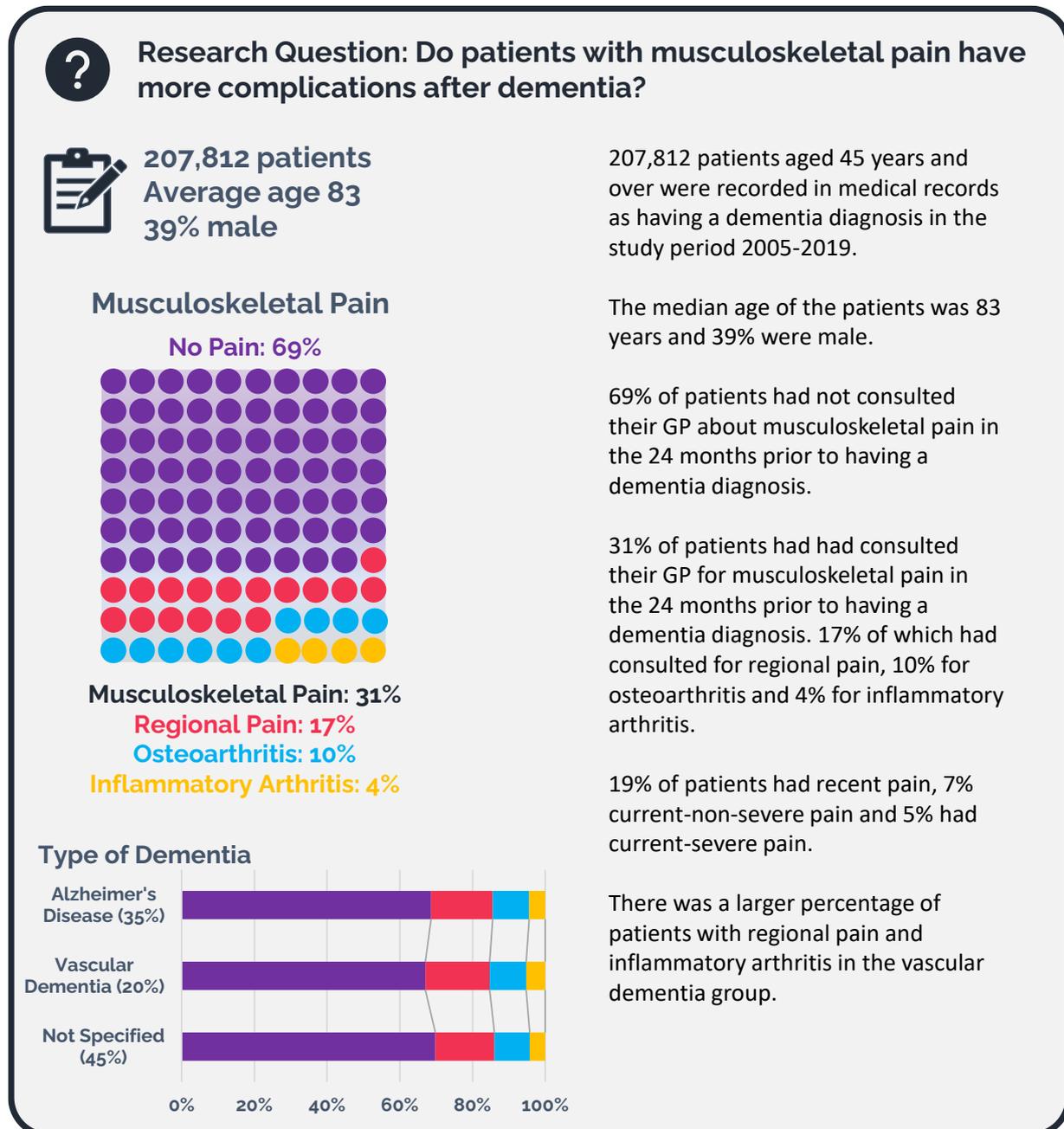
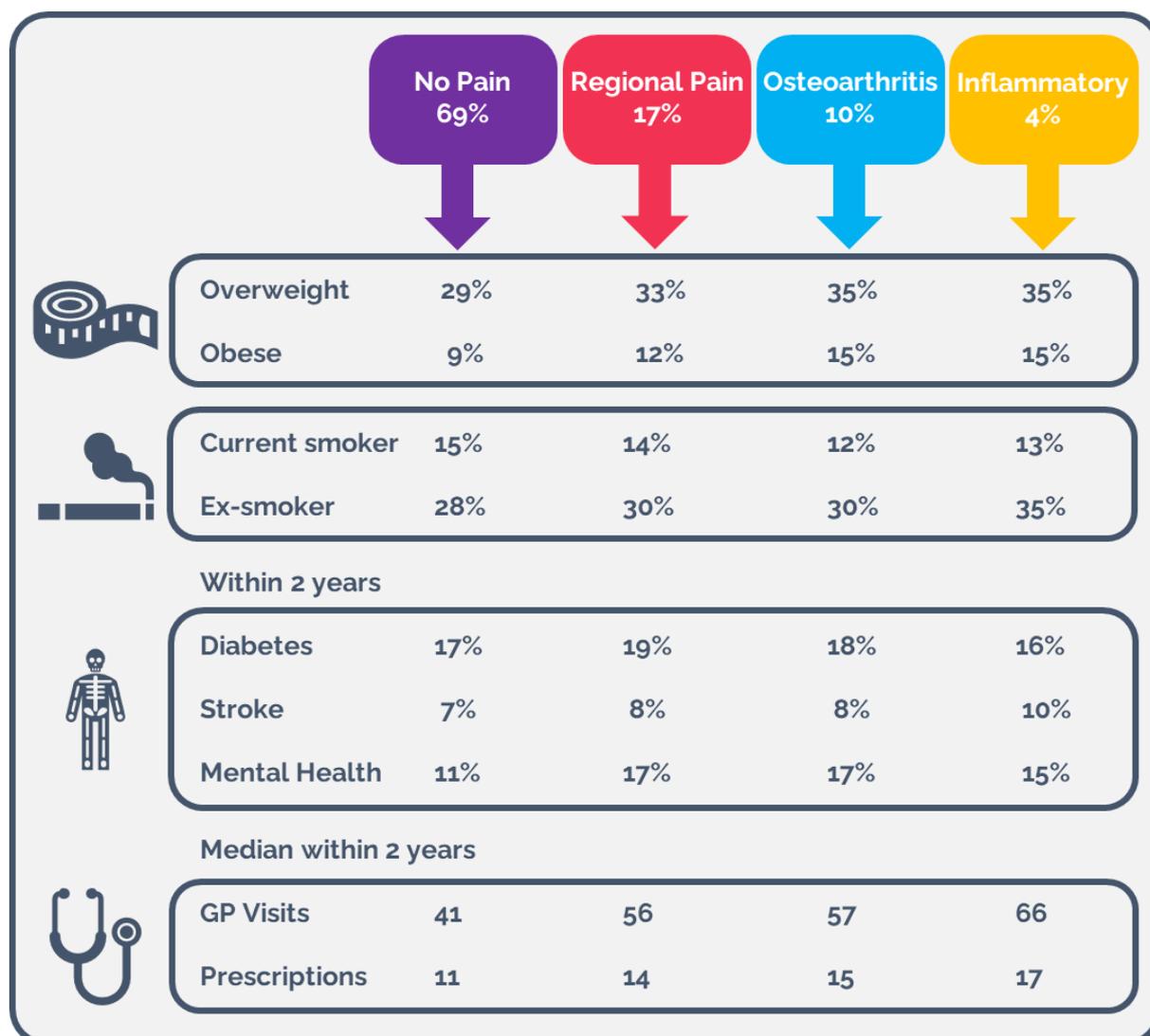


Figure 17. Lifestyle characteristics and frequency of other illnesses in dementia patients by presence of musculoskeletal pain

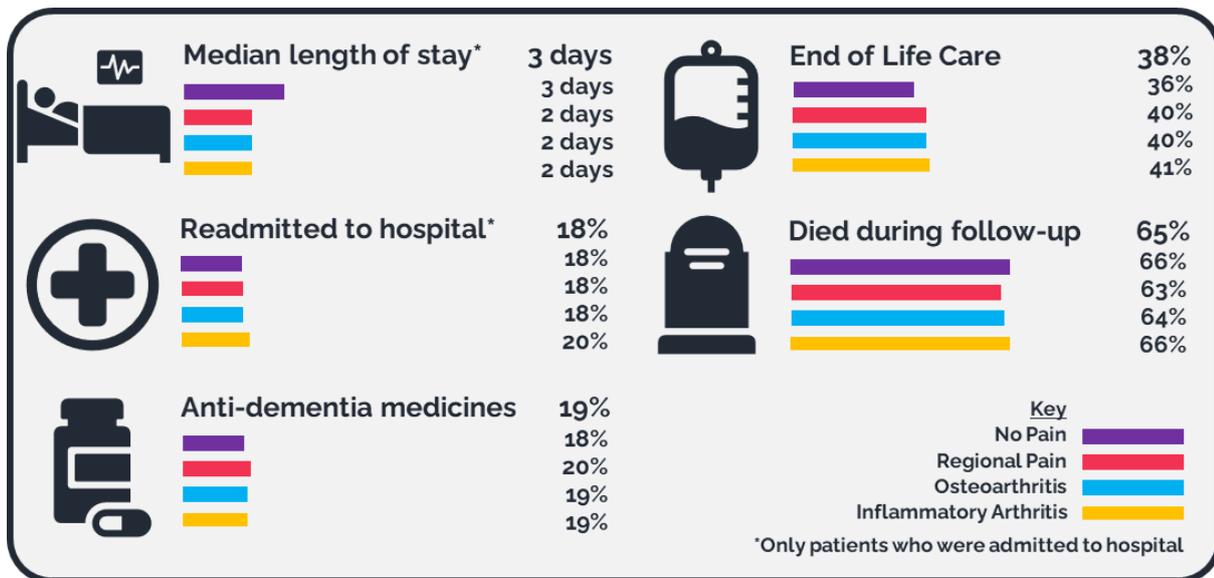


Patients diagnosed with dementia who had consulted with musculoskeletal pain were more likely to be overweight or obese compared to patients that had had not consulted their GP about musculoskeletal pain in the 24 months prior to being diagnosed with dementia as shown in Figure 17.

There were small differences in diabetes or stroke comorbidity between those with and without musculoskeletal pain in patients with dementia, although having a mental health condition was more common in those with musculoskeletal pain.

Patients diagnosed with dementia consulting with musculoskeletal pain had a much higher number of GP visits and prescriptions than those with no musculoskeletal pain.

Figure 18. Summary of outcomes for patients diagnosed with dementia grouped by the presence of musculoskeletal pain



Unadjusted results

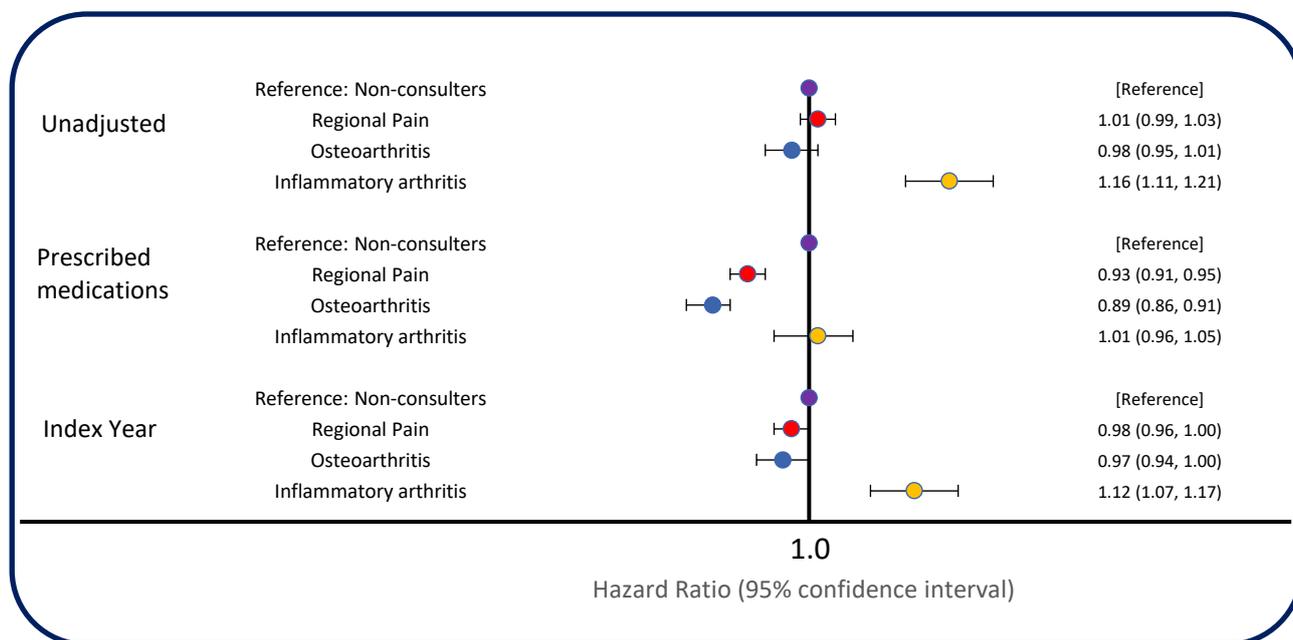
- Patients were followed in their records for a median of 4.6 years.
- Patients with all types of musculoskeletal pain were more likely to be admitted to hospital sooner compared to those with no musculoskeletal pain, with those with inflammatory arthritis likely to be admitted into hospital the most quickly.
- A slightly high proportion of patients with inflammatory arthritis were readmitted to hospital within 30 days after discharge (Figure 18).
- Patients with inflammatory arthritis had the highest rates of end-of-life care (incidence rate 461 per 1,000 person years) compared to those who did not consult for musculoskeletal pain (incidence rate 428 per 1,000 person years).

- Patients with inflammatory arthritis were also more likely to die earlier (incidence rate 241 per 1,000 person years) compared to those with no musculoskeletal pain (incidence rate 222 per 1,000 person years).
- Patients with musculoskeletal pain were more likely to develop a new marker of dementia progression in the first year after diagnosis when compared to patients with no musculoskeletal pain.

Adjusting for covariates

- After adjustment for other factors, having osteoarthritis was independently associated with a small risk of being admitted into hospital sooner than individuals with no musculoskeletal pain.
- The increased risk of developing new markers of dementia progression for all musculoskeletal groups compared to those with no musculoskeletal pain persisted after adjustment.
- However, having musculoskeletal pain was not independently associated with increased risk of the other outcomes compared to those with no musculoskeletal pain.
- The main characteristics which seemed to explain the relationship found in the unadjusted analyses were:
 - PRESCRIBED MEDICATIONS - patients with musculoskeletal pain had been prescribed more medicine and this also explained some of the differences in outcomes.
 - INDEX YEAR – patients diagnosed with dementia more recently had improved outcomes.

Figure 19. A plot showing the risk of long-term death in patients that had been diagnosed with dementia by groups of musculoskeletal pain



Management outcomes

- Patients with musculoskeletal pain were more likely to be prescribed anti-dementia medicines in the 3 months following diagnosis. This increased likelihood remained for all musculoskeletal pain groups compared to no musculoskeletal pain after adjustment for other factors.

Secondary analysis

- When we examined by recency and severity of pain, having current-severe pain was associated with an increased rate of hospitalization after adjustment for covariates, and recent pain was associated with prescribed anti-dementia medicines.
- All musculoskeletal severity groups had increased risk of developing a new marker of progression in the first year after diagnosis.

What the evidence tells us about musculoskeletal pain and pneumonia

Figure 20. Summary of characteristics of patients in the pneumonia cohort

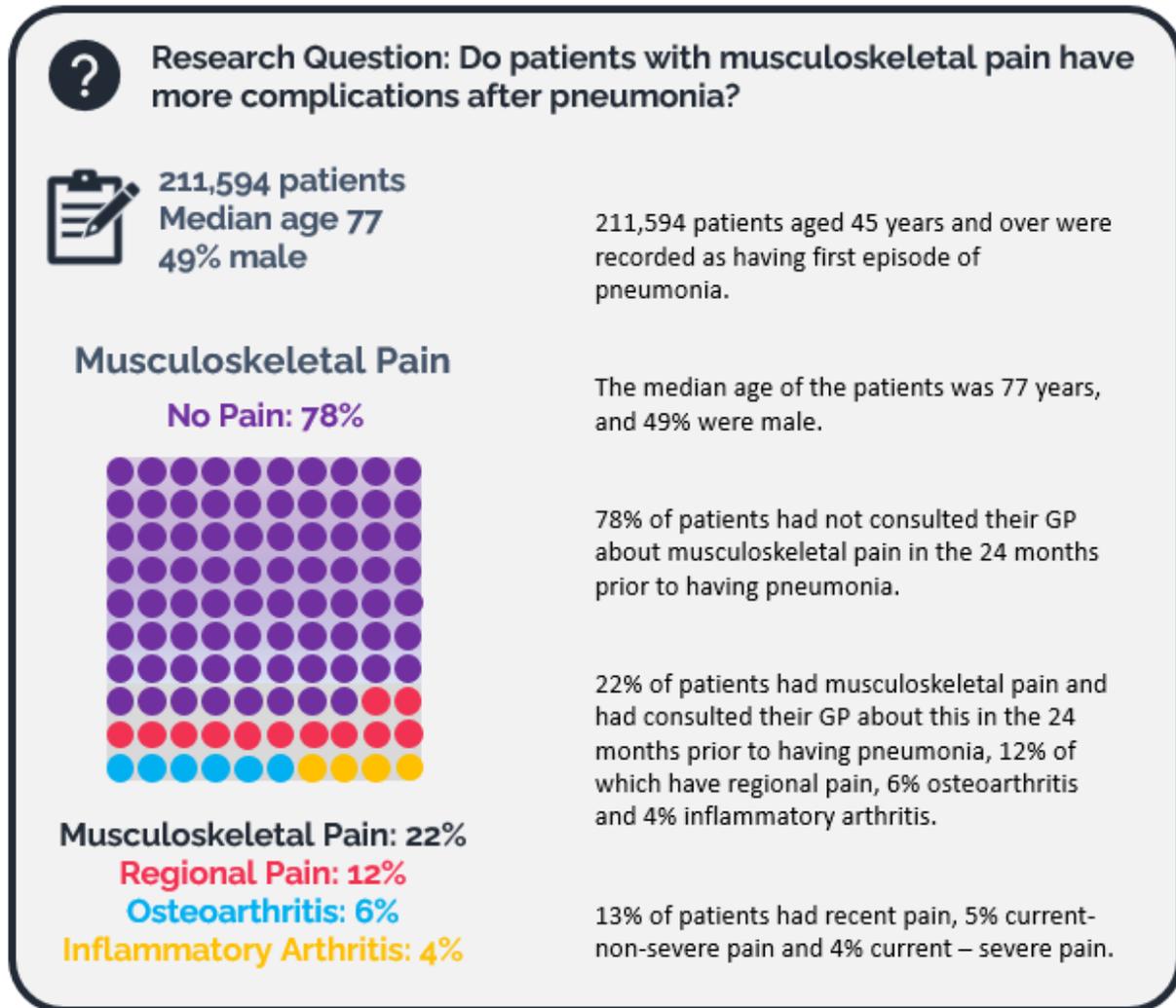
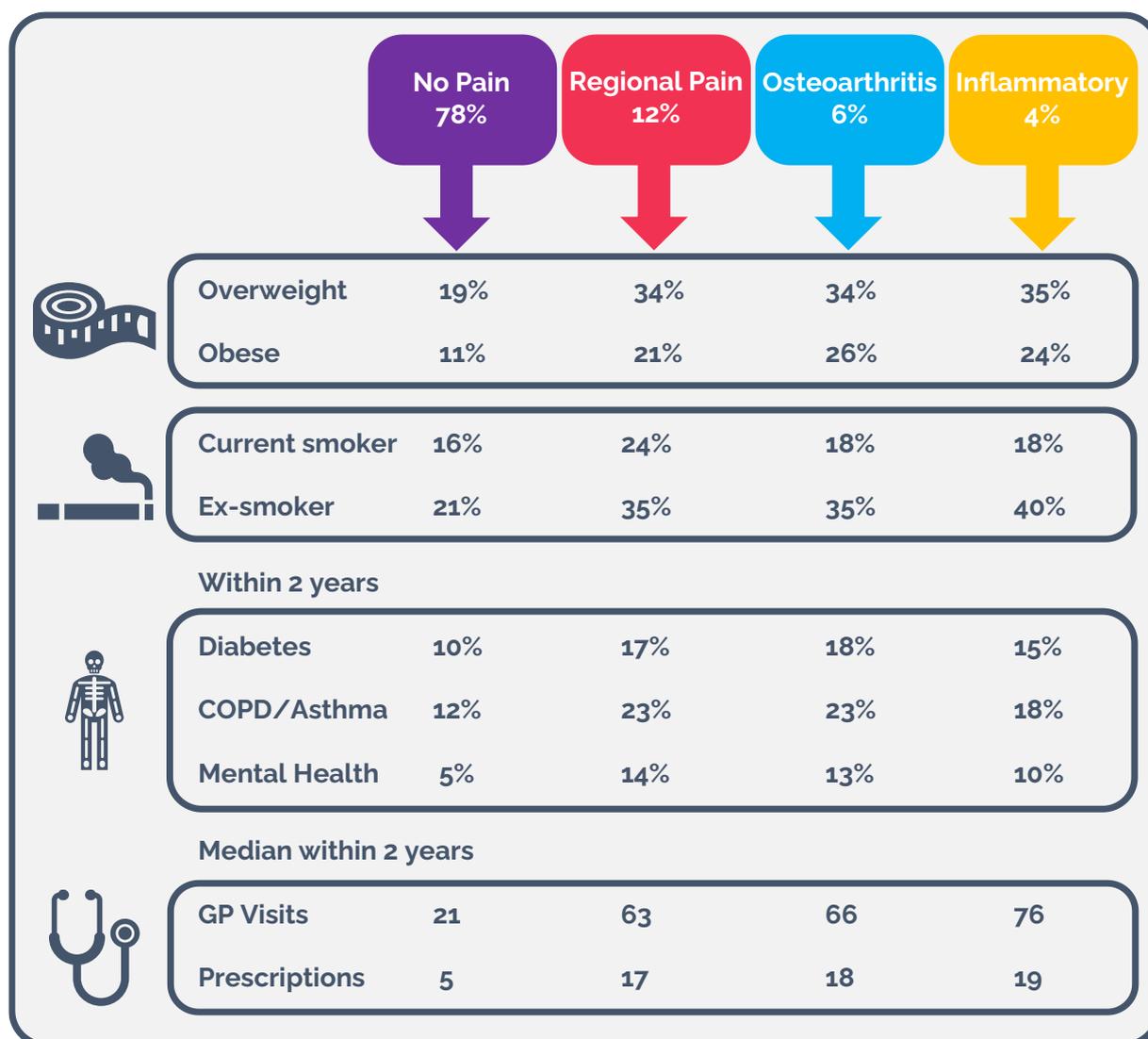


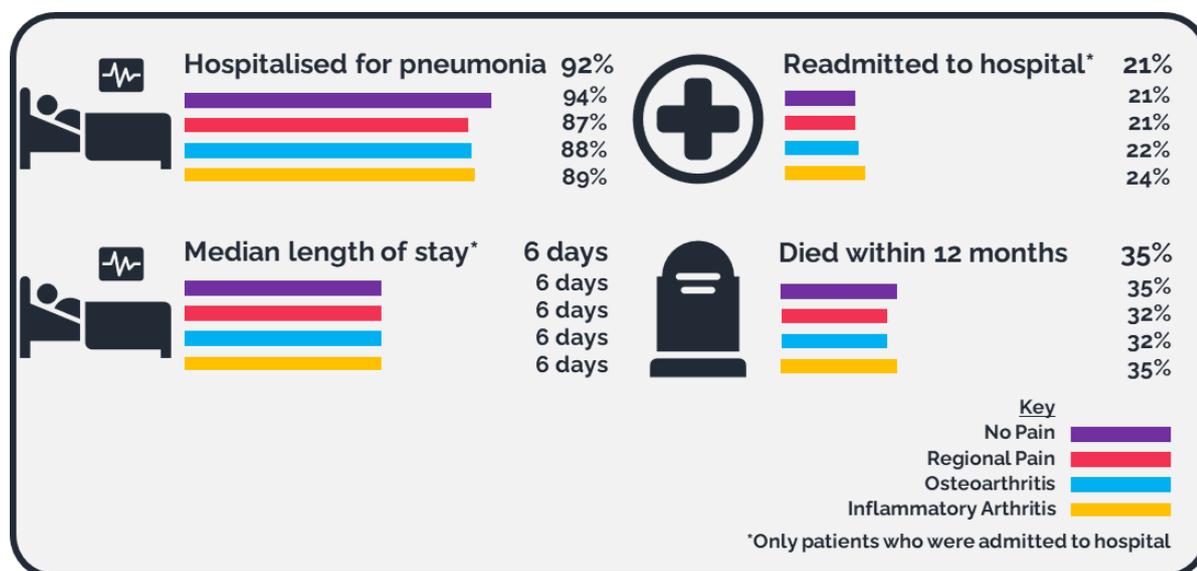
Figure 21. Lifestyle characteristics and frequency of other illnesses in pneumonia patients by presence of musculoskeletal pain



Patients with a new diagnosis of pneumonia who had consulted with musculoskeletal pain were more likely to be overweight or obese compared to patients that had had not consulted their GP about musculoskeletal pain in the 24 months prior to being diagnosed with pneumonia.

Patients consulting with musculoskeletal pain were more likely to have had other health conditions, including diabetes, chronic obstructive pulmonary disease (COPD) or severe asthma, and had higher numbers of GP visits and prescriptions as shown in Figure 21.

Figure 22. Summary of outcomes for patients diagnosed with pneumonia grouped by the presence of musculoskeletal pain



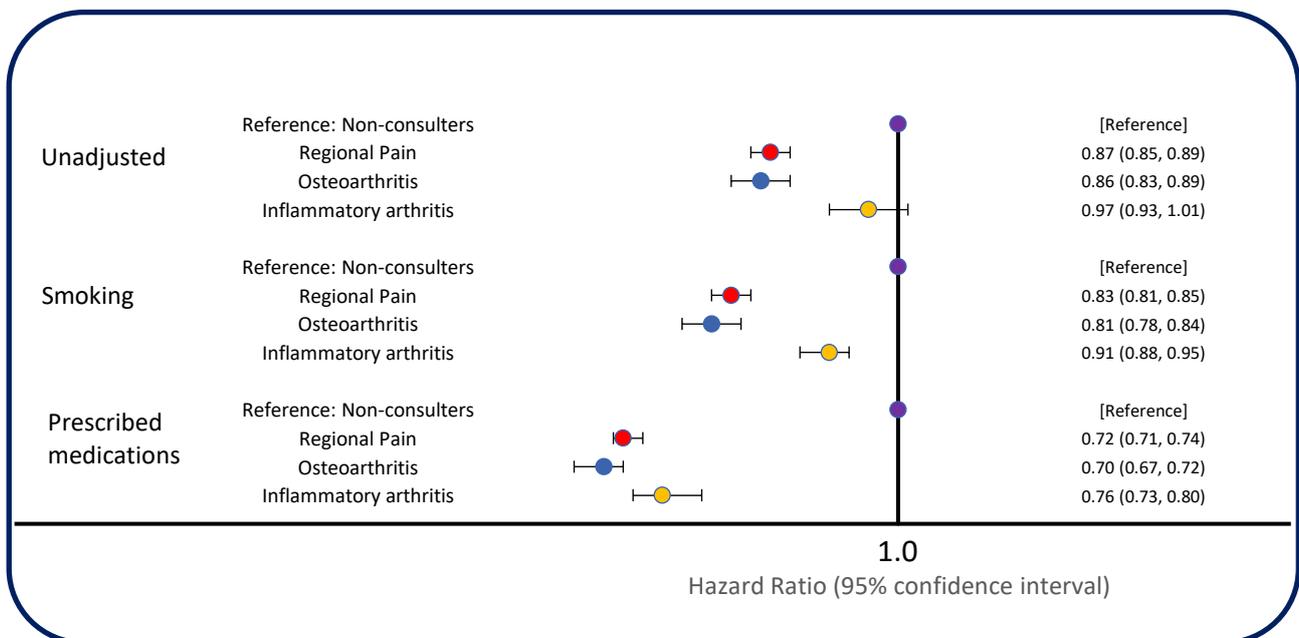
Unadjusted results

- Patients were followed in their records for an average of 4.5 years.
- In patients who were admitted to hospital, the length of admission was similar between patients with and without musculoskeletal pain (median 6 days) (Figure 22).
- However, patients with inflammatory arthritis were most likely to be readmitted to hospital within 30 days for any reason (24% vs 21% in those without musculoskeletal pain) (Figure 22).
- Patients with regional pain (incidence rate 105 per 1,000 persons) or osteoarthritis (incidence rate 107 per 1,000 persons) were less likely to die within 12 months of having pneumonia compared to those with inflammatory arthritis (incidence rate 125 per 1,000 persons) or no musculoskeletal pain (incidence rate 127 per 1,000 persons).

Adjusting for covariates

- The higher risk of readmission to hospital for patients with inflammatory arthritis was no longer evident after adjusting for smoking and the number of prescribed medications.
- There was a decreased risk of mortality at 12 months for patients with musculoskeletal pain after adjusting for age, smoking, and number of prescribed medications (Figure 23).

Figure 23. A plot showing the risk of long-term death in patients that had been diagnosed with pneumonia by groups of musculoskeletal pain unadjusted and after adjustment for i) age, ii) smoking status, and iii) number of prescribed medications



Secondary analysis

- When we examined by recency and severity of pain, people with current-severe pain had increased rates of readmission to hospital within 30 days for pneumonia which remained after adjustment

- However, no other associations remained after adjustment for age and the number of prescribed medications.

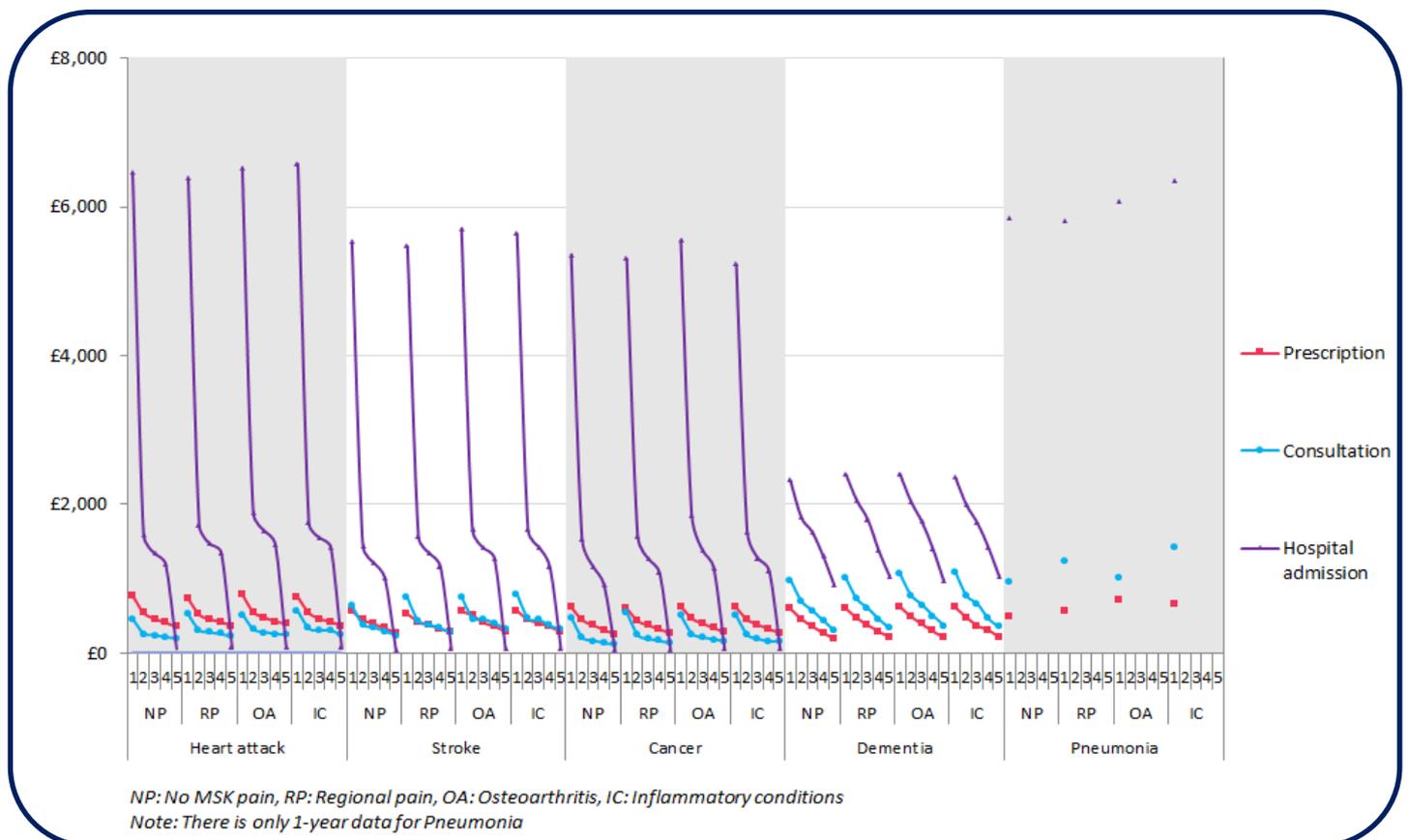
Moderation Analysis

- There was no evidence of a differing association of musculoskeletal pain with the outcomes by sex, age, deprivation, ethnicity, geographical region, or mental health consultation in any of the cohorts.

What the health economics analysis tells us

In general, patients across the illness cohorts had the highest health care costs during the first year of diagnosis and their economic costs decreased over time (Figure 24). This was driven by the high initial hospitalization rate and/or expensive procedures during the first year, which is especially noticeable for patients in the heart attack cohort (Figure 24). The main cost driver was hospital admissions.

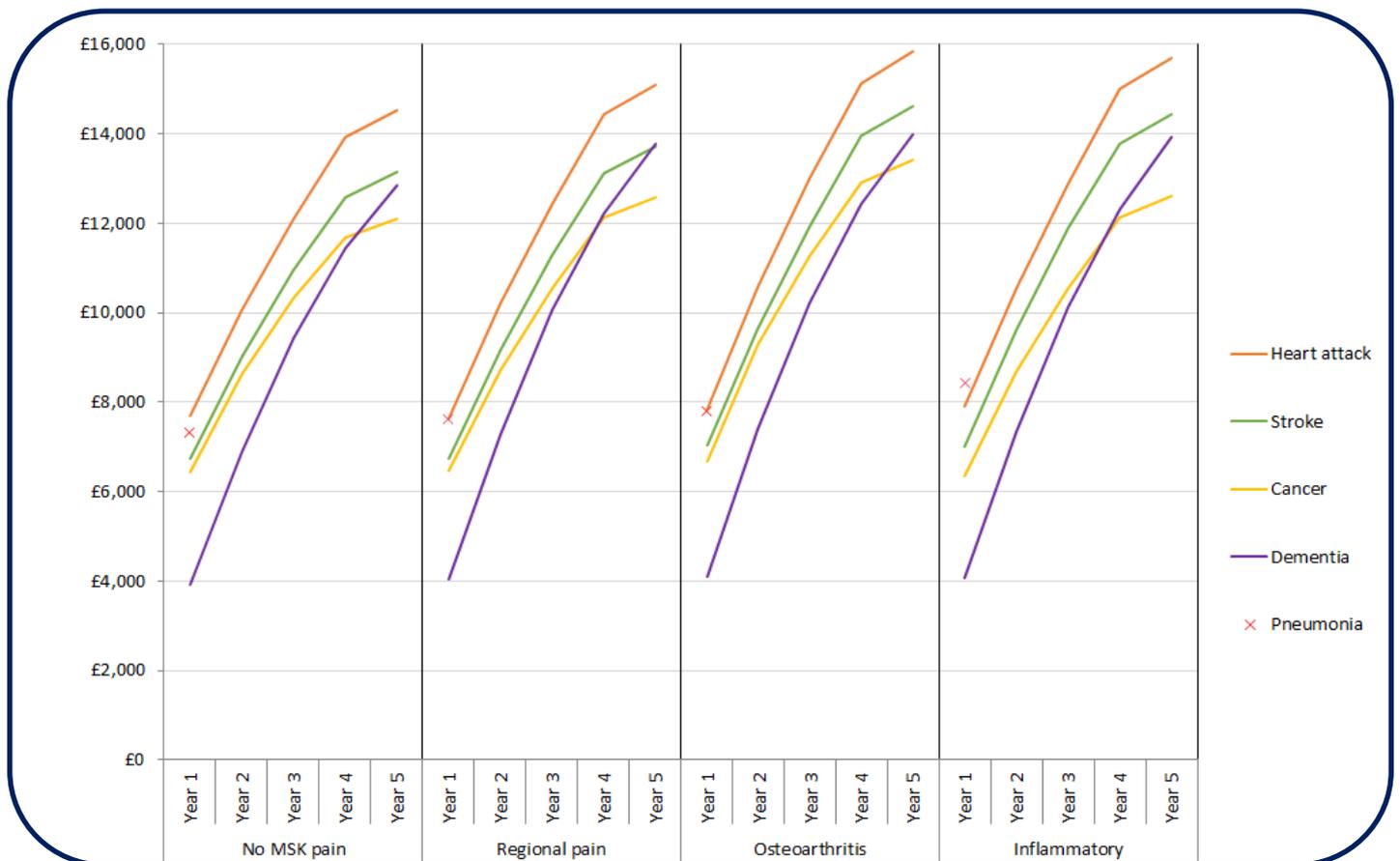
Figure 24. Adjusted mean cost of each resource category in each cohort over five years (one-year for the pneumonia cohort) (£, 2020/21 prices)



Patients with osteoarthritis in the heart attack, stroke, cancer, and dementia cohorts incurred the highest costs over five years while patients with inflammatory conditions in the pneumonia cohort incurred the highest costs in the first year after a diagnosis (Figure 25).

Overall, the patients in each cohort with musculoskeletal pain had a higher total cost than those without musculoskeletal pain. Patients with musculoskeletal pain in the heart attack cohort had around 4%-12% higher cost than those without musculoskeletal pain over five years (Figure 25). This value was around 6%-13% for stroke patients, 3%-30% for cancer patients, 8%-12% for dementia patients, and 2%-7% for pneumonia patients. This meant that patients with musculoskeletal pain were incurring around £339 to £1,250 more for their consultations, prescriptions, and hospital admissions than those without musculoskeletal pain over five years for heart attack, stroke, cancer, and the dementia cohorts; and around £167 to £785 over one year for the pneumonia cohort.

Figure 25. Adjusted cumulative mean total cost of each cohort over five years (one year for the pneumonia cohort) (£, 2020/21 prices)



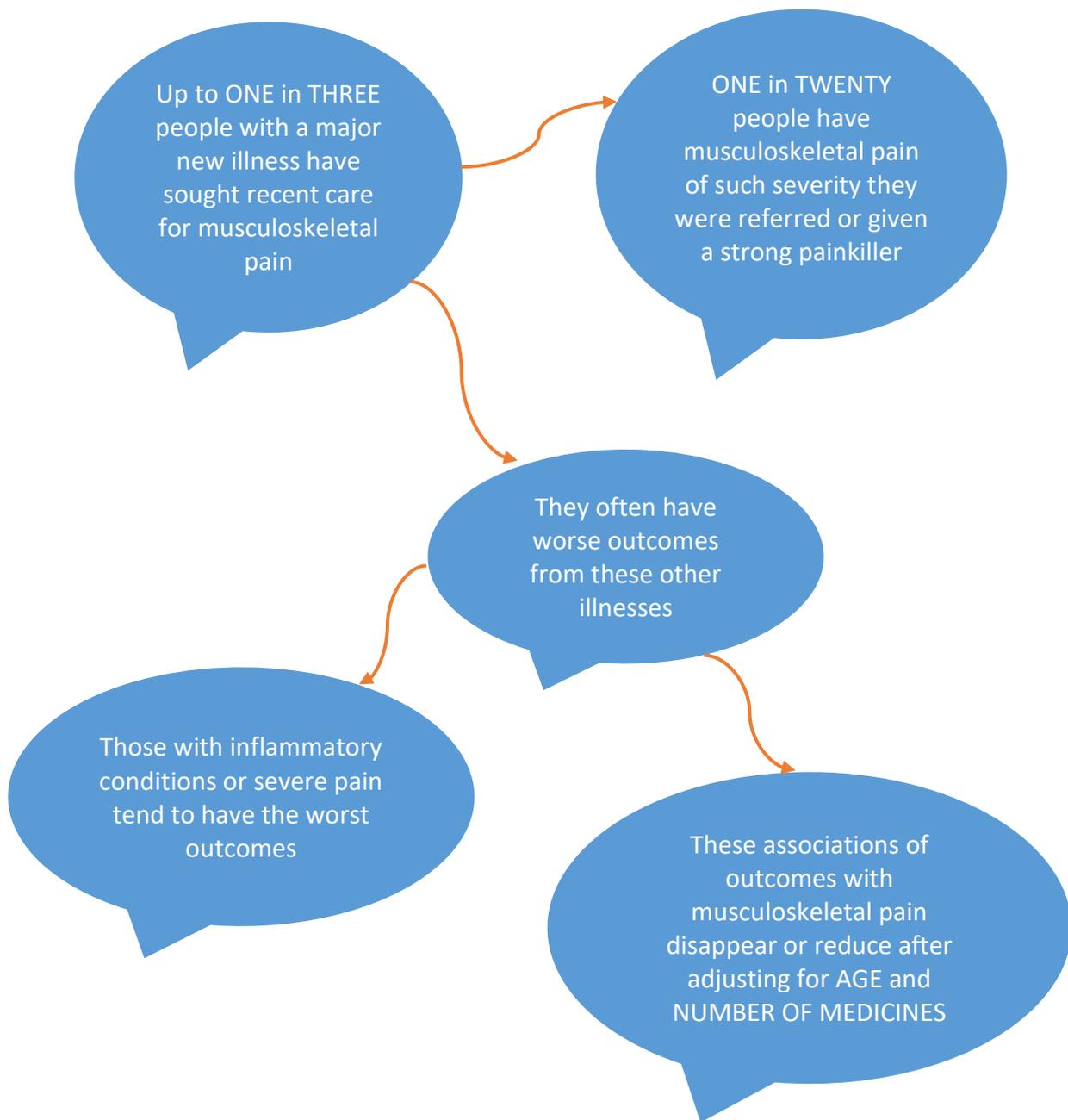
Key findings, messages, and implications

Summary of main findings

The main findings of our study are displayed in Figure 26.

This study examined the electronic health records of people across the UK who have been newly diagnosed with a heart attack, stroke, cancer, dementia, or pneumonia. Up to a third of patients with each new illness had consulted their GP for a painful musculoskeletal condition in the previous two years. Our study showed that these people had increased risks of several worse outcomes relating to their new illness compared to those who had not consulted for a painful musculoskeletal condition. Patients with inflammatory arthritis or current and severe musculoskeletal pain (defined as referral onwards or prescription of a strong painkiller) tended to have greater risk. However, when investigating further, once we adjusted for the age of the patient and the number of medicines they had been prescribed, the association of musculoskeletal pain with poorer outcomes generally disappeared (meaning musculoskeletal pain was not independently associated with outcomes) or reduced. This study highlights that a consultation for musculoskeletal pain in older adults is an indicator of complexity, with such patients being older and having more comorbidities and prescribed medicines, with increased risk of poorer outcomes from other illnesses and higher costs related to their care.

Figure 26. A summary of the main findings



Reflections on study design

The MSKCOM study used anonymised health care information contained in CPRD Aurum, a large nationally representative database of routinely recorded primary care information currently including around 20% of the English population. The majority of the English population are registered with a general practice and general practice is the gateway to the NHS; typically, the first point of contact for a new symptom and the place where most chronic conditions are managed in the UK. Recorded illnesses and conditions in primary care databases such as CPRD have been shown to be highly valid.

A novelty of this study is its assessment of whether people with existing regional pain, osteoarthritis, and inflammatory musculoskeletal conditions have an increased risk of a different experience and outcomes following diagnosis of five different, yet common and impactful, illnesses. This new research expands on previous studies which show that musculoskeletal painful conditions are risk factors for developing these illnesses. The limited number of previous studies assessing the impact of musculoskeletal conditions on outcomes of other illnesses have given mixed findings and tended to be small and/or based outside of the UK. The use here of data from an EHR research database gives advantages over prospective new data collections such as surveys including the ability to analyse large numbers of patients and follow them up for a long-time following diagnosis. All our cohorts included over 100,000 patients and the largest had over 400,000 patients, with several years of follow-up after diagnosis of each index condition. Use of EHR data also means we did not have to rely on large numbers of people completing multiple questionnaires over time as would be necessary for a study using self-reported information from patients. In contrast the generalisability of surveys is often affected by poor response as not everyone eligible to take part will take part, and of those who do take part many will drop out of subsequent stages of the study over time.

The study used a robust approach to study design and in developing definitions of musculoskeletal pain and the index illnesses from EHR including derivation of code lists. This drew on previously developed code lists and included obtaining consensus on definitions and codes to include from clinical and non-clinical experts in EHR research. The code lists used to derive musculoskeletal pain

and the index illnesses are freely available for other researchers to use and are available online (<https://doi.org/10.21252/878s-x990>).

There are always challenges in defining health conditions using EHR databases as they rely on patients consulting health care and on what is recorded by the health care professional (who will record information for clinical rather than research purposes). Defining musculoskeletal pain as a recorded consultation up to 24 months prior to a new diagnosis may mean some patients did not have pain at time of the diagnosis. To overcome this, in a secondary analysis we categorised pain by recency of consultation including a subgroup with a more recent (in six months before new diagnosis) consultation to reflect increased likelihood of a current episode of pain. There will also be patients in the non-musculoskeletal pain comparison group who have musculoskeletal pain but have not sought healthcare for it. By using a 24-month baseline period, the subgroup of patients labelled as having no musculoskeletal pain who do actually have pain should be small, and these patients are likely to have less severe or less chronic pain. A limitation of using EHR databases is that severity of painful symptoms is not recorded. A recorded consultation suggests the musculoskeletal pain was of a severity which prompted the need to seek healthcare. However, we also used a recent musculoskeletal referral or prescription of a strong opioid analgesic (which cannot be bought over the counter) as a proxy for severity on the understanding that patients with more severe pain would be more likely to be referred or get a strong painkiller. There are issues with missing data for some of our covariates, for example, ethnicity is not always fully recorded in EHR, which needed to be addressed in the analyses. All our outcomes also had to be collated from the records. There are other outcomes from our chosen illnesses such as impact on everyday life and support needed from family or carers that would have been informative to have assessed and are of importance to patients but are not recorded in EHR. Despite the limitations of surveys noted above, it would therefore be of value for future research to complement the MSKCOM study by investigating the impact of musculoskeletal pain using self-reported information on pain and on outcomes of other illnesses.

The pneumonia cohort was mainly driven by people with a hospital admission for pneumonia. Pneumonia may not always be recorded in primary care unless diagnosed in hospital, with GPs preferring to use labels such as chest infection. This and the older age and increased prior

consultation rate for this cohort may signify higher rates of pre-existing chronic or severe comorbidity than the other cohorts.

We did not examine all types of musculoskeletal conditions but restricted to the most common painful conditions previously shown to be associated with the other morbidity. We adjusted in our models for consultation for other musculoskeletal conditions. Again, further research could broaden our study to include all types of musculoskeletal conditions, but it would need to be recognised that the impact may vary across conditions.

Discussion and recommendations

We discussed our findings with a range of stakeholders including:

- Our Patient and Public Involvement Engagement Group
- Clinical researchers: GPs, rheumatologists, cardiologist, dementia specialists, physiotherapists, pharmacists
- Methodologists in statistics, epidemiology, social science, health services research
- The Keele University Impact Accelerator Unit whose aim is to close the evidence-to-practice gap, by accelerating both the uptake and impact of research evidence
- Clinical and non-clinical experts in EHR research.

The code lists used to derive musculoskeletal pain and the index illnesses are freely available for other researchers to use and are available online (<https://doi.org/10.21252/878s-x990>).

1. *Up to a third of people newly diagnosed with heart attack, stroke, cancer, dementia, and pneumonia have consulted for a common musculoskeletal painful problem in the previous 2 years.*

Musculoskeletal pain is a common comorbidity across all types of illness. Many of these patients are suffering from severe pain with associated impact on everyday life including restricting ability to be physically active, causing anxiety and low mood, and interfering with sleep. It is likely more have musculoskeletal pain but have not consulted healthcare for this pain in those two years.

2. *Patients with painful musculoskeletal conditions such as inflammatory arthritis and osteoarthritis had higher rates of worse outcomes from other illnesses than patients without musculoskeletal pain. Musculoskeletal pain though is not generally independently associated with poor outcomes after taking into account other characteristics such as age and number of medicines prescribed to the patient.*

This suggests it is not just musculoskeletal pain which directly causes poorer outcomes, and that musculoskeletal pain is an indicator that patients may be more complex, being more likely to be older and have more comorbidities and medications and increased costs of care. Previous studies have highlighted musculoskeletal conditions may be risk factors for onset of these new illnesses and whilst musculoskeletal pain may not directly impact on the outcomes from these illnesses, it may make successful rehabilitation from other illnesses harder. There were indications from the secondary analyses of our study that those with more severe pain may have worse outcomes. Severe pain may worsen quality of sleep and mental health and reduce exercise levels and the ability to take part in everyday activities. Ensuring rehabilitation plans for other illnesses includes awareness of musculoskeletal pain may help remove barriers to successful outcomes and improve the overall quality of life of older people with arthritis and other musculoskeletal conditions. This may include appropriate use of exercise and physiotherapy interventions, aids and devices for walking and daily living activities, and better drug treatment of musculoskeletal pain in patients with these conditions. There were also many patients with musculoskeletal pain within our cohorts who are prescribed strong opioids, and this is a concern given the risk of adverse effects associated with long term use of opioids (Bedson et al, 2019).

- Clinicians need to be aware of the risk of other illnesses for people with musculoskeletal pain and ensure appropriate management of the musculoskeletal pain and targeting of common risk factors.
- Improving recognition and management of musculoskeletal pain and its impact on everyday life in people across co-occurring conditions, including integration within rehabilitation, may help improve their outcomes.

3. *Patients with musculoskeletal pain have a high number of prescribed medicines (polypharmacy) that appears to be associated with an increased risk of poor outcomes from other conditions.*

The impact of polypharmacy on what happens following a new diagnosis has been found more generally in patients in other studies, including those from Keele University (Rathod-Mistry et al., 2021). Polypharmacy is defined as the concurrent use of 5 or more regular medicines and is increasingly prevalent as the population ages (Masnoon et al., 2017). Patients with musculoskeletal pain were being prescribed an average of 13-19 different medicines over 2 years excluding painkillers. This does not take into account medicines purchased “over the counter” from places such as pharmacies and supermarkets and so the overall number of medicines they are taking is likely to be higher, particularly when also including painkillers for their musculoskeletal pain.

The number of different medicines that these patients are taking may reflect the likelihood they have a number of other illnesses and a higher frequency of consultation. This demonstrates the complexity of patients with musculoskeletal pain and highlights the need to take a person perspective in the management of newly diagnosed illnesses.

Whilst it is not possible to assess within the design of this study, the high number of medicines may also increase the risk patients are not taking them all as advised by their GP. A further important concern is whether there are specific medicines increasing risk of poor outcome (“inappropriate prescribing”), for example increasing risks of falls, episodes of delirium, and hospital admissions because of adverse drug reactions.

- Clinicians need to think about the patient as a whole when treating individual illnesses including consideration of all their illnesses and current medicines.
- Regular and detailed medicine reviews are needed in patients with musculoskeletal pain to assess appropriateness of all their prescribed medicine.
- Further research should explore the reasons for a relationship between prescriptions of multiple medicines and outcomes of illness in people with musculoskeletal pain.

4. *Patients with musculoskeletal pain have high rates of risk factors for other illnesses such as heart problems and stroke.*

These risk factors include having other illnesses such as diabetes, and lifestyle characteristics such as obesity and smoking.

- This highlights the need for surveillance of this group of patients presenting with a new illness. For example, in new heart attack or stroke, patients may be at risk of further heart problems or another stroke. This targeted surveillance could be undertaken within specialist cardiology clinics or carried out by GPs via commissioning of a specialist primary care service, similar to other high-risk conditions such as diabetes mellitus surveillance in GP.

5. *There is little indication people with musculoskeletal pain are managed differently*

This is reassuring given the potential for management to be impacted by concerns over interactions of medicine with prescribed analgesia such as NSAIDs, or the analgesic medicine increasing risk of bleeding following procedures such as percutaneous coronary intervention.

6. *Recognition of musculoskeletal pain in patients with other illnesses may vary. In particular, studies have highlighted there is a need to improve recognition and management of pain in people living with dementia.*

Studies have suggested that the recognition of pain in people living with dementia needs to be improved (Bullock et al., 2020, 2021; Rajkumar et al; 2017), and may be more likely to be reported by the person's caregiver than the person living with dementia (Bullock et al, 2020). This may mean that our dementia cohort includes people with unrecognised musculoskeletal pain which may have reduced our observed impact of musculoskeletal pain on dementia outcomes. Despite this, differences in outcomes were identified in people with recorded musculoskeletal pain. This may relate to sub-optimal primary care management of recognised pain in people living with dementia that has previously been noted in other studies (Bullock et al., 2020, 2021).

7. *There are higher healthcare costs for patients with musculoskeletal pain who develop other illnesses*

Musculoskeletal pain has a high impact on utilisation of healthcare services including increased consultations, prescriptions and hospital stays. Health care costs over five years were on average around £339 to £1,250 higher for patients with musculoskeletal pain after a new diagnosis of heart attack, stroke, cancer, and dementia; and around £167 to £785 over one year for patients with pneumonia. This again shows the complexity of patients with musculoskeletal pain. The main costs were in the first year after diagnosis and for hospital services. This has also been observed in other cost-of-illness studies (Boman et al., 2021; Fattore et al., 2012, Guy et al., 2013; Muller et al., 2014).

8. *This study used data from healthcare use before the COVID-19 virus pandemic.*

The impact of the COVID-19 virus pandemic on reduction in healthcare seeking and delays in referral and longer waits for surgery such as knee or hip replacements may mean there are now more people with severe musculoskeletal pain than for the time period that this study covered. The pandemic has also impacted on levels of presentation, screening, referral, and treatment of our index conditions. For example, cancer screening levels have reduced and referral waiting times have increased (Cancer Research UK, 2022). Dementia diagnoses also fell during the pandemic (NHS Digital, 2022). Rates of heart attack hospitalisations dropped by a half during the initial COVID period (Public Health England, 2020).

- Future research is needed to assess whether the COVID-19 pandemic has increased the impact of musculoskeletal pain on outcomes of other conditions and altered how patients with musculoskeletal pain are treated.

Conclusions

Musculoskeletal pain is common and a frequent reason for going to see a clinician. It can have a major impact on everyday life, reducing the ability to perform everyday tasks and impacting on sleep, mental health, and work. Older adults consulting for musculoskeletal pain often have many co-existing illnesses and be on multiple medicines, as a consequence when they have a new serious illness, they are more likely to have poorer outcomes compared to those without musculoskeletal pain.

Project outputs

Mason KJ, Jordan KP, Achana F, Bailey J, Chen Y, Frisher M, Heron N, Huntley AL, Mallen CD, Mamas MA, Marshall M, Png ME, Tatton S, White S, Edwards JJ.

Musculoskeletal pain and its impact on prognosis following hospitalisation for acute coronary syndrome or cerebrovascular accident: a linked electronic health record cohort study (MSKCOM). Society for Academic Primary Care North Conference 2021; Oral presentation.

<https://sapc.ac.uk/conference/2021sapcnorth>

Mason KJ, Jordan KP, Achana F, Bailey J, Chen Y, Frisher M, Herron N, Huntley AL, Mallen CD, Mamas MA, Marshall M, Png ME, Tatton S, White S, Edwards JJ.

Musculoskeletal pain and prognosis for acute coronary syndrome and cerebrovascular accident: a linked electronic health record cohort study.

British Society of Rheumatology Annual Conference 2022; Poster presentation.

https://academic.oup.com/rheumatology/issue/61/Supplement_1

Mason KJ, Achana FA, Bailey J, Chen Y, Frisher M, Heron N, Huntley AL, Mallen CD, Mamas MA, Png ME, Tatton S, White S, Edwards JJ, Marshall M.

Impact of musculoskeletal pain on outcome of comorbidities: the MSKCOM study. KP Jordan, KJ National Musculoskeletal Health Data Group (Versus Arthritis) 2022; Oral presentation.

Mason KJ, Bailey J, Heron N, Marshall M, Achana F, Chen Y, Edwards JJ, Frisher M, Huntley AL, Mallen CD, Mamas MA, Png ME, Tatton S, White S, Jordan KP.

Musculoskeletal pain and its impact on rates of hospitalisation and mortality in cancer: a linked electronic health record cohort study (MSKCOM).

Society for Academic Primary care Annual Scientific Meeting 2022; Oral Presentation.

https://sapc.ac.uk/sites/default/files/2022_asm_abstract_book.pdf

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