Delays in Diagnosis of Degenerative Cervical Myelopathy: A Population-Based Study using the Clinical Practice Research Datalink

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Contents

Abstract (English)

Background: Degenerative cervical myelopathy (DCM) is a significant public health concern that causes important dysfunction in individuals. Surgical intervention is an accepted, cost-effective treatment for DCM and should generally be completed early in the disease course to arrest the development of further neurological dysfunction. Unfortunately, the diagnosis of DCM is often difficult to establish, and many patients deteriorate before treatment due to delays in diagnosing the condition.

Objectives: This study aims to describe the time between initial presentation to a primary care provider (PCP) and final diagnosis of DCM in the general population of the United Kingdom while describing erroneous diagnoses that occur early in the disease course. A secondary objective is to assess the risk factors associated with delays in diagnosis of DCM within the same population. These risk factors include age, sex, socio-economic status, comorbidities (chronic pain, fibromyalgia, and anxiety) and Charlson Comorbidity Index (CCI).

Methods: The data source for this study is the Clinical Practice Research Datalink (CPRD), a UK-based network of PCP practices, providing anonymized medical records on over 16 million registered patients. A case series of all patients with a diagnosis of DCM over 18 years of age was identified between April 1997 and March 2022, with DCM defined based on specific procedural and diagnostic codes. All prior medical codes for DCM-related visits, defined using prespecified diagnoses and symptoms, were used to identify the date of first related visit to a PCP. Survival analysis using Kaplan Meier plots were used to describe the time from first related visit to diagnosis. Risk factors for delay in diagnosis of DCM by a specialist were assessed using a Cox proportional hazards model.

Results: The case series of patients with a DCM diagnosis included 36612 patients. There were 51.1% male, with a mean (SD) and median (IQR) age at DCM diagnosis of 67.3 (12.4) and 68 (58, 77), respectively. The most common DCM-related diagnoses were pain (41.9%), falls (19.1%) and numbness or paresthesia (15.4%). For 43.4% of the subjects, there was no delay in the diagnosis of DCM. Among those with at least one DCM-related visit, the median (IQR) time from first visit to DCM diagnosis was 22.1 (5.7, 43.3) months. Comparatively, the median (IQR) time from initial DCM-related PCP visit to confirmed DCM diagnosis among those who only had a cervical spine MRI (vs. other imaging modalities) was 8.8 (0.03, 37.2) months. Male sex (HR: 1.18, 95% CI [1.15, 1.21]), and older age (>80) (HR: 1.29, 95% CI [1.13, 1.48]), were associated with shorter delays in DCM diagnosis. Further, being a previous or current smoker (HR: 0.94, 95% CI [0.91, 0.98]), and having a diagnosis of chronic pain or fibromyalgia (HR: 0.92, 95%CI [0.85, 0.99]) were associated with longer delays in DCM diagnosis.

Conclusions: Patients face significant delays in diagnosis of DCM. The most common DCM-related visits before a diagnosis is made are for pain, falls, and paresthesia. Imaging modality requests other than cervical spine MRIs may delay diagnosis and treatment. Female sex, age <80, being a

previous or current smoker, and having a diagnosis of chronic pain or fibromyalgia are associated with longer delays in diagnosis.

Abstract (French)

Contexte: La myélopathie cervicale dégénérative (MCD) est un problème de santé publique important qui provoque d'importants dysfonctionnements chez les patients. L'intervention chirurgicale est un traitement efficace et rentable de la myélopathie cervicale dégénérative et devrait généralement être effectuée tôt dans l'évolution de la maladie afin d'arrêter le développement d'autres atteintes neurologiques. Malheureusement, le diagnostic de MCD est souvent difficile à établir, et l'état de nombreux patients se détériore avant le traitement en raison de retards dans le diagnostic de la maladie.

Objectifs: Cette étude vise à décrire le délai entre la présentation initiale à un prestataire de soins primaires (PCP) et le diagnostic final de MCD dans la population générale du Royaume-Uni, tout en décrivant les diagnostics erronés qui sont évoqués au début de l'évolution de la maladie. Notre objectif secondaire est d'évaluer les facteurs de risque associés aux retards de diagnostic de la MCD au sein de la même population. Ces facteurs de risque comprennent l'âge, le sexe, le statut socio-économique, les comorbidités (douleur chronique, fibromyalgie et anxiété) et l'indice de comorbidité de Charlson (CCI).

Méthodes: La base de données utilisée dans cette étude est le Clinical Practice Research Datalink (CPRD), un réseau britannique de cabinets de médecins de famille, qui fournit des dossiers médicaux anonymes sur plus de 16 millions de patients. Une série de cas de tous les patients de plus de 18 ans ayant reçu un diagnostic de MCD a été identifiée entre avril 1997 et mars 2022, la MCD étant définie sur la base de codes de procédure et de diagnostic spécifiques. Tous les codes médicaux antérieurs pour les visites liées à la MCD, définis à l'aide de diagnostics et de symptômes préspécifiés, ont été utilisés pour identifier la date de la première visite liée à la MCD auprès d'un PCP. Une analyse de survie utilisant des diagrammes de Kaplan Meier a été utilisée pour décrire le délai entre la première visite et le diagnostic. Les facteurs de risque de retard dans le diagnostic de la MCD par un spécialiste ont été évalués à l'aide d'un modèle à risque proportionnel de Cox.

Résultats : La série de cas de patients ayant reçu un diagnostic de MCD comprenait 36612 patients. Il y avait 51,1% d'hommes, avec un âge moyen (SD) et médian (IQR) au moment du diagnostic de MCD de 67,3 (12,4) et 68 (58, 77), respectivement. Les diagnostics les plus fréquents liés à la MCD étaient la douleur (41,9 %), les chutes (19,1 %) et l'engourdissement ou la paresthésie (15,4 %). Pour 43,4 % des sujets, il n'y a pas eu de retard dans le diagnostic de la MCD. Parmi ceux qui ont eu au moins une visite liée au MCD, le délai médian (IQR) entre la première visite et le diagnostic du MCD était de 22,1 (5,7, 43,3) mois. Comparativement, le délai médian (IQR) entre la première visite au PCP liée à la MCD et le diagnostic confirmé de MCD chez ceux qui ont seulement subi une IRM du rachis cervical (vs. autres modalités d'imagerie) était de 8,8 (0,03, 37,2) mois. Le sexe masculin (HR : 1.18, 95% CI [1.15, 1.21]) et l'âge avancé (>80) (HR : 1.29, 95% CI [1.13, 1.48]) étaient associés à des délais plus courts pour le diagnostic de MCD. En outre, le fait d'être un ancien fumeur ou un fumeur actif (HR : 0,94, 95% CI [0,91, 0,98]) et d'avoir

un diagnostic de douleur chronique ou de fibromyalgie (HR : 0,92, 95%CI [0,85, 0,99]) étaient associés à des retards plus importants dans le diagnostic de la MCD.

Conclusions : Les patients sont confrontés à des retards importants dans le diagnostic du MCD. Les consultations liées à la MCD les plus fréquentes avant qu'un diagnostic ne soit posé concernent la douleur, les chutes et les paresthésies. Les demandes de modalités d'imagerie autres que les IRM de la colonne cervicale peuvent retarder le diagnostic et le traitement. Le sexe féminin, l'âge inférieur à 80 ans, le fait d'être ou d'avoir été fumeur et le diagnostic de douleur chronique ou de fibromyalgie sont associés à des délais de diagnostic plus longs.

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Contribution to Original Knowledge

The current thesis is written to define the time-window in degenerative cervical myelopathy (DCM) from initial presentation at a primary care physician (PCP) to final diagnosis. Administrative health data from the United Kingdom population covered by the Clinical Practice Research Datalink (CPRD) was used. Several other analyses were performed, including identification of risk factors for longer delays in diagnosis, and describing trends in radiological imaging use during the diagnostic workup. This study adds to a very limited body of literature assessing the time to diagnosis in patients with DCM. It is the first to analyze this time-window using a large sample size, the first to use administrative health data, and the first to use the CPRD. Several secondary objectives, including describing the trends in radiological imaging used during the diagnostic workup, and identification of risk factors predictive of longer delays in diagnosis, are also novel. This research, defining the time-window for diagnosis of DCM, also provides a foundation for advancing research to benefit DCM populations. The identified risk factors for delayed diagnosis can inform clinical guidelines and help optimize healthcare practices. Understanding trends in radiological imaging requests can help guide resource-efficient diagnostic processes. Finally, policymakers can utilize findings for effective resource allocation, decreasing societal DCM burden.

Contribution of Authors

Lior Elkaim, through discussions with Dr. Oliver Lasry, identified a gap in the current understanding of DCM. Lior Elkaim performed a literature review and identified a research question, of which the focus was narrowed with the help of Dr. Oliver Lasry. Objectives were set by Dr. Oliver Lasry in cooperation with Dr. Samy Suissa. Dr. Oliver Lasry helped provide relevant pathophysiological and clinical expertise necessary to guide the research. Dr. Samy Suissa was responsible for providing access to the Clinical Practice Research Datalink (CPRD) and guided the formal data application. Data were obtained by application written by Lior Elkaim and revised by Dr. Suissa and Dr. Lasry.

Both Dr. Oliver Lasry and Dr. Samy Suissa helped throughout the thesis manuscript composition with revisions, suggestions, and supervision. They were also instrumental in helping guide the statistical analysis, along with Hui Yin. The methodology employed during this thesis was planned by Lior Elkaim under close supervision with Dr. Oliver Lasry and Dr. Samy Suissa. Lior Elkaim was directly involved in the planning and writing of every chapter included in this thesis.

Chapter 1.1: Introduction to Degenerative Cervical Myelopathy

Degenerative cervical myelopathy (DCM, also called cervical spondylotic myelopathy) is a disease characterized by progressive cervical spinal cord compression caused by degenerative changes in the spine, which lead to progressive neurologic dysfunction and disability[1]. The term "degenerative" within DCM is used to encompass several age-related changes in the cervical spine, including osteoarthritic changes, spondylosis (age-related degeneration of the neck), disk herniations, facet arthropathy, and ligamentous hypertrophy, calcification, or ossification[2]. DCM is considered an acquired form of non-traumatic spinal cord injury (NTSCI)[3], and is the most common cause of spinal cord dysfunction worldwide[4]. The precise pathophysiology of DCM remains unclear, but the manifestation of the disease is multifactorial, with genetic[5] and environmental[1] contributing elements. Most DCM diagnoses are made in patients in their 50s, with rare diagnoses given before age 40[6]. As patients age, their risk of DCM diagnosis and progression is thought to increase[4]. DCM, as a progressive disease affecting neurologic function, is associated with significant individual and societal burden. For patients, several activities of daily life can be affected[7], including limited mobility, loss of hand dexterity affecting the ability to write or self-care, bowel or bladder (sphincter) dysfunction, and even wheelchair dependence and paralysis. Some imperfect estimates place the incidence and prevalence of DCM in North America at 41 and 605 per million, respectively[4]. These numbers significantly underestimate the true incidence and prevalence, as the data are of low quality and sometimes include only patients with severe disability (i.e. tetraplegia or quadriplegia). From a societal perspective, the current best available data estimates that DCM leads to an annual cost of over £681 million annually in the UK, mainly due to admissions costs, lost productivity, and disability[8]. Further, in the United

States, three DCM-related conditions were identified as a top 100 national priority for research by the Institute of Medicine[9]. These priorities were for: 1) establishing a prospective registry to compare treatments for patients with DCM 2) Compare the effectiveness of different treatments for patients with cervical disc and neck pain and 3) compare the effectiveness of different surgical strategies for symptomatic disc herniation. The best strategy to decrease individual and societal disease burden associated with DCM is to improve disease recognition and refer patients for timely surgical intervention. If done early, surgery is recognized as the gold-standard treatment for DCM, halting disease progression[10,11]. Unfortunately, the diagnosis of DCM can be challenging, and many patients irreversibly deteriorate before surgery due to delays in diagnosis[12]. Specifically, patients often first visit their primary care providers (PCP), who may have difficulty recognizing the early signs and symptoms of DCM[13]. This clinical time window from initial PCP visit to DCM diagnosis has not yet been adequately described.

This thesis will estimate the time to diagnosis for DCM using administrative health data. Specifically, the clinical window from an initial PCP visit for a DCM-related complaint to final recorded diagnosis of DCM is described. Further, risk factors for lengthier delays in diagnosis, including age, sex, comorbidities, and socioeconomic status are analyzed. In doing so, we hope to help guide PCPs and other physicians with the diagnosis of DCM, ultimately helping patients to be referred for surgical assessment sooner. In the upcoming chapter, the various elements surrounding DCM are discussed, including the pathophysiology, diagnosis, natural history, treatment options, and epidemiology. Formal study aims and objectives will then be presented. Chapter 2 will focus on a literature review surrounding the time to diagnosis in patients with DCM.

Chapter 1.2: Pathophysiology of Degenerative Cervical Myelopathy

DCM is caused by compression of the cervical spinal cord[14]. Underlying causes of cervical cord compression include herniated intervertebral discs, degeneration of stabilizing structures like joints, ligaments, and connective tissue, bone spur growth caused by inflammation, and thickening of the ligamentum flavum or facet joints[1]. These factors cause spinal cord compression through static and dynamic factors[1]. Static factors are those that are either congenital or caused by degeneration; underlying disease processes that lead to myelopathy through static forces include acquired spondylosis and disc degeneration, ossification of the posterior longitudinal ligament (OPLL), a disease with higher prevalence in Asian populations[15], and ossification and or calcification of ligamentum flavum[16]. In spondylosis, due to aging and the accompanying repetitive stresses on the cervical spine, the composition of the intervertebral disc (specifically the nucleus) changes to become more rigid and less capable of redistributing vertical compressive loads[14]. As a result, the surrounding supporting structures, including the facet and uncovertebral joints, are exposed to greater mechanical forces, leading to structural disc failure, osteophyte formation, and ligamentum hypertrophy and calcification[14]. Another potential cause of myelopathy, through static factors, is ossification of the posterior longitudinal ligament (OPLL). OPLL is a rare disease caused by bone deposition throughout the posterior longitudinal ligament. It is thought to be influenced by multiple genetic and environmental factors, which eventually lead to spinal cord compression[17].

Dynamic factors associated with DCM further decrease the area of the spinal canal through neck movement. For example, flexion at cervical spine level may exacerbate spinal cord compression against ventral spondylotic spurs[18]. Moreover, flexion may also lead to increased spinal cord

compression through lateral and ventral column deformation[19]. Extension of the cervical spine may also lead to increased transient cord compression through posterior buckling of the ligamentum flavum. Other processes that contribute to cervical myelopathy through dynamic forces include acute traumatic spinal cord injury (and central cord syndrome especially)[14], hyperextension[19], and telescoping or subluxation[20].

The repetitive biomechanical stressors on the cervical spinal cord caused by static and dynamic factors lead to progressive neuronal injury and spinal cord damage through ischemia and hypoxia, neuroinflammation, and blood-spinal cord barrier disruption[14]. The spinal cord is highly sensitive to decreased blood flow[21]. In DCM, chronic compression can cause reduced perfusion through direct compression of arterial blood flow[18] and adaptive changes to blood vessels[22]. The resultant hypoxia leads to blood-spinal cord disruption and neuroinflammation, which causes progressive spinal cord injury and dysfunction through several steps described elsewhere[14]. Ultimately, the damage to the cervical spinal cord manifests as a myriad of symptoms which may be difficult for some clinicians to diagnose. These symptoms, along with the diagnosis, natural history, and prognosis, are discussed in the upcoming section.

Chapter 1.3: Signs, Symptoms, and Diagnosis

There are currently no widely accepted diagnostic criteria for DCM, further adding to the challenges of making an accurate diagnosis[23]. Currently, most clinicians rely on severity scoring systems like the modified Japanese Orthopaedic Association (mJOA) to characterize myelopathy[24]. While relevant, the mJOA primarily assesses disease severity and is less useful for establishing a DCM diagnosis. More specifically, the mJOA score descriptively assesses various functions that may be affected in patients with DCM, e.g. the ability to eat with a spoon or to use

stairs with or without a handrail. To improve diagnostic delays and prioritize early treatment, an established diagnostic framework for DCM has been named as the number 3 priority by the AO Spine RECODE-DCM (Research Objectives and Common Data Elements for DCM), an international consensus initiative aimed at improving outcomes in DCM[25]. As of now, diagnosis of DCM relies on a high degree of clinical suspicion combined with clinical and imaging findings[14]. Practically, the diagnostic process usually begins with a patient visit to a PCP for any number of symptoms (see next section below)[6]. The patient is subsequently referred for imaging (CT or MRI)[26] before being referred to a specialist (spine surgeon, physiatrist, or neurologist) for a final diagnosis. It is important to note that the diagnosis of DCM by a specialist is not a gold standard test for diagnosing the pathology, especially in the absence of accepted diagnostic criteria. However, there is currently no gold standard for DCM diagnosis. The clinical window between an initial PCP visit for a DCM-related complaint and a final DCM diagnosis is plagued with delays. Some factors that may influence the delay in diagnosis are lack of familiarity of PCPs with DCM signs and symptoms[27], multiple other mimicking diagnoses[6], non-specific symptoms overlapping with other neurological conditions[28], and delays in referral to a spine surgeon[29].

Signs and Symptoms

One of the principal causes of diagnostic delays in patients with DCM is the non-specific early disease signs and symptoms that are seen in several other neurological pathologies[6]. Symptoms associated with DCM include non-specific neck pain, sensory loss and paresthesia, abnormal gait, loss of manual dexterity, genitourinary and bowl dysfunction[30]. Further, several differential diagnoses for DCM exist, including amyotrophic lateral sclerosis (ALS), carpal tunnel disease and radiculopathy[28]. These can confound the diagnosis of DCM due to the similarity of the progressive

neurologic symptoms of certain diagnoses like ALS or due to the non-specific symptoms of DCM often seen with other pathologies like carpal tunnel disease or radiculopathy. A dedicated literature review of DCM's signs, symptoms, and differential diagnoses can be found in Chapter 2 of the thesis.

Imaging

An adequate diagnosis of DCM relies on strong clinical suspicion coupled with clear evidence of myelopathy (compression of the spinal cord) seen on radiological imaging. Imaging in DCM is not limited to diagnosis; it is essential for surgical planning, prognostication, and postoperative follow-ups.

Radiographs (or plain films, X-rays) are a cheap and simple imaging modality that can provide information on cervical spine alignment, osteophytic structures, OPLL, and bony lesions[31]. While relevant for surgeons' intent on operating on patients with DCM, the use of plain films to demonstrate underlying spinal cord compression, and therefore to diagnose myelopathy, is insufficient[32].

Computed tomography (CT) scans provide high-resolution tomographic (cross-sectional) images of the body. Like X-rays, CT scans are an effective imaging modality that can provide accurate views of underlying bony anatomy. Further, CT scans are widely available, fast, cheap, and easy to organize from a PCP perspective[31]. Despite these advantages, CT scans are not as detailed as MRIs for the characterization of spinal cord compression. They are, therefore, not the imaging modality of choice for a DCM diagnosis. Further, CT scans are associated with ionizing radiation and should be avoided, when possible, in younger patients[33].

MRI is the imaging modality of choice for the characterization and diagnosis of DCM[34]. An MRI provides a detailed view of most of the underlying structures involved in the pathophysiology of DCM, including discs, ligaments, the cross-sectional space surrounding the cord, and the spinal cord[30]. A detailed review of the structural changes seen in DCM on MRI and the several measurement techniques used to evaluate DCM on MRI is provided elsewhere[35]. Despite the clear superiority of MRI for DCM characterization and diagnosis, several practical limitations exist. These include, among others, the significant increase in costs of MRI relative to other, cheaper imaging (i.e., CT-scans)[36], lengthy wait times and difficulty organizing outpatient MRIs for patients in PCP settings[37], and claustrophobia among some patients[38].

The relative disadvantages of MRIs mentioned above, coupled with the convenience of 'simpler' imaging modalities like CT scans and X-rays, may contribute to delays in diagnosis for patients with DCM. For example, a PCP may order a CT scan or X-ray in a patient with DCM and may only order an MRI once the results from the initial radiologic tests are received and interpreted. Ideally, PCP physicians should immediately order an MRI (the gold standard for DCM diagnosis) when suspecting DCM. Ultimately, both X-rays and CT scans remain relevant in some patients with DCM; however, they should mostly be used to 1) screen patients with vague symptomatology (provided it is ordered at the same time as an MRI), 2) after the diagnosis is made, they can be used to characterize certain anatomical osseous features relevant for surgery. The relationship between the effects of certain imaging modalities on diagnostic delays in patients with DCM is further explored in this thesis.

Chapter 1.4: Natural History and Treatment Options

As mentioned above, the diagnosis of DCM can be challenging. However, surgical and non-surgical clinicians must arrive at an early diagnosis because there is a clear and accepted treatment strategy for moderate and severe DCM (described below), in which effectiveness relies heavily on early diagnosis and treatment. The treatment strategies for DCM, including surgical and non-surgical options and the natural history of the disease, are described in the upcoming section.

Natural History

The natural history of patients with DCM is highly variable[14]. Generally, patients experience a stepwise and progressive decline in neurologic function if left untreated, marked by periods of relative stability[39]. One randomized control trial showed no significant deterioration in mJOA score or timed 10m walk in patients with DCM managed conservatively over a 2-year follow-up[40]. By contrast, several studies have shown that patients managed conservatively have non-negligible (>30%) deterioration rates without surgery[41–45]. In 2017, Rhee and colleagues systematically reviewed the literature. They showed that the percentage of patients with DCM experiencing a neurologic deterioration (decrease in mJOA by one point or more) after 3-6 years of follow-up ranged from 20-62%[46]. While relevant, these studies sometimes did not evaluate the progression of DCM, stratified by severity. Thus, the authors have noted a need for prospective studies assessing the rate of neurologic deterioration in patients with mild DCM[39]. The need for accurate estimates of clinical deterioration in patients with mild or minimal DCM and predictors of deterioration within this same population has been named as the number 2 research priority by the AO Spine RECODE-DCM[47].

Treatment

In 2017, the current, best available clinical practice guidelines for treating DCM were published by AO Spine North America and the Cervical Spine Research Society[48,49]. The guidelines stipulate that patients should be treated operatively or, in some cases, closely monitored with nonoperative treatment.

Nonoperative

Nonoperative treatment options for patients with DCM may include, among others, cervical traction[43], rest[42], and closely monitored physiotherapy[50]. While nonoperative treatment allows patients to avoid invasive surgical treatments, minimal data supports its effectiveness for treating DCM[14]. Among a group of 78 patients with mild DCM initially treated conservatively, 21 patients eventually deteriorated and required surgery. This group, when compared to those who were treated conservatively throughout the study, showed no significant difference in mean mJOA score at last follow up[51]. Based on very low to low-quality evidence, the following weak-strength recommendation is given regarding nonoperative management in DCM: "We suggest surgical intervention or a supervised trial of structured rehabilitation for patients with mild DCM. If initial nonoperative management is pursued, we recommend operative intervention if there is neurological deterioration and suggest operative intervention if the patient fails to improve"[48,49]. More recent evidence has shown that surgery can effectively treat patients with mild-DCM[52,53].

Operative

Surgery is the mainstay of treatment for DCM[54], with the primary objective of decompressing the cervical spinal cord. Based on moderate quality evidence, current guidelines strongly recommend

surgical intervention for patients with severe (mJOA score ≤ 11) or moderate (mJOA 12-14) DCM. These recommendations are based on comprehensive systematic reviews[46,55], large prospective studies[56] and expert opinion[14]. One multi-center, prospective study by Fehlings and colleagues followed 260 North American adult patients with symptomatic myelopathy and cervical spine compression on MRI. All patients underwent surgical decompression and instrumented fusion, with specifics determined by the treating physician. Data were available for 222 patients after 1-year follow-up; overall, significant improvements from baseline (when adjusting for possible confounders) were seen in mJOA scores (β: 2.88, 95% CI [2.52, 3.24]), Nurick grades (β: -1.59, 95% CI [-1.77, -1.40]), Neck Disability Index (NDI) scores (β: -11.28, 95% CI [-13.77, -8.79]), and SF-36v2 (all dimensions except general health). Further, except for mJOA, the improvement did not significantly change when adjusting for severity (mild versus moderate versus severe, based on mJOA score)[56]. Several other studies also support the role of surgery in patients with DCM[57–60].

Beyond significant improvements in several clinical scoring systems (i.e. mJOA, Nurick, SF-36), surgery for DCM can be cost-effective[8,61,62]. A 2017 study by Witiw and colleagues sought to evaluate surgery for DCM through a QOL and health economics lens[62]. The paper analyzed quality-adjusted life year (QALY) gains over the study period using an area under the curve calculation with linear interpolation estimates in a prospective cohort of DCM patients. Lifetime incremental cost-to-utility ratios (ICUR) for surgery were also used. Overall, Witiw et al. found that the mean QALY gained (3% discount per annum of gains and costs) over 24 months was 0.139 (95% CI [0.109-0.170]). Further, they estimated the lifetime ICUR of surgical intervention

as $20,547.84/QALY gained, which, as per the World Health Organization, is considered “very cost-effective”[63].

Thus, the above section highlights that surgery is an effective treatment for most patients with DCM and that surgery for DCM is cost-effective. However, early diagnosis and prompt referral of patients with DCM to a spine surgeon has been strongly advocated[14,29,39], as studies have identified worse clinical outcomes after surgery in patients with a longer duration of symptoms and higher preoperative severity (mJOA)[2,57]. These studies are further discussed in the upcoming literature review (chapter 2.2). Historically, surgical intervention for DCM was done to halt disease progression and maintain neurologic status. However, some authors have recently suggested that surgery for DCM can improve neurologic function[14].

Chapter 1.5: Study Aim and Objective

In this chapter, we have highlighted that DCM is a significant public health concern, that there is an available, cost-effective treatment (surgery) for DCM, and that surgery should be done as early as possible in patients with moderate to severe DCM. Unfortunately, many patients deteriorate irreversibly before treatment due to delays in the diagnosis of DCM. Further, a paucity of evidence (explored in the upcoming chapter) describes the clinical window to diagnosing and treating patients with DCM. Improving DCM awareness, specifically for early diagnosis and surgical treatment, has been named the number one research priority by AO Spine RECODE-DCM[64]. Thus, the objectives of this thesis are to:

1. Estimate the time between initial presentation with DCM-related symptoms to diagnosis of DCM in the general population of the United Kingdom, while describing erroneous diagnoses that occur early in the disease course.
2. Estimate the association between age at time 0, sex, socio-economic status (using Patient Level Index of Multiple Deprivation Domains (PIMD), and comorbidities (chronic pain, fibromyalgia, and anxiety) and delays in diagnosis of DCM within the same population.

Chapter 2.1: Literature review

The following chapter discusses findings from two comprehensive literature reviews that provide information necessary to complete the abovementioned objectives and identifies knowledge gaps in the management of DCM that this thesis addresses. The first focuses on identifying all signs, symptoms, and differential diagnoses related to DCM. A thorough understanding of the multiple presentations and mimicking diagnoses of DCM is essential to identify all initial PCP visits before an official DCM diagnosis is made. The second literature review focuses on the clinical window from symptom onset to diagnosis in patients with DCM. Describing the clinical time window for patients with DCM, from initial PCP visit to diagnosis, will help improve the awareness of DCM and hopefully help patients be treated faster. Analysis of the risk factors (comorbidities, age, sex, socioeconomic status) associated with lengthier diagnostic delays could further help clinicians identify those at highest risk. Of note, the objective of this thesis is not to provide a formal systematic review of the literature on these topics; Instead, both rely on a query of only one database (PubMed). Specific search terms for each review can be found in the Appendix.

Chapter 2.2: Signs, Symptoms, and Differential Diagnosis

DCM, especially early in the disease course, can be challenging to diagnose. The difficulty of making an accurate DCM diagnosis is due to several factors, including 1) the similarity of the DCM presentation to several other neurologic and musculoskeletal conditions[65] 2) Non-specific, early disease features[6] 3) Limited knowledge and awareness of DCM in primary care, where patients most often first present[27]. The following section will review the different signs and symptoms of DCM (table 1).

Several signs can be seen during a physical examination in a patient with DCM. Motor signs include pyramidal and segmental weakness[6], usually in the extensors more than flexors in the upper limbs and vice-versa in the lower limbs. Sensory changes can also be seen, such as decreased sensation or Lhermitte's sign[30]. Changes related to patient reflexes are also characteristic of DCM; these include, among others, hyperreflexia below the level of compression, positive Hoffmann sign (thumb flexion after forced flexion and release of the tip of the long finger), positive finger flexor reflexes, positive Babinski signs, and spasticity[66]. Abnormal gait, especially if spastic, can also be suggestive of myelopathy[27].

Several patient-reported symptoms can also be suggestive of myelopathy. Unfortunately, many of these symptoms lack specificity and overlap with other degenerative and neurologic diagnosis. Our literature review identified the following clusters of symptoms reported by patients: decreased manual dexterity, urinary and fecal symptoms, recurrent gait and balance disturbances, falls, numbness or paresthesia, weakness, and pain. Decreased manual dexterity is a common complaint and can manifest in multiple ways, depending on the patient's everyday life. For example, the mJOA assigns different scores based on the patient's ability to button a shirt, or to eat with a spoon[53]. Decreased manual dexterity can also present as handwriting

changes, frequent dropping of objects, or difficulty clasping small items. Bowel and urinary function can also be affected in patients with advanced DCM, and often presents as incontinence[27]. Among the most common findings in patients with DCM are abnormal gait and balance[67]. On an individual level, this can manifest in several ways, including a general feeling of incoordination[68], difficulty climbing up or down stairs[69], the need for walking aids[58] (i.e. cane or walker), and recurrent falls[70]. Patients with DCM may also complain of numbness or tingling, usually in the upper extremities[71]. They may describe an overall loss of sensation affecting the hands, which can contribute (along with weakness) to a loss of manual dexterity. Perhaps the least specific early symptom of myelopathy is pain, which can be seen in 41% of patients[72]. The pain seen in DCM can be radiculopathic or axial/mechanical[73]. It is important to note that DCM is a global disease that affects people differently depending on their daily activities. For example, standard evaluations for patients with DCM in East-Asian countries include assessment of a patient's ability to use chopsticks[74]. Thus, physicians should always consider cultural implications when evaluating a patient with a DCM diagnosis.

Many neurologic and musculoskeletal disorders can be confused with DCM based on clinical presentations. The large spectrum of differential diagnoses is due in part to the variety of non-specific signs and symptoms seen in several other pathologies. A 2013 literature review by Kim and colleagues was performed to identify a comprehensive differential diagnosis for DCM[75]. The paper queried one database (PubMed, supplemented with review articles and textbooks) to identify English case series describing conditions that may be confused with DCM. Overall, they reported results from 35 papers (474 patients) and organized the differential diagnoses into 7 categories: congenital/anatomic, degenerative, neoplastic, inflammatory/autoimmune,

idiopathic, circulatory, and metabolic. The paper identified 35 differential diagnoses associated with DCM, of which the most common were amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), and spinal tumors[75]. Table 1 summarizes the signs and symptoms of DCM identified in this literature review.

Chapter 2.3: Literature review part 2: Time to Diagnosis

Many authors have cited delays in accurate diagnosis of DCM as a principal factor contributing to the significant neurologic disability associated with the disease[29,39]. International experts have highlighted that developing strategies to increase awareness and understanding of DCM, among healthcare professionals and the public, may help improve timely diagnosis and therefore management of DCM[76]. Several reasons have been proposed for the delays and under diagnosis of DCM, including low awareness about the pathology in the PCP setting, lack of investment in research (compared to other neurologic pathologies), non-specific signs, symptoms and a wide differential diagnosis, and a complex care pathway sometimes involving physicians from several different specialties[64]. A 2020 study evaluated the education gap along the PCP training pathway[77]. Using modal ranks and standardized online-questions, researchers compared knowledge of DCM to other conditions with similar presentations and epidemiology (i.e. ALS, MS). DCM was the least cited in curricula and learning resources among all compared conditions. Further, despite above average knowledge on DCM in general, knowledge pertaining to management was poor[77]. Another study by Hilton and colleagues examined how DCM is assessed in a clinical setting, and how the assessment differs depending on specialist training[29]. The clinical

documentation of several signs and symptoms were tracked at three phases of clinical care: primary (PCP or physiotherapist), secondary (first specialist appointment) and surgical (first assessment by a spinal surgeon). The authors found that upper limb paresthesia and urinary dysfunction were the most and least common reported symptoms in 43 patients with DCM, respectively. Further, significant differences (unspecified) in assessments for several key features of DCM were noted, including presence of limb pain, hyperreflexia, Hoffman reflex, and spasticity. Among PCPs, pathological reflexes were least frequently assessed. The paper suggests that incomplete assessment by PCPs may contribute to delays in diagnosis for patients with DCM. However, several issues limit the findings, including discrepancies between clinical exams and documentation and small sample size.

Overall, we found only three studies that quantify the clinical time window to diagnosis in patients with DCM. Pope et. al used an online survey to question 778 patients with self-reported DCM. Results showed that the self-reported average delay in diagnosis was "1-2 years", with greater delays among Black or African American patients. The paper also found an association between longer self-reported delays in diagnosis and more severe disease (mJOA score), greater support dependence, and unemployment[13] . Although relevant, the study is potentially limited by several factors, including lack of generalizability (patients recruited via Internet using social media), recall bias, and missing data.

Perhaps the most thorough study evaluating the time to diagnosis in patients with DCM is a retrospective cohort study by Behrbalk and colleagues, in which the medical files of patients who underwent surgical intervention at a single tertiary hospital in Israel were analyzed[78]. Of 146 patients undergoing surgery for DCM, only 42 having complete hospital and community level

data were included in the analysis. The mean (SD) time to diagnosis of DCM from first visit to a physician with a DCM-related sign or symptom was 2.2 (2.3) years. During that time, the mean (SD) number of physician visits with DCM-related complaints before arriving at a final diagnosis was 5.2 (3.6). Notably, none of the patients presenting with myelopathic symptoms were diagnosed correctly after their first visit to a PCP. The most frequent visits before a formal DCM diagnosis was given were for carpal tunnel syndrome (43.1%) and radiculopathy (35.7%). The most common workups requested included EMG (83.7%), cervical CT scans (63.1%), and bone scans (35.8%). Per the authors, the main reason for diagnostic delay in their cohort was the lack of awareness of the pathology by PCPs and orthopedic surgeons. Further contributing factors include MRI and physician availability, although no formal analysis exploring this relationship was performed. This study also suffers several drawbacks, including: 1) The small sample size 2) Data were only available in 42 of 146 patients undergoing surgery 3) Only patients who underwent surgery were included.

More recently, Hilton et. al aimed to characterize the route to diagnosis in patients with DCM in the United Kingdom (UK)[29]. The authors screened MRI scans at one tertiary care center to identify patients with potential DCM. Overall, 43 meeting inclusion criteria (non-traumatic cord compression on MRI due to degeneration, clinical diagnosis of DCM given, and adequate clinical documentation to characterize referral pathways) were included in the analysis. The authors specify that their tertiary care serves an estimated 5.9 million people; it is therefore alarming that only 43 patients with DCM were identified. Further, the authors do not specify what constituted “adequate” documentation. The time from symptom onset to DCM diagnosis was determined by retrospective review of PCP charts. For example, if a PCP note stated that a patient

had been experiencing neck pain for 5 months, then the onset of symptoms was defined as 5 months before the date of referral. This data collection method is limited by patient recall bias and potentially poor documentation often seen in PCP settings. Overall, the authors found that the average (SD) time to referral after symptom onset was 6.4 (7.7) months, while the average (SD) time to neurosurgical review was 15.8 (13.5) months. No clinical features or demographic factors were associated with longer delays in diagnosis.

In summary, three estimates are currently available in the literature describing the time to diagnosis in patients with DCM (table 2). These are "1-2 years" in a survey-based study, 2.2 (2.3) years in a study of 42 patients in Israel, and 15.8 (13.5) months (to neurosurgical review) in 43 patients in a UK-based study. While relevant, all these studies suffer from several limitations, and none seek to describe the clinical window to diagnosis using a large administrative health database.

Chapter 2.4: Knowledge Gaps and Contribution to Medicine

The preceding chapters emphasize that DCM is a disease associated with significant morbidity, and while surgery is a widely accepted treatment, diagnoses are frequently delayed. These delays contribute to increased morbidity, patient distress, and societal impact. Only three manuscripts have endeavored to delineate the time to diagnosis in patients with DCM. These studies are important; however, several limitations (including small sample sizes and data quality) limit their generalizability. Further, few studies seek to define predictors of longer delays in diagnosis. This thesis aims to bridge the gaps in the literature by providing the most accurate estimate of time from the initial PCP visit to DCM diagnosis and pinpointing patients who face the greatest risk of prolonged delays. These findings will enhance DCM awareness and aid clinicians in prioritizing

early diagnosis and surgical intervention, which has been identified as the top research priority by AO Spine RECODE-DCM. We anticipate that earlier diagnoses will result in swifter specialist referrals, more timely surgical interventions, and ultimately, reduced neurological dysfunction.

Chapter 3.1: Methods

The general objective of this thesis is to describe the clinical window from initial presentation at a PCP to final diagnosis of DCM. It will also evaluate the factors associated with lengthier delays in diagnosing DCM.

Chapter 3.2: Specific Objectives

The specific objectives of this thesis are as follows:

1. Estimate the time between initial presentation with DCM symptoms (termed DCM-related visit throughout the study) to diagnosis of DCM in the general population of the United Kingdom, while describing erroneous diagnoses that occur early in the disease course.
2. Estimate the association between age at time 0, sex, socio-economic status (using Patient Level Index of Multiple Deprivation Domains (PIMD), and comorbidities (chronic pain, fibromyalgia, and anxiety) and delays in diagnosis of DCM within the same population.

Chapter 3.3: Overview of study design

This project is a case-series, while the study type is observational and descriptive. The study is centered on the UK population covered by the Clinical Practice Research Datalink (CPRD) suffering from DCM. Patients with a diagnosis of DCM from April 1997 to March 2022 and aged 18 or more at the time of diagnosis were candidates for inclusion in the study. Using these

criteria, a series of over 36000 patients was assembled. The following data were collected or calculated: the time from initial PCP visit for a complaint related to DCM (termed “DCM-related visit”) to the final diagnosis of myelopathy, the prevalence of DCM-related visits, patterns in diagnostic imaging tests, patient baseline characteristics, and patient comorbidities.

Chapter 3.4: Data Source and Population

The CPRD was queried to identify all patients with a diagnosis of DCM from April 1997 to the study start date in March 2022. CPRD data is collected both prospectively. The CPRD (Aurum and linked datasets) is the primary and only data source used for this thesis. The CPRD is a UK-based network of PCP practices, providing anonymized medical records on over 16 million registered patients[79]. The target population are any adult patients suffering from DCM in high-income countries. The source population is patients suffering from DCM in the UK. Finally, the sample population is patients included in our analysis, or those who suffer from DCM and have data available through CPRD.

The recruitment period for this study was from April 1997 to March 2022. April 1997 was chosen as an initial cut-off as it represents the start of Hospital Episode Statistics (HES) linked data, a databank which includes details of hospital admissions in England[80]. Only patients permanently registered with standard follow-up (minimum of 1 year) were included to ensure that data is available for patients at initial PCP visits and up to the final DCM diagnosis. We also used data from the Diagnostic Imaging Dataset (DID)[81]. The DID collects information about diagnostic imaging tests taken from NHS providers' radiological imaging programs, including X-rays, CT scans, and MRIs. These data are available from tests carried out as of April 1st, 2012, in England.

Chapter 3.5: Series Definition and Definition of Myelopathy

Patients included in this study are adult patients (age >18) with available CPRD (and linked HES and DID data) from April 1997 to March 2022 with a diagnosis of myelopathy. A one-year minimum follow-up is also required for inclusion in the study.

Definition of Myelopathy

To be included in this study, a patient must have a diagnosis of myelopathy as defined by the following:

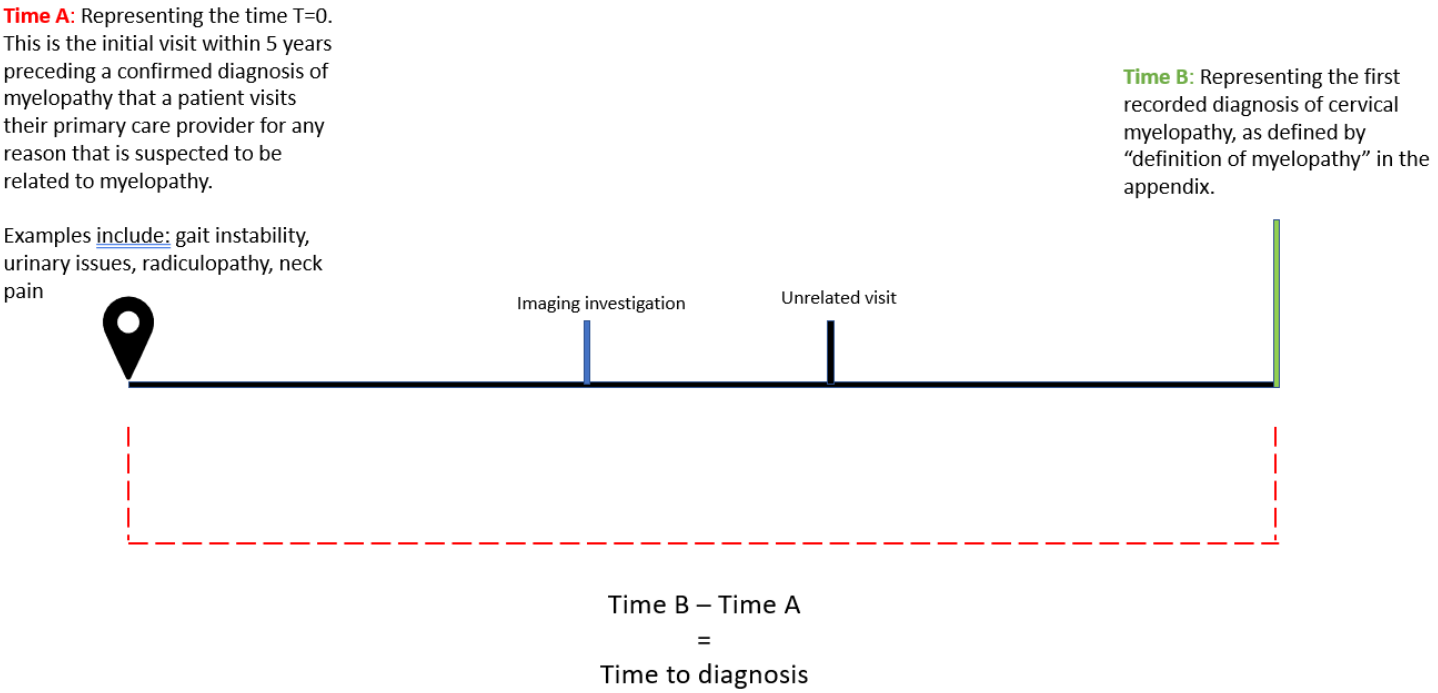
1. Clear, demonstrated and highly specific diagnostic code for myelopathy within CPRD and HES data, as identified using ICD-10 and CPRD code browsers and the key terms "myelopathy" and "cervical". These codes can be found in tables 1 and 2 in the appendix.

The codes identifying a myelopathy diagnosis were found through manual query of ICD-10 and CPRD code browsers using the keywords "myelopathy" and "cervical". Only the terms and codes highly specific for DCM, as determined by L.M.E and reviewed by an expert neurosurgeon (Dr. Oliver Lasry) were included. These were supplemented with recognized ICD-10 codes for non-traumatic spinal cord injury that have previously been published using Canadian administrative health data[3]. While relevant, the algorithm developed by Jaglal and colleagues did not focus specifically on DCM, and, as such, was not exclusively used to identify cases of DCM within the CPRD.

Chapter 3.6: Main outcome and time to diagnosis

As mentioned above, Read codes for CPRD Aurum and ICD-10 codes for HES were used to identify a DCM diagnosis. Using this series of patients, this thesis assesses "DCM-related

visits" for diagnoses, symptoms, investigations, and time-delays that patients face in the 5 years prior to their confirmed DCM diagnosis. Of note, a DCM-related visit, as defined in this study, precedes the official DCM diagnosis (see image below). We also used Kaplan Meier plots to describe the time from an initial primary care visit for a DCM-related complaint (time 0) to official diagnosis of the condition (time 1). Read codes for symptoms and differential diagnoses (obtained through our literature review, see **table 1**) were used to identify the initial DCM-related visit. These codes were collected by manually searching a CRPD code browser using keywords corresponding to each diagnosis or symptom. For example, for pain, the term "pain" was used to search a CPRD code browser, and all codes thought to potentially relate to myelopathy were included, i.e. "arm pain", "chronic neck pain" and "mechanical neck pain". A full list of diagnoses, signs, and symptoms, along with their corresponding Medical, Read, SnomedCT and ICD-10 (if available) codes are in the appendix (table 3). The first read code thought to relate to DCM identified within a 5-year window preceding the confirmed DCM diagnosis were used to identify the first DCM-related physician visit. **If there were no primary care visits within 5 years of DCM diagnosis corresponding to a DCM-related visits, then that patient was given a time of t=0.** The time difference from the first DCM-related visit to the final DCM diagnosis was then calculated. The following image illustrates this strategy.



Chapter 3.7: Covariates and Diagnostic Imaging Data

We also described the clinical course from initial primary care visit to final DCM diagnosis. As such, the frequency of certain DCM-related visits and the average number of visits before a DCM diagnosis is made was calculated. We also described the imaging modalities requested by PCPs en-route to a DCM diagnosis, as identified by the DID. Specifically, the entire DID was queried to collect codes about potential investigations requested by PCPs when investigating DCM or its related differential diagnoses or symptoms, i.e. "MRI spine cervical" if suspecting myelopathy, or "MRI brachial plexus" if suspecting a brachial plexus injury. A full list of included diagnostic imaging codes are available in the Table 4 in the supplementary materials.

Finally, to identify patients at higher risk for delays in diagnosis, we assessed risk factors for delays in diagnosis including age at time 0, sex, socio-economic status (using Patient Level Index of Multiple Deprivation Domains (PIMD)), and comorbidities (chronic pain, fibromyalgia, and

anxiety). Further, the Charlson Comorbidity Index (CCI) is used as a surrogate for comorbidities when analyzing risk factors[82]. A pre-identified comorbidity ICD-10 list corresponding to the CCI published in a previous manuscript is used[83]. The three comorbidities (chronic pain, fibromyalgia, and anxiety) were only included if they were registered before time A (e.g before the initial visit for a symptom that is thought to be DCM).

Chapter 3.8: Statistical analyses and sensitivity analyses

This study is descriptive. As such, measures of central tendency (mean, median, SD, IQR) were used to describe the primary outcome (time to diagnosis). We used Kaplan Meier plots to describe the time from an initial visit for DCM-related symptoms to diagnosis of the condition. Correlation between many variables (including comorbidities, mental illness, and investigations) were analyzed using regression models. We assessed risk factors for delays in diagnosis, including factors such as age, sex, medical comorbidities (listed above), socio-economic status, and rural/urban status. These risk factors were assessed through regression modelling using a Cox Proportional Hazards Model to analyze the association of these factors and time to diagnosis.

Sensitivity analysis: time window

Multiple sensitivity analyses were conducted. The first included changing the time window retroactive to the final diagnosis of DCM. The main analysis used a 5-year window from DCM diagnosis to identify all DCM-related visits. Subsequent calculations used a 3- and 7-year time window, which provided insight into the clinical course of myelopathy and provide clues on the natural history of the disease as well as ensuring the robustness of the results of our primary analysis that used a 5-year window.

Sensitivity analysis: DCM-related visits and related symptoms

The second sensitivity analysis reran the main outcome (time from initial PCP visit to final DCM diagnosis) calculation using different DCM-related visits based on their specificity and likelihood of being mistaken for DCM. For example, diagnoses like “bilateral carpal tunnel syndrome” or “gait-related disturbance” are very likely to represent a missed DCM diagnosis based on literature review and expert knowledge (table 3, appendix). Thus, we reran our analyses using only highly specific DCM-related diagnostic codes to assess the robustness of our results.

Chapter 3.9: Ethical considerations

Several measures protect confidentiality and safeguard patient information within the CPRD. CPRD provides no information that can identify a patient, and the CPRD never receives any patient identification from a GP practice (i.e., name, address, NHS number, full DOB, or medical notes). Further, the CPRD has ethics approval from the Health Research Authority and provides anonymized data to researchers. This study protocol was also reviewed and approved by the Medical/Biomedical Research Ethics Committee (REC) members of the CIUSSS West-Central Montreal Research Ethics Board (REB). The project meets the scientific and ethical standards for conduct as highlighted by the CIUSSS West-Central Montreal REB (project 2022-3265).

Chapter 4: Results

The CPRD search revealed 36612 patients that met inclusion criteria (fig 1). Each of these patients had a diagnosis of DCM between April 1997 to March 2022 and was over the age of 18.

Chapter 4.1: Descriptive Statistics

Overall, 19949 (51.1%) of patients were male. The mean (SD) age at DCM diagnosis was 67.5 (12.3), while the median (IQR) age at DCM diagnosis was 68 (58, 77). The range for age at DCM diagnosis was 29 to 100. 31171 (79.9%) of patients were current or past smokers. An overview of patient characteristics can be seen in Table 2.

Chapter 4.2: DCM-related visits

Overall, 22,103 (56.6%) patients had at least one DCM-related visit before the final diagnosis of DCM was made. The rest did not have any-DCM related visit before the first registered DCM diagnosis. The most common DCM-related visits were pain seen in 41.9% of patients, falls seen in 19.1%, and numbness or paresthesia seen in 15.4%. The average number of visits for DCM-related features before a DCM diagnosis was made among the entire series was 1.8 (4.4). Comparatively, among only those who had at least one DCM-related visit, the average number of DCM-related visits was 3.2 (5.4). The DCM-related visits can be grouped into broader categories, as seen in Table 2. Among these groups, the most common visits were for pain, falls, numbness, or paresthesia.

Chapter 4.3: Comorbidities

The presence of several comorbidities was analyzed among the entire patient group. The average (SD) CCI among the entire series was 2.3 (2.4). Overall, chronic pain and fibromyalgia were seen

in 1030 (2.6%) patients. Depression and anxiety were present in 11,357 (29.1%) and 6840 (17.5%) of patients, respectively.

Chapter 4.4: Imaging characteristics

Overall, out of 21891 patients who had a DCM diagnosis between April 1st, 2012 and October 31st, 2020 (time for HES DID data), 13905 (63.5%) patients had at least one imaging modality requested by their PCP between their initial PCP visit and confirmed DCM diagnosis. The most common imaging modality requested between the initial PCP visit and diagnosis of DCM was a cervical MRI, seen in 55.7% of patients. This was followed by X-rays, ordered in 45.6% of patients, and head CT, seen in 21.3%. Patients had an average (SD) of 1.2 (1.5) requested imaging modalities between the initial PCP visit and confirmed diagnosis. Cervical X-rays were requested in 29.0% of patients, and CT scans in 21.7%. The median (IQR) time from the initial PCP visit to the first cervical spine MRI was 12.5 (2.9, 31.8) months. Comparatively, the median (IQR) time from the initial PCP visit to confirmed DCM diagnosis among those who only had a cervical spine MRI was 8.8 (0.03, 37.2) months.

Among those undergoing surgery for DCM, MRI requests were seen in 64.2% of patients. Practically, all patients undergoing surgery for DMC will have had an MRI. It is possible that many patients in this case-series had MRIs done in private settings; these data would therefore not be captured by the DID. The median (IQR) time from an initial PCP visit to confirmed DCM diagnosis among those with a cervical X-ray or CT scan was 10.6 (0.03, 39.4) months. Details on imaging modality requests and characteristics can be found in Table 3.

Chapter 4.5: Main outcome and time to diagnosis

Among patients with at least one DCM-related visit, the median (IQR) time from first DCM-related visit to DCM diagnosis (including patients whose first DCM-related visits were on the day of DCM diagnosis) was 22.1 (5.7, 43.3) months. The Kaplan-Meier curve demonstrating the time from the first DCM-related visit to the first confirmed DCM diagnosis (among those with at least one DCM-related visit) is shown in Fig 2. When excluding patients whose first DCM-related visit was on the day of DCM diagnosis, the median (IQR) time from first DCM-related visit to DCM diagnosis was 25.9 (9.3, 45.1) months.

In the entire series (including both patients with and without a DCM-related visit), the mean (SD) time from the initial DCM-related visit to the first recorded DCM diagnosis was 14.3 (19.6) months. Comparatively, the median (IQR) time from the initial DCM-related visit to the first recorded DCM diagnosis was 0.8(0.03, 27.1) months (fig 3).

Chapter 4.6: Risk Factors

The following risk factors were considered when identifying predictors of a longer delay from initial outpatient PCP visit to first confirmed DCM diagnosis: sex, age, CCI, PMID, smoker status, chronic pain diagnosis, fibromyalgia diagnosis, or anxiety diagnosis. These risk factors were assessed using a Cox Proportional Hazards Model to analyze crude and adjusted hazard ratios. The results showed that male sex (HR: 1.18, 95% CI [1.15, 1.21]) and older age (>80) (HR: 1.29, 95% CI [1.13, 1.48]) were associated with shorter delays in DCM diagnosis. Meanwhile, being a previous or current smoker (HR: 0.94, 95% CI [0.91, 0.98]) and having a diagnosis of chronic pain

or fibromyalgia (HR: 0.92, 95%CI [0.85, 0.99]) were associated with longer delays in DCM diagnosis. These model results can be found in Table 4. A Kaplan-Meier curve demonstrating the time from initial PCP visit to diagnosis stratified by age is presented in Fig 4. A Kaplan-Meier curve demonstrating the time from the initial PCP visit to diagnosis, stratified by sex, is presented in Fig 5.

Chapter 4.7: Results from sensitivity analyses

The first sensitivity analysis changed the clinical time window retroactive to the first confirmed DCM diagnosis code. The previous analyses outlined in this manuscript used a 5-year window retroactive to the initial DCM diagnosis to identify all DCM-related visits. The sensitivity analyses used a 3 and 7-year time window for the median time from the initial PCP visit to the confirmed DCM diagnosis. When using the 3-year time window in patients with at least 1 false diagnosis, the median (IQR) time from the initial PCP visit to the first confirmed DCM diagnosis was 12.87 (3.20, 25.77) months. Using the 7-year time window, the median (IQR) time from the initial PCP visit to the first confirmed DCM diagnosis was 31.47(8.07, 60.97) months.

The second sensitivity analysis involved rerunning the main outcome using only certain DCM-related visit codes based on the specificity and likelihood of being mistaken for DCM. As a reminder, certain diagnoses (i.e. Carpal Tunnel Syndrome) are very likely to represent a missed DCM diagnosis (Table 3, appendix). When including only diagnoses considered very likely to represent DCM (Table 3, appendix), the median time from initial PCP visit to DCM diagnosis was 0.03 (0.03, 21.4) months. Comparatively, the median time was 0.2 (0.03, 25.6) months when including diagnoses with a medium to high likelihood of representing DCM.

Chapter 5: Discussion

This thesis aims to estimate the time from an initial PCP visit for a DCM-related complaint to final diagnosis of DCM in the general population of the UK while describing erroneous diagnoses that occur in the early disease course. Further objectives include assessing risk factors associated with lengthier delays in diagnosis within the same population. The CPRD was queried from April 1997 to March 2022 to answer these questions, and data from 36612 patients were analyzed. Several important findings are reported, including 1) the median time to DCM diagnosis is almost two years among those with at least one DCM-related visit. 2) Requests for additional imaging modalities (CT and X-rays), compared with MRI requests alone, seem to be associated with longer delays in diagnosis. 4) Male sex, older age, and higher CCI are associated with shorter delays in DCM diagnosis, while being a current or past smoker and having a diagnosis of chronic pain or fibromyalgia is associated with a longer delay in DCM diagnosis.

Chapter 5.1: Patient Characteristics and Epidemiology

Over 36000 patients diagnosed with DCM in the CPRD between April 1997 and March 2022 were included in our analyses. The male-to-female ratio of DCM prevalence is variable in the literature; however, most studies report a male predominance[4,84]. A 2013, 12-year nationwide database in Taiwan showed a marked male predominance for DCM incidence, peaking in patients over 70 (28.9 and 15.3 cases per 100,000 person-years for males and females, respectively)[84]. A 2012 study of 41 patients in Leicester found a male-to-female ratio of 2.1:1[85]. A 2013 study of Japanese

patients undergoing surgery for DCM had 636 male patients, compared to only 380 female patients (1.67:1 ratio). Our study showed a slight male predominance, with just over 50% of patients being male; however, the predominance was less marked than what has been noted in previous studies. Comparatively, our study represents the largest series of patients with DCM. Therefore, the previous manuscripts citing a male predominance may have needed a larger sample size. It is also possible that the epidemiology of DCM differs based on genetics[86–88] and that there is a higher male predominance in certain countries (i.e. the UK) versus others. We found an average age at DCM diagnosis of 67.5 (12.3), in line with previous studies. Wu and colleagues found a mean (SD) age at hospitalization of 60.35 (14), while Matsunaga and colleagues found a mean (SD) age at diagnosis of 61.8 (17.6), specifically in patients with OPLL[84,89].

The incidence and prevalence of DCM are variably reported in the literature and are the subject of significant discussion[4,84,85]. A 2015 systematic review did not reveal any article reporting an incidence or prevalence of DCM[90]; the article presents its own estimate of 1.6 surgical cases per 100,000 inhabitants based on case volumes ascertained from two Dutch Hospital centers[90]. Another systematic review from 2015 by Nouri and colleagues presented several estimates of DCM incidence and prevalence derived from low-quality data[4]. The estimates provided include an incidence and prevalence minimum of 41 and 605 per million, respectively, based on non-traumatic SCI data. Finally, Wu and colleagues estimated an overall incidence of DCM-related hospitalization of 4.04 per 100,000 person-years, based on a 12-year nationwide database[84].

Recently, Grodzinski and colleagues evaluated age-stratified estimates of DCM prevalence based on spinal cord compression data derived from UK HES data. The authors queried the UK HES

database for any admission with a primary DCM diagnosis and then calculated age-stratified incidence rates. This was done by adjusting population-level life expectancy to a standardized mortality ratio of DCM. From 2012 to 2019, the authors identified 28517 admissions for DCM and found a mean prevalence of DCM across all age groups at 0.19% (0.17, 0.21). Comparatively, we identified 21891 patients with a DCM diagnosis between April 1, 2012 and October 31, 2020, using HES data. There are several potential explanations for the discrepancy. First, the ICD-10 codes used for inclusion in our study (Table 2) were more specific to DCM than those used by Grodzinski and colleagues. Further, they cite the total number of admissions for DCM but do not specify whether these are all unique patients. Thus, it is possible that patients were admitted multiple times. In contrast, we only included unique patient IDs.

Chapter 5.2: Main Outcome and DCM-related Visits

Among patients with at least one DCM-related visit, the median (IQR) time from the first PCP visit to DCM diagnosis was 22.1 (5.7, 43.4) months or just under two years. This value is in keeping with previous estimates of time to diagnosis available in the current literature. Pope and colleagues used an online survey to survey patients with self-reported DCM (i.e., no formal diagnosis was required for study inclusion). The average reported delay in diagnosis was “1-2 years”, with greater delays reported by those identifying as Black or African Americans. Further, greater reported delays in diagnosis were associated with disease severity (on mJOA score), support dependence, and employment status. The average reported age was 54.04, with 70.8% of respondents being women. Further, roughly 55% of patients reported significant delays in diagnosis, defined as a diagnostic delay of greater than 1 year. Almost 20% of patients reported a diagnostic delay of over 5 years.

Our findings are also similar to those described by Berhbalk and colleagues. They used a retrospective study to analyze medical files of patients undergoing surgery for DCM in a single tertiary hospital in Israel. Specifically, the article retrospectively reviews the medical charts of 146 patients undergoing surgery from DCM between January 2009 and December 2010. Complete data (undefined by the authors) were available for 42 patients. These patients were then contacted by phone for additional data, including demographic information, number of physician visits, and time delay from first symptom to final diagnosis. The authors report a mean time to diagnosis of DCM from initial physician visits of 2.2 years (SD 2.3), with a mean of 5.2 (SD 3.6) physician visits for DCM-related complaints. Comparatively, we found a mean of 3.2 (5.4) physician visits for DCM-related complaints before final diagnosis. The authors also describe the most common DCM-related complaints, namely paresthesia (seen in 85.7% of patients) and gait disturbances (seen in 66.6%). Importantly, the two most common DCM-related visits given were carpal tunnel syndrome (43.1%) and radiculopathy (35.7%). The study is comparable to ours in a few ways. First, Israel's healthcare system is modern and government-funded, like the UK's. Further, patients mostly present to their family physician before being referred to a specialized physician. Despite this, the article suffers from several limitations. First, the sample size is small, reporting on only 42 patients. Second, complete data were only obtained for 42 of 146 patients eligible for inclusion, and there is no explanation for what constituted complete data. Further, the data were collected from chart reviews and through telephone conversations; both methods of data collection can lack precision due to the quality of data found in physical charts and the likelihood of recall bias from phone calls. Finally, only surgical patients were included, which may be selection bias.

In 2018, Hilton and colleagues sought to characterize the route to diagnosis and surgical assessment in patients with DCM in the UK. The authors screened 1123 cervical MRIs for signs of spinal cord compression and subsequently reviewed patient documentation to determine cases of DCM. Specifically, the clinical records of patients with spinal cord compression on MRI were examined for mention of a clinical DCM diagnosis. If this was available along with adequate clinical documentation (undefined by authors), then the patients were included in the analysis. The authors state that their referral center serves an estimated population of 5.9 million people; however, only 43 patients were included in the analysis. Of the included cases, the mean age at symptom onset was 61.4 (13.9) years, with most (65%) of patients being male. On average, patients were referred to secondary care (specialists) 6.4 months after symptom onset, with MRI scanning and neurosurgical review occurring at 12.5±13.0 and 15.8±13.5 months after symptom onset, respectively. The exact time from symptom onset to DCM diagnosis was not defined. The study also suffers from several limitations. Despite covering a population of several million, only 43 cases of DCM were analyzed over 1 year. The authors address this limitation, stating that most patients receiving treatment at their center presented with external imaging and were not eligible for inclusion in their study.

Overall, our median time from initial PCP visit for a DCM-related complaint to DCM diagnosis was 22.1 months (5.7, 43.3) among those with at least one DCM-related complaint; this is similar to the reported delays in diagnosis previously reported[13,29,78]. These results highlight the often-lengthy delays patient face before an adequate diagnosis is made. This is important, as many patients deteriorate before definitive treatment (surgery) is given[29,91]. It is important to note that the natural history of DCM is not completely understood, and but that 20-62% of patients are

thought to deteriorate at 3 to 6 year follow up[39]. The role of surgery for patients with mild disease is also not completely understood.

Significantly, our analysis revealed that 43.4% of patients received a diagnosis of DCM without having a related medical visit recorded beforehand. In essence, almost half of these patients experienced no discernible delay in the detection of DCM. Notably, the diagnosis of DCM typically falls within the purview of specialized medical professionals such as neurosurgeons, neurologists, orthopedic surgeons, or physiatrists. This observation prompts various potential explanations. Firstly, it is plausible that these patients did not initially consult a general practitioner, leading to their diagnosis being outside the scope of data captured by the CPRD. Another conceivable factor is the possibility of inaccurate data entry by primary care physicians (information bias). Despite our diligent efforts, an additional consideration is that certain symptoms, diagnoses, and signs related to DCM were not included in our compiled list (refer to Appendix, Table 3). Consequently, these aspects might not have been recognized as indicators of a DCM-related visit preceding the formal diagnosis.

Chapter 5.3: Risk factors for delays

A Cox proportional hazards model (Table 4) was used to identify predictors of a longer delay from an initial DCM-related visit to a confirmed DCM diagnosis. The results showed that male sex (fig 5) (HR: 1.18, 95% CI [1.15, 1.21]) and older age (>80, fig 4) (HR: 1.29, 95% CI [1.13, 1.48]), were associated with shorter delays in DCM diagnosis.

These results align with similar studies indicating prolonged diagnostic delays in females, as observed in cases such as tuberculosis or myocardial infarction[92,93]. These delays may be

explained by different symptomatology among women, or other socio-cultural factors. Of note, the shorter delays in diagnosis for men is not in line with previous analyses showing that women are more likely to visit their doctor than men and that women are 100 percent better at following screening and scheduled preventative care"[94].

For age (>80), it is possible that care for elderly patients is prioritized (both by the healthcare system and by patients themselves), which may explain the faster diagnosis seen among this age group. Further, being a previous or current smoker (HR: 0.94, 95% CI [0.91, 0.98]) and having a diagnosis of chronic pain or fibromyalgia (HR: 0.92, 95%CI [0.85, 0.99]) were associated with longer delays in DCM diagnosis (Table 4). These results may be due to a decreased desire to investigate smokers presenting with unexplainable signs and symptoms. The finding that chronic pain and fibromyalgia patients have longer delays in diagnosis of DCM is understandable given that many of the complaints (e.g. pain) associated with DCM may be falsely attributed to the fibromyalgia diagnosis. It is also possible that physicians treat complaints from these populations less seriously, in certain cases. The time from an initial PCP visit to surgery was not assessed in this manuscript. While several risk factors may overlap with time to diagnosis, there are likely differences. For example, while female sex is a risk factor for delays in DCM diagnosis, it may not necessarily be a risk factor for time to surgery. Future manuscripts that analyze the time from DCM diagnosis to surgery will be valuable, as they can help clinicians identify at-risk patients and streamline surgical pathways.

Chapter 5.4: Imaging modalities

An accurate DCM diagnosis requires compatible clinical suspicion and evidence of myelopathic compression on radiological imaging. While several imaging modalities are often requested in

patients with DCM (i.e. CT scans, X-rays, EMGs), MRIs remain the gold standard for diagnosing DCM. Patients in our study had an average (SD) of 1.2 (1.5) imaging requests. Our study showed that MRIs were the most common (55.7%) imaging modality (Table 3) requested by their PCP in patients with DCM. While expected, these percentages likely underrepresent the true number of patients with DCM who have had an MRI. Practically, MRIs are requested in every patient with a DCM diagnosis; a formal DCM diagnosis is rarely made without an MRI[14,26,31]. The diagnostic imaging dataset (DID) collects detailed information about diagnostic imaging tests taken from NHS providers' radiological information systems[81]. Thus, the DID will not collect data from patients who elect to undergo their imaging in private settings. Our results may, therefore, indicate that a significant proportion of patients in the UK choose to have their imaging workup done in private practices. This is supported by the lengthy median wait from initial PCP visit to first cervical MRI, which was 12.5 (2.9, 31.8) months in our series. Further, the median (IQR) time from initial PCP visit to DCM diagnosis among patients with only a cervical spine MRI was 8.8 months (0.03, 37.2), significantly less than the time to diagnosis among those who had a cervical X-ray or CT scan was 10.6 (0.03, 39.4) months. This finding suggests that PCP physicians wait to screen patients with suspected DCM with an X-ray or cervical CT, before referring them for an MRI. PCPs may elect to start their investigation with simpler imaging modalities rather than MRIs due their limitations, including long wait times, convenience, and cost[36,37]. However, our results highlight that PCP physicians should instead immediately order an MRI when DCM is suspected. If the PCP sees value in cervical X-rays and CT scans, they should order the investigations concomitantly, along with an MRI.

Chapter 5.5: Strengths and Limitations

The current report represents the most comprehensive analysis of the time window from clinical presentation to diagnosis in patients with DCM. Three previous manuscripts have attempted to define the time to diagnosis in patients with DCM; however, they have several limitations, including small sample size, data quality, and lack of defined predictors associated with longer delays in diagnosis. Our sample size is significant, including over 36000 patients from the CPRD, an anonymized UK-based data network of PCP practices covering over 16 million registered patients. The CPRD data has many strengths, including its coverage, size, follow-up time, and data quality. Further, a systematic review was used to generate a complete list of signs and symptoms of DCM to optimize the identification of DCM patients. Several Kaplan-Meier curves for time to diagnosis were computed, including among the entire series, stratified by age and stratified by sex. We also repeated many analyses for time from initial PCP visit to surgical treatment, which is particularly interesting to clinicians. Further, Cox-proportional hazards models were used to assess factors associated with longer delays in diagnosis and longer delays to surgical treatment. The Cox regression model assesses multiple factors associated with "longer-survival", which in our study was defined as longer time to diagnosis. Further, a Cox proportional hazards model was preferred over a logistic regression model since the former has more statistical power; this is because we analyzed the time from initial PCP visit to diagnosis.

This study also has limitations. Although highly generalizable to the UK and likely to European and Western Countries, the findings described in this manuscript are less applicable elsewhere. A time-window of 5 years before DCM diagnosis was set to identify the first visit for a DCM-related complaint, potentially representing selection bias. This time-window was set somewhat arbitrarily based on the opinions of expert surgeons who manage this condition regularly. This

time window may have missed some patients who presented very early, e.g. if the first signs and symptoms appeared over 5 years before the DCM diagnosis was given. To address this, we conducted a sensitivity analysis using a time-window of 7 years. We found that the analysis that used a 7-year window increased the median time to diagnosis from 22.1 months (5-year window) to 31.47 months (7-year window). These findings suggest that DCM may present very early, with subtle findings.

As an observational study, confounding is likely. We included a variety of factors in our Cox proportional hazards model to address confounding. Residual confounding is still possible, as it is likely that other confounding factors were not adjusted for due to data not being readily available. It is also possible that residual confounding existed between variables included in the model, i.e. within age brackets. However, only the oldest age bracket (>80 years) was associated with shorter delays in DCM diagnosis.

Another limitation is the lack of clinically accepted gold-standard criteria for the diagnosis of DCM. The diagnosis currently relies on imaging and clinical findings and assessments from expert physicians. Likewise, there is no gold-standard criteria for an administrative DCM diagnosis. We attempted to circumvent this by using only highly specific diagnostic codes for DCM, which include the keywords “myelopathy” and “cervical”. However, despite great efforts to identify all possible DCM-related initial visits in patients with DCM using a systematic review, several patients with alternate diagnostic codes were likely missed. Overall, the results from this manuscript are also limited by the inherent quality of large administrative health data, including missing, incomplete, or misclassified data. The data included in the CPRD also does not readily

include metrics that can define DCM severity, which is of significant interest when determining which patients should be sent for surgical treatment.

Chapter 6: Conclusions

The median time from an initial DCM-related visit to a formal DCM diagnosis is 22.1 months. The most common DCM-related visits were for pain, falls, numbness or paresthesia. Imaging requests other than cervical spine MRIs may cause further delays in diagnosis and treatment. Female sex, age <80, being a previous or current smoker, and having a diagnosis of chronic pain or fibromyalgia are associated with longer delays in DCM diagnosis. Future manuscripts should analyze delays from diagnosis to surgery and quantify the impact of these delays on post-operative neurologic course.

Tables and Figures

Signs	Symptoms
Motor: -Pyramidal weakness -Segmental weakness Sensory: -Sensory loss Reflexes: -Hyperreflexia -Hoffman sign -Lhermitte's sign -Finger Flexor Reflex -Babinski Other: -Spasticity, especially in lower extremities -Gait disturbance	Decreased manual dexterity: -Difficulty with fine motor tasks, i.e. buttoning a shirt, eating with a spoon -Handwriting changes -Frequent dropping of objects -Difficulty clasping small items Bowel and Bladder: -Urinary or fecal incontinence Abnormal gait and balance -Difficulty walking on flat surface -Difficulty with stairs -Need for walking aids (i.e. cane) -Frequent falls Sensory changes -Paresthesia -Loss of sensation Pain -Radiculopathy -Axial/mechanical

Table 1: Signs, symptoms, and differential diagnoses associated with DCM.[75].

Characteristic	**N=36612**
Sex, male N(%)	19949 (51.1%)
Age at diagnosis Mean, (SD)	67.5 (12.3)
Age at diagnosis Median, (IQR)	68 (58,77)
Smoker N (%)	31171 (79.9%)
At least one DCM-related visit N(%)	22103 (56.6%)
Visits for a DCM-related visit before final DCM diagnosis* Mean, (SD)	3.2 (5.4)
DCM-related visits categories, %	
Pain	41.9
Falls	19.1
Paresthesia	15.4
Other	23.6

Table 2: Baseline characteristics of patients included in the series. *Among those with at least one DCM-related visit.

Imaging characteristic	**N=21891***
Patients with at least one imaging modality N, (%)	13905 (63.5%)
Cervical MRI %	55.7%
Cervical X-rays %	29.0%
Head CT %	21.3%

Number of imaging requests before DCM diagnosis, Mean (SD)	1.2 (1.5)
Time to cervical MRI from first related-visit, months†, Median, (IQR)	12.5 (2.9, 31.8)
Time to cervical MRI from first related-visit, months, Median, (IQR) ‡	8.8 (0.03, 37.2)

Table 3: Table demonstrating the characteristics of imaging modalities. *Represents the number of patients with HES DID data, between April 1st 2012 and October 31st 2020. †Among entire series. ‡Among those who only had a cervical MRI.

Risk factor	**Crude HR (95% CI)**	**Adjusted HR (95% CI)**
Male	1.17 (1.14-1.20)	1.18 (1.15-1.21)
Age		
< 40	1.00 (Reference)	1.00 (Reference)

40-49	0.94 (0.82-1.07)	0.95 (0.83-1.09)
50-59	1.03 (0.90-1.18)	1.04 (0.91-1.19)
60-69	1.01 (0.89-1.16)	1.02 (0.90-1.17)
70-79	1.06 (0.93-1.21)	1.07 (0.94-1.22)
≥ 80	1.29 (1.13-1.47)	1.29 (1.13-1.48)
CCI		
0	1.00 (Reference)	1.00 (Reference)
1-2	0.98 (0.95-1.01)	0.97 (0.94-1.00) [§]
3-4	1.01 (0.97-1.05)	0.98 (0.95-1.02)
≥5	1.08 (1.03-1.12)	1.03 (0.99-1.08)
PMID		
1	1.00 (Reference)	1.00 (Reference)
2	0.97 (0.93-1.01)	0.98 (0.94-1.02)
3	0.97 (0.93-1.01)	0.98 (0.94-1.02)
4	0.96 (0.92-1.00)*	0.99 (0.95-1.03)
5	0.96 (0.92-1.00)[‡]	0.99 (0.95-1.03)
Smoking		
Never	1.00 (Reference)	1.00 (Reference)
Ever	0.96 (0.92-0.99)	0.94 (0.91-0.98)
Unknown	1.48 (1.17-1.88)	1.40 (1.10-1.77)
Chronic pain or fibromyalgia	0.96 (0.79-0.93)	0.92 (0.85-0.99)
Depression	0.93 (0.90-0.95)	0.98 (0.95-1.01)
Anxiety	0.93 (0.90-0.96)	0.98 (0.94-1.02)

Table 4: Hazard ratio of risk factors for a longer delay from initial DCM-related visit to outpatient PCP to first confirmed DCM diagnosis. Abbreviations: HR, hazard ratio; CI, confidence interval; CCI, Charlson-comorbidity-index; PMID, patient level index of multiple deprivation. * The upper limit is 1.0046 [‡] The upper limit is 0.997. [§]The upper limit is 1.003.

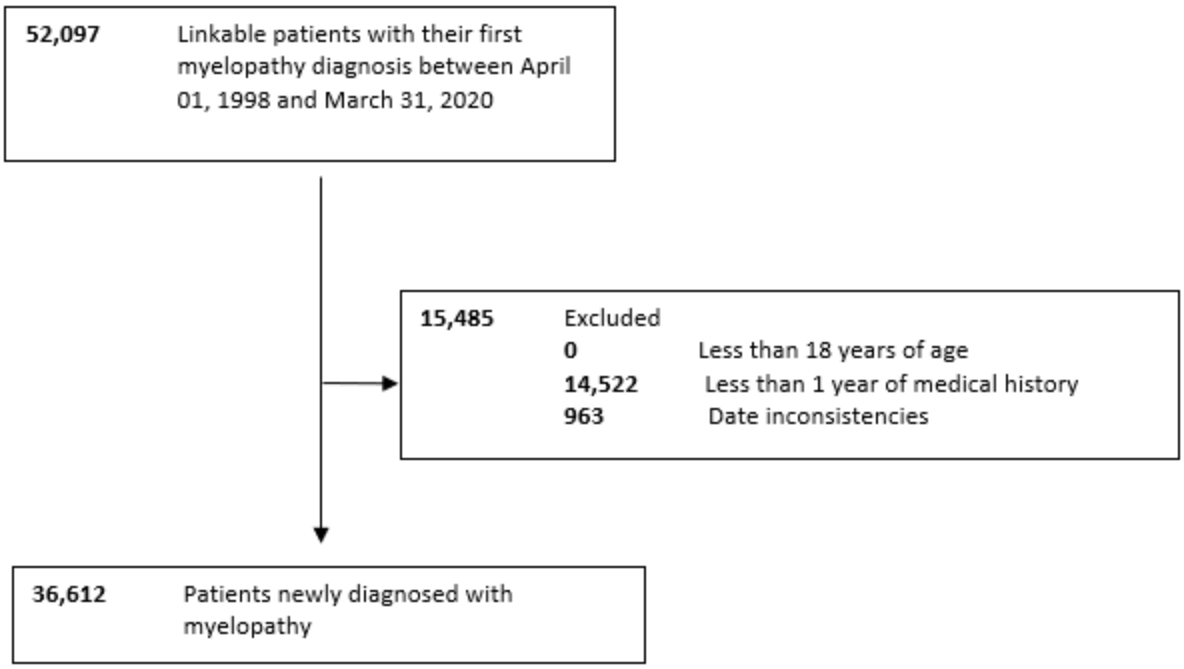


Fig 1: Study flow chart showing included patients.

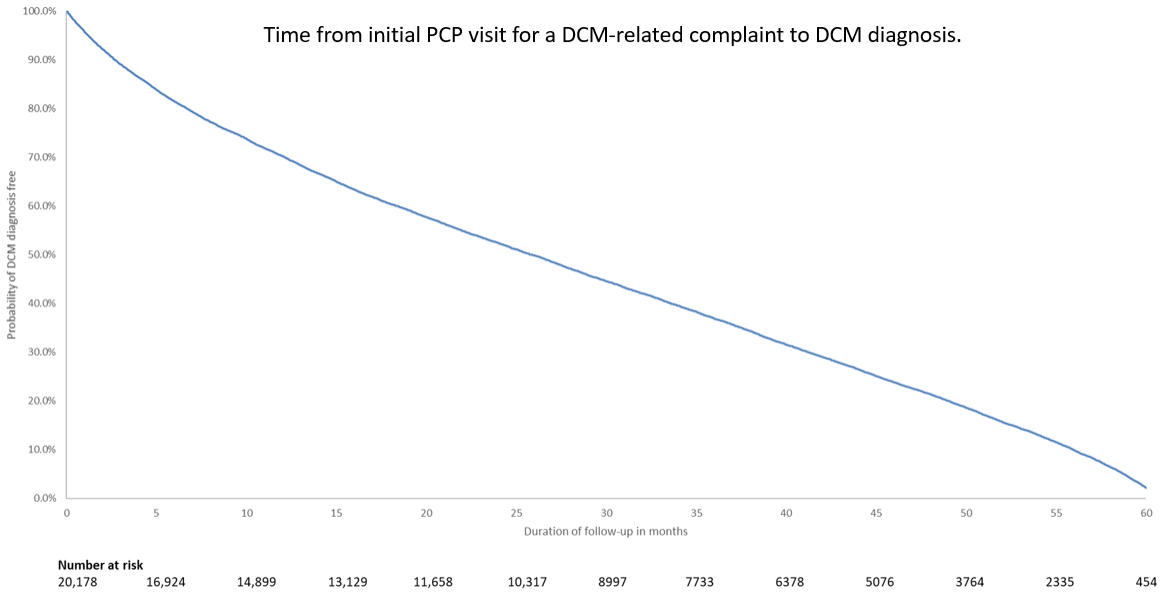


Fig 2: Kaplan Meier curve demonstrating the time to diagnosis among those with at least one prior PCP visit for a DCM-related complaint.

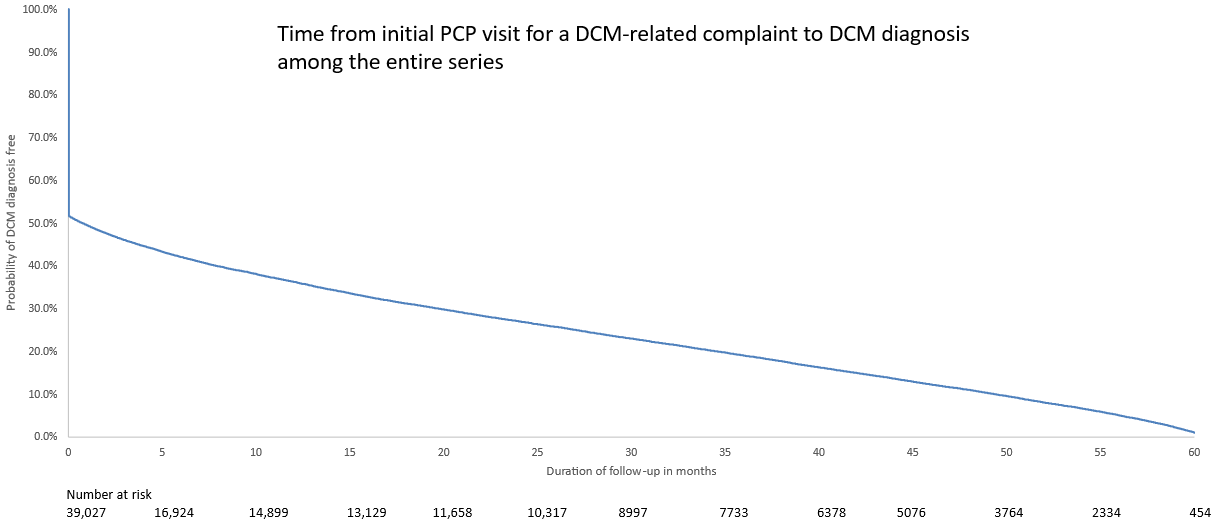


Fig 3: Kaplan Meier curve demonstrating the time to diagnosis in the entire series. This includes all patients identified in the series, including those with no identified DCM-related visit prior to DCM-diagnosis.

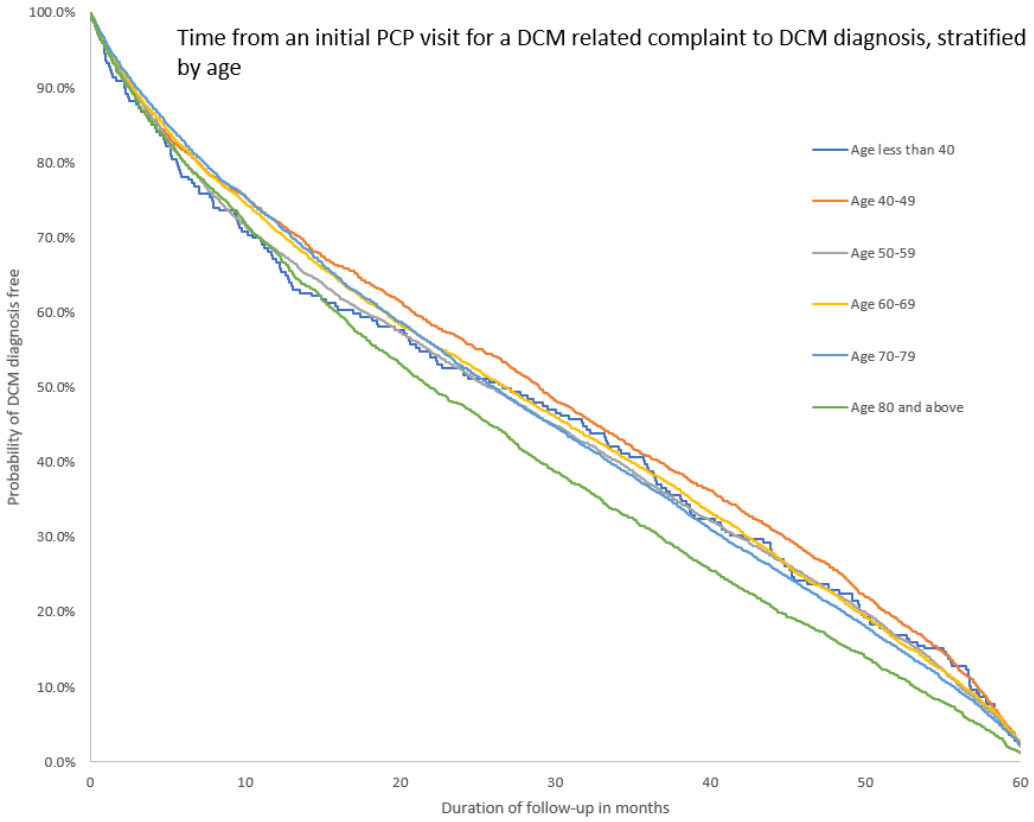


Fig 4: Kaplan Meier curve demonstrating the time from initial PCP visit to diagnosis, stratified by age.

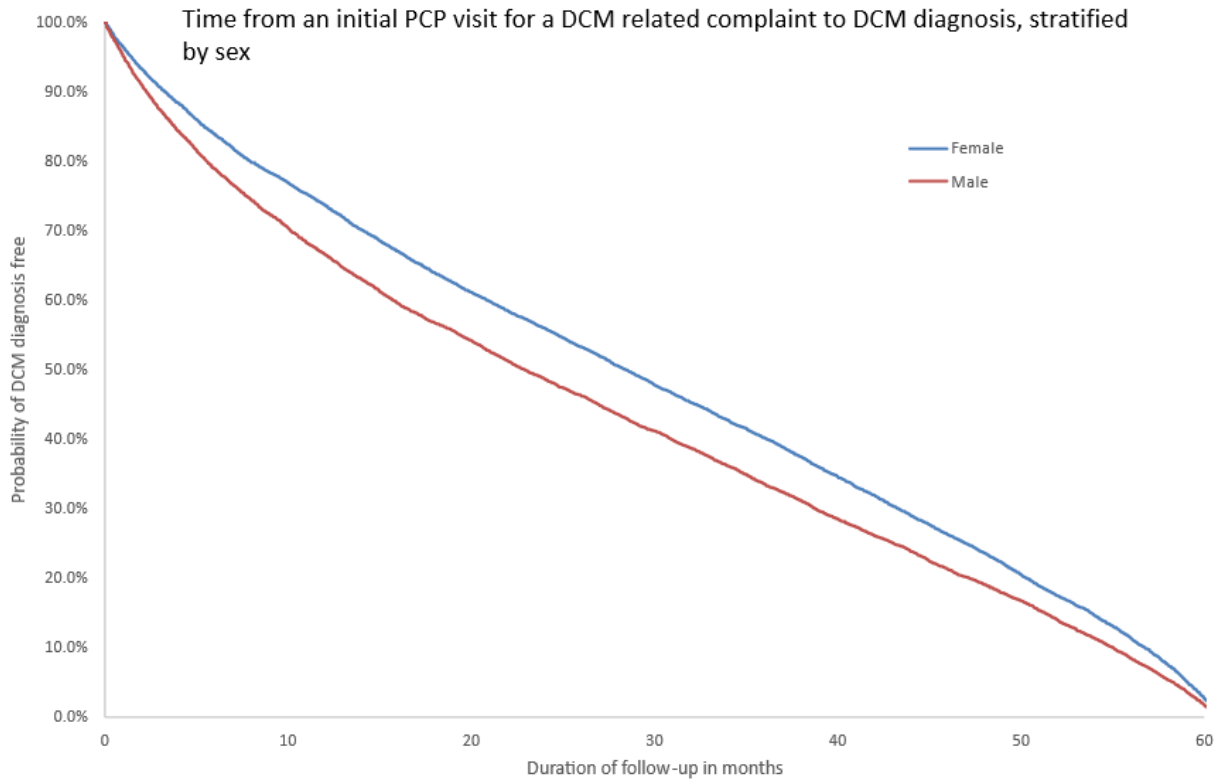


Fig 5: Kaplan Meier curve demonstrating the time from initial PCP visit to diagnosis, stratified by sex.

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Appendix:

Literature review 1- Signs, symptoms, and differential diagnosis of DCM:

Many pathologies can be identified as DCM-related visits of DCM. The following list was made using a literature review of diagnoses of DCM and using the clinical knowledge and expertise of senior authors.

The following search terms were used to query Pubmed: “differential diagnosis degenerative cervical myelopathy” = 1538 results AND “cervical myelopathy mimic” = 134 results.

Total: 1672

Literature review 2-Time to diagnosis in patients with DCM:

The following literature review was done to capture all current available estimates of the time from initial presentation to final diagnosis of DCM.

The following search terms were used to query Pubmed:

“Delay diagnosis cervical myelopathy” = 685 results AND “time diagnosis cervical myelopathy” = 2867 results.

Total: 3552

Definition of myelopathy:

The following terms and corresponding SNOMED-CT and medical codes, identified through a manual search of CPRD code browsers, ICD-10 code browsers, and a previous publication by Jaglal and colleagues are presented below. The CPRD was queried using medical codes (table 1), while HES was queried using ICD-10 codes (table 2).

Table 1: Codes identifying a diagnosis of myelopathy within CPRD data.

Term	SNOMED Concept ID	Medical Code

Spinal stenosis in cervical region	83561009	3859631000006115
Myelopathy	48522003	12704511000006114
Cervical myelopathy	202664003	311064012
Degenerative myelopathy	70350007	NA
Disc prolapse with myelopathy	202728009	311159011
cervical disk prolapse with myelopathy	202729001	311160018
Myelopathy due to cervical spondylosis	1156963006	NA
spinal stenosis of neck with myelopathy	9971000119105	NA
Intervertebral disc disorder with myelopathy	44983007	NA
Myelopathy due to two-level cervical spondylosis (disorder)	1156969005	NA
Recurrent atlantoaxial subluxation with myelopathy (disorder)	202830000	311304017
Myelopathy due to single-level cervical spondylosis (disorder)	1156965004	NA
Myelopathy due to multiple-level cervical spondylosis (disorder)	1156967007	NA
Intervertebral disc disorder of cervical region with myelopathy (disorder)	75467001	NA
Spondylosis of cervical spine	445018004	NA
Degenerative cervical stenosis	202761002	311195015
stenosis of spinal canal due to	203713000	312501014, 4822371000006116
Spinal stenosis in cervical region	83561009	138588018
Myelopathy due to spinal cord compression	16219341000119105	NA
myelopathy due to intervertbral disc disease	192905004	297148015

Table 2: Codes identifying a diagnosis of myelopathy within HES data.

ICD-10 term	ICD-10 code
Other spondylosis, with myelopathy	M.47.1
Spinal stenosis, cervical region	M48.02
Melopathy, NOS	G95.9
cervical disc disorder with myelopathy	M50.0, G99.2
Recurrent atlantoaxial subluxation with myelopathy	M43.3

Table 3: Codes identifying a diagnosis suspicious for myelopathy. *denotes the likelihood that the registered code is a missed diagnosis of DCM, as determined by literature review and the authors' clinical knowledge.

Diagnosis	Term	MedCodeId	Likelihood*
Abscess	Intraspinal abscess	3482014	Low
Abscess	Intraspinal abscess NOS	296927014	Low
Abscess	Intraspinal epidural abscess	3.53472E+15	Low
Abscess	Tuberculous intraspinal abscess	8.3031E+13	Low
ALS	Amyotrophic lateral sclerosis	142653015	High
ALS	Amyotrophic lateral sclerosis with dementia	5.00542E+15	High
Arachnoid Cyst	Arachnoid cyst	56081016	Low
Arachnoid Cyst	Arachnoid cyst	1.36464E+16	Low
Arachnoid Cyst	Intradural spinal arachnoid cyst	5.32642E+15	Low
Arachnoid Cyst	Spinal arachnoid cyst	5.32641E+15	Low
Behcet syndrome	Behcet syndrome	6.00282E+15	Low
Behcet syndrome	Behcet's disease	6.00279E+15	Low
Behcet syndrome	Behcet's syndrome	454287012	Low
Carpal Tunnel	Bilateral Carpal Tunnel Decompression	9.03921E+14	High
Carpal Tunnel	Carpal tunnel decompression	2551763014	High
Carpal Tunnel	Carpal tunnel nerve release	9.03931E+14	High
Carpal Tunnel	Carpal tunnel release	494859016	High
Carpal Tunnel	Carpal tunnel syndrome	95473010	High
Carpal Tunnel	CTD - Carpal tunnel decompression	3.2686E+15	High
Carpal Tunnel	CTR - Carpal tunnel release	3.26859E+15	High
Carpal Tunnel	CTS - Carpal tunnel syndrome	497880019	High

Carpal Tunnel	Endoscopic carpal tunnel release	266128011	High
Carpal Tunnel	Injection of carpal tunnel	282332019	High
Carpal Tunnel	Referral for carpal tunnel injection	2.20373E+15	High
Carpal Tunnel	Release of carpal tunnel for median nerve decompression	3.26854E+15	High
Carpal Tunnel	Release of carpal tunnel for nerve decompression	3.26853E+15	High
Carpal Tunnel	Re-release of carpal tunnel	266126010	High
Carpal Tunnel	Revision of carpal tunnel release	7.26617E+15	High
Carpal Tunnel	Revision of decompression of carpal tunnel	7.26615E+15	High
Central cord syndrome	Central cord syndrome	5.66908E+15	High
Central cord syndrome	Central cord syndrome of cervical spinal cord	7.81638E+15	High
Central cord syndrome	Central cord syndrome of cervical spinal cord at C3 level	7.81643E+15	High
Chiari Malformation	Chiari malformation	5.46731E+14	Low
Congenital cervical spondylolisthesis	Congenital cervical spondylolisthesis	7.05068E+15	Low
Copper deficiency	Copper deficiency	479672013	Low
Cubital tunnel	Cubital tunnel release	266153014	Medium
Cubital tunnel	Cubital tunnel syndrome	93418010	Medium
Decreased manual dexterity	Poor manual dexterity	449865015	High
DISH	Diffuse idiopathic skeletal hyperostosis	484890016	High
DISH	DISH - Diffuse idiopathic skeletal hyperostosis	3.0073E+15	High
dural av fistula	Type I spinal dural AV fistula	7.37657E+15	Low
Epidural abscess	Epidural abscess	103013011	Low
Epidural abscess	Epidural intraspinal abscess	7.68811E+14	Low
Epidural abscess	Spinal epidural abscess	3.5347E+15	Low
Epidural hematoma	Epidural haematoma	7.58304E+15	Low
Extradural Abscess	Extradural intraspinal abscess	1232479011	Low
Faecal incontinence	Faecal incontinence with faecal urgency	8.04514E+15	Medium
Faecal incontinence	Fecal incontinence with fecal urgency	8.04515E+15	Medium
Falls	Accidental falls NOS	329383013	High

Falls	At risk for falls	4.4317E+15	High
Falls	At risk of falls	1495651015	High
Falls	Discussion about falls	8.46579E+15	High
Falls	Fall on stairs	2534630017	High
falls	Falls	252318014	High
falls	Falls education	6.51735E+15	High
Falls	History of falls	9.82461E+14	High
Falls	Number of falls in last month	8.35261E+15	High
falls	Number of fractures due to falls in last 12 months	8.3526E+15	High
Falls	Number of visits to general practitioner due to falls in past 12 months	8.35262E+15	High
Falls	Observation of falls	5.8517E+15	High
Falls	Other falls	329380011	High
Falls	Recurrent falls	417481019	High
Falls	Referral to elderly falls prevention clinic	4.06941E+14	High
Falls	Referral to falls service	4.05101E+14	High
Falls	Streamed from emergency department to falls service following initial assessment	8.4521E+15	High
falls	Unexplained falls	6.70525E+15	High
Falls	Unexplained recurrent falls	6.70524E+15	High
fecal incontinence	Daytime faecal incontinence	8.26341E+15	Medium
fecal incontinence	Night time faecal incontinence	8.2635E+15	Medium
fecal incontinence	Complete faecal incontinence	8.46581E+15	Medium
fecal incontinence	Idiopathic faecal incontinence	6.45992E+15	Medium
fecal incontinence	Functional faecal incontinence	7.83749E+15	Medium
fecal incontinence	Neuromyopathic faecal incontinence	5.08946E+15	Medium
Folic acid deficiency	Folic acid deficiency	293006011	Low
Gait/balance	Abnormal coordination	5.9051E+15	High
Gait/balance	Abnormal gait	37486015	High
Gait/balance	Abnormal gait	318013019	High
Gait/balance	Abnormal gait due to impairment of balance	7.13972E+15	High
Gait/balance	Balance assessment	3.71341E+14	High
Gait/balance	Balance impairment	6.47434E+15	High
Gait/balance	Coordination problem	5.90509E+15	High

Gait/balance	Decreased balance	9.60081E+14	High
Gait/balance	Decreased coordination	6.99215E+15	High
Gait/balance	Deterioration in ability to walk up stairs	1.7549E+15	High
Gait/balance	Difficulty climbing stairs	5.66178E+15	High
Gait/balance	Difficulty managing stairs	5.89587E+15	High
Gait/balance	Difficulty managing steps and stairs	5.8958E+15	High
Gait/balance	Difficulty walking down stairs	5.66185E+15	High
Gait/balance	Does not manage stairs	5.89586E+15	High
Gait/balance	Does not manage steps and stairs	5.89579E+15	High
Gait/balance	Examination of gait	5.56635E+15	High
Gait/balance	Feels off balance	372880015	High
Gait/balance	Functional gait abnormality	8.02176E+15	High
Gait/balance	Gait abnormality	317119019	High
Gait/balance	Gait problem	2.85572E+15	High
Gait/balance	Gait/ambulation disturbance	9.60101E+14	High
Gait/balance	Impairment of balance	6.47432E+15	High
Gait/balance	Incoordination	317130016	High
Gait/balance	Incoordination	318014013	High
Gait/balance	Incoordination	1.80708E+15	High
Gait/balance	Incoordination symptom	397975013	High
Gait/balance	Incoordination symptom NOS	253033018	High
Gait/balance	Keeps losing balance	5.2792E+15	High
Gait/balance	Lack of coordination	317126019	High
Gait/balance	Loss of balance	5.66305E+15	High
Gait/balance	Multifactorial gait problem	7.08374E+15	High
Gait/balance	Needs help on stairs	256969015	High
Gait/balance	No incoordination	253027010	High
Gait/balance	O/E - gait NOS	402515019	High
Gait/balance	O/E - generally off balance	255070013	High
Gait/balance	O/E - Parkinson gait	402514015	High
Gait/balance	O/E-festination-Parkinson gait	402512016	High
Gait/balance	Poor balance	5.27921E+15	High
Gait/balance	Problem with balance	6.47433E+15	High
Gait/balance	Reason for referral: Dizziness/Balance Problems	1.7766E+15	High
Gait/balance	Unable to balance when bending	5.68725E+15	High

Gait/balance	Unable to balance when reaching	5.68731E+15	High
Gait/balance	Unable to balance when standing	5.66319E+15	High
Gait/balance	Unable to balance when standing with feet apart	2.73413E+15	High
Gait/balance	Unable to balance when standing with feet in semi-tandem stance	2.73417E+15	High
Gait/balance	Unable to balance when standing with feet in tandem stance	2.73419E+15	High
Gait/balance	Unable to balance when standing with feet together	2.73415E+15	High
Gait/balance	Unable to climb stairs	256968011	High
Gait/balance	Unable to manage stairs	5.89583E+15	High
Gait/balance	Unable to manage steps and stairs	5.89576E+15	High
Gait/balance	Unable to run up stairs	5.66604E+15	High
Gait/balance	Unable to walk down stairs	5.66181E+15	High
Gait/balance	Unsteady gait	6.54593E+15	High
Gait/balance	Unsteady gait [D]	9.31931E+14	High
Gait/balance	Waddling gait	5.52809E+15	High
Gait/balance	Worsening balance	1.74625E+15	High
Gait/balance	Needs walking aid in home	250470015	High
Gait/balance	Walking difficulty due to unspecified site	310951016	High
Gait/balance	Difficulty walking	310958010	High
Gait/balance	Walking distance reduced	370598017	High
Gait/balance	Uses single walking stick	2838470011	High
Gait/balance	Walking disability	6.20911E+14	High
Gait/balance	Unsteady when walking	2.86069E+15	High
Gait/balance	Walking aid	4.93373E+15	High
Gait/balance	Difficulty walking on the flat	5.66109E+15	High
Gait/balance	Difficulty walking up hill	5.66136E+15	High
Gliomatosis cerebri	Gliomatosis cerebri	2.91829E+15	Low
Guillain barre	Guillain Barre syndrome	3.15984E+15	low
Hematomyelia	Myelopathy due to haematomyelia	297142019	low
HTLV	Human T-lymphotropic virus 1	3.76004E+15	low
HTLV	Human T-lymphotropic virus 1 infection	7.1067E+15	low
Hyperreflexia	Hyperreflexia	3.91213E+15	high

lupus	Systemic lupus erythematosus	92208011	low
Lyme disease	Lyme disease	39462014	low
Lyme disease	Suspected Lyme disease	2.39003E+15	low
meningioma	Spinal meningioma	290627016	low
Multiple sclerosis	Generalised multiple sclerosis	297179016	Medium
Multiple sclerosis	Management of multiple sclerosis in early disease phase	6.99731E+14	Medium
Multiple sclerosis	Management of multiple sclerosis in onset phase	6.99671E+14	Medium
Multiple sclerosis	Management of multiple sclerosis in stable disability phase	6.99791E+14	Medium
Multiple sclerosis	Multiple sclerosis	41398015	Medium
Multiple sclerosis	Multiple sclerosis NOS	297181019	Medium
Multiple sclerosis	Multiple sclerosis of the spinal cord	297177019	Medium
Multiple sclerosis	Primary progressive multiple sclerosis	2692565012	Medium
Multiple sclerosis	Secondary progressive multiple sclerosis	2674605012	Medium
Nerve injury	Injury of nerve of upper extremity	325422012	Medium
Nerve injury	Injury of nerve of upper extremity	3.91071E+14	Medium
Nerve injury	Intraspinal nerve root divisn.	9.03801E+14	Medium
Nerve injury	Nerve conduction testing	256245010	Medium
Nerve injury	Periph. nerve action potential	262723014	Medium
Nerve injury	Peripheral nerve entrapment syndrome	3.23934E+15	Medium
Neuromyelitis optica	Neuromyelitis optica	41961013	low
Neurosurgeon	Private referral to neurosurgeon	284089011	Medium
Neurosurgeon	Referral to neurosurgeon	451837010	Medium
Neurosurgeon	Referral to neurosurgical service	4.72461E+15	Medium
NPH	Dementia associated with normal pressure hydrocephalus	7.51073E+15	Medium
NPH	Normal pressure hydrocephalus	51470011	Medium
NPH	NPH - Normal pressure hydrocephalus	2.99575E+15	Medium

Numbness/parasthesia	Complaining of paraesthesia	1.40774E+16	High
Numbness/parasthesia	Numbness	253009012	High
Numbness/parasthesia	Numbness and tingling of skin	7.9648E+15	High
Numbness/parasthesia	Numbness of finger	5.99003E+15	High
Numbness/parasthesia	Numbness of hand	452966011	High
Numbness/parasthesia	Numbness of limbs	454088013	High
Numbness/parasthesia	Numbness of upper limb	1.8052E+15	High
Numbness/parasthesia	O/E - paraesthesia in hands	254993010	High
Numbness/parasthesia	O/E - paraesthesia present	254992017	High
Numbness/parasthesia	Paraesthesia	317163011	High
Numbness/parasthesia	Paraesthesia (numbness/tingling)	3.9792E+15	High
Numbness/parasthesia	Paraesthesia of arm	4.06078E+15	High
Numbness/parasthesia	Paraesthesia of bilateral hands	1.39413E+16	High
Numbness/parasthesia	Paraesthesia of finger	3637373011	High
Numbness/parasthesia	Paraesthesia of foot	5.9847E+15	High
Numbness/parasthesia	Paraesthesia of hand	5.98468E+15	High
Numbness/parasthesia	Paraesthesia of lower limb	7.10857E+15	High
Numbness/parasthesia	Paraesthesia of upper limb	4.06074E+15	High
Numbness/parasthesia	Paralysis	450557012	High
Numbness/parasthesia	Paralysis present	253000011	High
Numbness/parasthesia	Paraplegic gait	5.27985E+15	High
Numbness/parasthesia	Paresthesia (numbness/tingling)	3.97921E+15	High
Numbness/parasthesia	Paresthesia (numbness/tingling) of arm	4.0608E+15	High
Numbness/parasthesia	Transient paraesthesia	216639013	High
Orthopedics	Private referral to orthopaedic surgeon	284088015	Medium
Orthopedics	Referral to orthodontic clinic	284061013	Medium
Orthopedics	Referral to orthopaedic physiotherapist practitioner	4.07341E+14	Medium
Orthopedics	Referral to orthopaedic service	4.72457E+15	Medium
Orthopedics	Referral to orthopaedic special interest general practitioner	1.63855E+15	Medium
Orthopedics	Referral to orthopaedic surgeon	451836018	Medium
Orthopedics	Referral to orthopaedic triage service	2.16931E+15	Medium

Orthopedics	Referral to orthopedic service	4.7246E+15	Medium
Orthopedics	Referral to orthopedic surgeon	5.9792E+15	Medium
Pain	Arm pain	165844010	High
Pain	Chronic neck pain	7.96763E+15	High
Pain	Mechanical neck pain	1.27354E+16	High
Pain	Neck pain	2.15271E+14	High
Pain	Neck pain co-occurrent with neck stiffness following whiplash injury to neck	7.86394E+15	High
pseudogout	Pseudogout	359360013	Low
Radiculopathy	Cervical radiculopathy	3.38273E+15	High
Radiculopathy	Cervical spondylosis with radiculopathy	311091014	High
Radiculopathy	Radicular pain	2.68593E+15	High
Radiculopathy	Radiculopathy	8.54731E+14	High
Rheumatoid arthritis	Myopathy due to rheumatoid arthritis	297641010	Medium
Rheumatoid arthritis	Polyneuropathy in rheumatoid arthritis	297544012	Medium
Rheumatoid arthritis	Rheumatoid arthritis	116082011	Medium
Spasticity	Exercises for spasticity	283317016	High
Spasticity	Lower limb spasticity	1488401018	High
Spasticity	O/E - gait spastic	254948019	High
Spasticity	O/E - spastic gait	254949010	High
Spasticity	Spastic gait	317122017	High
Spasticity	Spasticity	4.91448E+15	High
Spasticity	Upper limb spasticity	1488402013	High
Spasticity	Worsening limb spasticity	1.74785E+15	High
synovial cyst	Synovial cyst	4.35295E+15	low
syringomyelia	Syringomyelia	178736016	low
transverse myelitis	Transverse myelitis	28148010	low
transverse myelitis	Transverse myelitis	9.1711E+13	low
tuberculous myelitis	Tuberculous myelitis	57296016	low
tuberculous osteomyelitis	Tuberculous osteomyelitis	3.45467E+15	low
urinary symptoms	Functional urinary symptoms	208692015	High
urinary symptoms	Intermittent urinary symptoms	7.38396E+15	High
urinary symptoms	Postural urinary symptoms	1.93669E+15	High
urinary symptoms	Total urinary symptoms	208698016	High
urinary symptoms	UI - urinary symptoms	4.59025E+15	High
urinary symptoms	Urge urinary symptoms	3.92321E+15	High

urinary symptoms	Urgency - urination	3.72084E+15	High
urinary symptoms	Urgency of micturition	124716012	High
urinary symptoms	Urgency to micturate	3.72088E+15	High
urinary symptoms	Urgency to pass urine	3.7209E+15	High
urinary symptoms	urinary symptoms	305212011	High
urinary symptoms	urinary symptoms	317524010	High
urinary symptoms	urinary symptoms of non-organic origin	478855012	High
urinary symptoms	Urinary sphincter weakness incontinence	6.34273E+15	High
Vitamin B12 deficiency	Neuromyelopathy due to vitamin B12 deficiency	3.48404E+15	Low
Vitamin B12 deficiency	Vitamin B12 deficiency	293008012	low
Weakness	General weakness	2.71865E+15	High
Weakness	Hand muscle weakness	5.85074E+15	High
Weakness	Muscle weakness	5.8981E+13	High
Weakness	Muscle weakness of limb	7.70508E+15	High
Weakness	Muscle weakness of upper limb	7.70507E+15	High
Weakness	O/E - paresis (weakness)	254826012	High
Weakness	Proximal muscle weakness	5.27843E+15	High
Weakness	Quadriceps weakness	5.88707E+15	High
Weakness	Weakness	2.71868E+15	High
Weakness	Weakness - general	2.98141E+14	High
Weakness	Weakness of arm	372825010	High
Weakness	Weakness of bilateral hands	9.83589E+15	High
Weakness	Weakness of distal arms and legs	5.27847E+15	High
Weakness	Weakness of foot	5.8674E+15	High
Weakness	Weakness of hand	5.86204E+15	High
Weakness	Weakness of left hand	9.83587E+15	High
Weakness	Weakness of leg	372826011	High
Weakness	Weakness of lower arm	1.80705E+15	High
Weakness	Weakness of upper arm	1.80571E+15	High
Weakness	Weakness present	252995016	High

Table 4: Included imaging tests investigated using the DID.

DI_Term	**SCT_Description**
CT Brachial plexus	Computed tomography of brachial plexus (procedure)
CT Brachial plexus with contrast	Computed tomography of brachial plexus with contrast (procedure)
CT Facet joint injection cervical	Injection of cervical zygapophyseal joint using computed tomography guidance (procedure)

CT Spine cervical discogram	Computed tomography discogram of cervical region (procedure)
CT Spine cervical	Computed tomography of cervical spine (procedure)
CT Spine cervical with contrast	Computerized axial tomography of cervical spine with contrast (procedure)
CT Spine cervical myelogram	Computed tomography myelogram of cervical region (procedure)
CT Bone densitometry	Computerized tomography, bone density study (procedure)
CT Head and neck with contrast	Computed tomography of head and neck with contrast (procedure)
CT Arthrogram cervical facet joint	Computed tomography arthrography of cervical facet joint with contrast (procedure)
CT Spine lumbar discogram	Computed tomography discogram of lumbar region (procedure)
CT Spine lumbar	Computed tomography of lumbar spine (procedure)
CT Spine lumbar with contrast	Computerized axial tomography of lumbar spine with contrast (procedure)
CT Neck	Computed tomography of neck (procedure)
CT Neck with contrast	Computed tomography of neck with contrast (procedure)
CT Head and orbits	Computed tomography of head and orbits (procedure)
CT Head and orbits with contrast	Computed tomography of head and orbits with contrast (procedure)
CT Skeletal survey	Computed tomography of entire skeleton (procedure)
CT Head and neck	Computed tomography of head and neck (procedure)
CT Head	Computed tomography of entire head (procedure)
CT Spine thoracic myelogram	Computed tomography myelogram of thoracic region (procedure)
CT Spine thoracic	Computed tomography of thoracic spine (procedure)
CT Spine thoracic with contrast	Computerized axial tomography of thoracic spine with contrast (procedure)
CT Whole spine	Computed tomography of whole spine (procedure)
CT Spine C T L S with contrast	Computed tomography of whole spine with contrast (procedure)
Discogram cervical	Cervical discography (procedure)
Myelogram cervical	Fluoroscopic cervical myelogram (procedure)
Fluoroscopy cervical spine	Fluoroscopy - cervical column (procedure)
Discogram	Fluoroscopic discography (procedure)

Myelogram thoracic	Fluoroscopic thoracic myelogram (procedure)
MRI Brachial plexus	Magnetic resonance imaging of brachial plexus (procedure)
MRI Brachial plexus with contrast	Magnetic resonance imaging of brachial plexus with contrast (procedure)
MRI Cerebrospinal fluid flow	Magnetic resonance imaging of cerebrospinal fluid flow (procedure)
MRI Spine cervical	Magnetic resonance imaging of cervical spine (procedure)
MRI Spine cervical with contrast	Magnetic resonance imaging of cervical spine with contrast (procedure)
MRI Spine cervical myelogram	Magnetic resonance imaging myelography of cervical spine (procedure)
MRI Spine cervicothoracic	Magnetic resonance imaging of cervicothoracic spine (procedure)
MRI Spine cervicothoracic with contrast	Magnetic resonance imaging of cervicothoracic spine with contrast (procedure)
MRI Lumbosacral plexus	Magnetic resonance imaging of lumbosacral plexus (procedure)
MRI Lumbosacral plexus with contrast	Magnetic resonance imaging of lumbosacral plexus with contrast (procedure)
MRI Spine lumbar	Magnetic resonance imaging of lumbar spine (procedure)
MRI Lumbar spine with contrast	Magnetic resonance imaging of lumbar spine with contrast (procedure)
MRI Neck	Magnetic resonance imaging of neck (procedure)
MRI Neck with contrast	Magnetic resonance imaging of neck with contrast (procedure)
MRI Head	Magnetic resonance imaging of head (procedure)
MRI Head with contrast	Magnetic resonance imaging of head with contrast (procedure)
MRI Spinal cord	Magnetic resonance imaging of spinal cord (procedure)
MRI Spinal cord with contrast	Magnetic resonance imaging of spinal cord with contrast (procedure)
MRI Spine whole	Magnetic resonance imaging of spine (procedure)
MRI Spine whole with contrast	Magnetic resonance imaging of spine with contrast (procedure)
MRI Spine thoracic lumbar with contrast	Magnetic resonance imaging of thoracic and lumbar spine with contrast (procedure)
MRI Spine thoracolumbar	Magnetic resonance imaging of thoracolumbar spine (procedure)
MRI Spine thoracic	Magnetic resonance imaging of thoracic spine (procedure)
MRI Spine thoracic with contrast	Magnetic resonance imaging of thoracic spine with contrast (procedure)

MRI Spine thoracic myelogram	Magnetic resonance imaging myelography of thoracic spine with contrast (procedure)
XR Cervical spine flexion and extension	Diagnostic radiography of cervical spine with flexion and extension studies (procedure)
XR Cervical spine	Radiography of cervical spine (procedure)
XR Cervicothoracic junction	Cervicothoracic junction X-ray (procedure)
XR Lumbar spine and pelvis	X-ray of lumbar spine and pelvis (procedure)
XR Lumbar spine	Diagnostic radiography of lumbar spine (procedure)
XR Lumbar spine and sacroiliac joint	X-ray of lumbar spine and sacroiliac joints (procedure)
XR Whole spine	Radiography of spine (procedure)