Study Report C1-007

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Version 2.1

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Document History

Version	Date	Description
V1.0	31/10/2023	**Final Version (Interim without CPRD) for EMA review**
V2.0	21/11/2023	**Reviewed version with CPRD**
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Study Title	DARWIN EU® - Natural history of dermatomyositis (DM) and polymyositis (PM) in adults and paediatric populations
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Research question and objectives	The overall objective of this study is to describe and characterise dermatomyositis (DM), polymyositis (PM) and their juvenile forms (JDM and JPM), in terms of prevalence, natural history of the disease, disease severity, and treatment. The specific objectives of this study are: 1. To estimate the yearly prevalence of DM and PM in adult (18+ years) and paediatric populations (0 to less than 2 years, 2 to less than 6 years, 6 to less than 12 years, 12 to less than 18 years), overall, and by sex. 2. To characterise patients and describe age at disease onset, for DM, PM, JDM and JPM. 3. To describe the occurrence in adults and children of biomarker measurements (e.g. creatinine kinase, tests for myositis auto-antibodies - INF-b levels, INF type I gene signature) before, at the time of, and after a diagnosis of DM, PM, JDM and JPM. 4. To describe the occurrence of clinical manifestations (muscle inflammation, muscle weakness, connective tissue disease overlap, presence of calcinosis in children) before, at the time, and after a diagnosis of DM, PM, JDM and JPM. 5. To describe disease severity including organ involvement (skin, joints, lung, heart, GI tract) before, at the time, and after a diagnosis of DM, PM, JDM and JPM. 6. To describe treatment administered (including combinations and sequences) after a diagnosis of DM, PM, JDM and JPM All results were reported by database, overall, and stratified by age and sex when possible.
Country(-ies)ofstudy	The study included data sources from Estonia, France, Germany, Spain, United Kingdom

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1. DESCRIPTION OF STUDY TEAM

Study team Role	Names	Organisation
Study Project Manager/ Principal Investigator	Albert Prats-Uribe	University of Oxford
Epidemiologist	Albert Prats-Uribe Ed Burn	University of Oxford University of Oxford
Clinical Domain Expert	Daniel Prieto-Alhambra	University of Oxford
Data Analysts/statisticians	Ed Burn Mike Du	University of Oxford University of Oxford
Data Partner*	**Names**	**Organisation**
Local Study Coordinator/Data Analyst	James Brash Hanne van Ballegooijen Talita Duarte Salles Laura Pérez Crespo Romain Griffier Antonella Delmestri Hezekiah Omulo Wai Yi (Teen) Man Raivo Kolde	IQVIA - DA Germany IQVIA - DA Germany IDIAPJGol - SIDIAP IDIAPJGol - SIDIAP University of Bordeaux - CDWBordeaux University of Oxford – CPRD GOLD University of Oxford – CPRD GOLD University of Oxford – CPRD GOLD Estonian Biobank

*Data partners' role is only to execute code at their data source, review and approve their results. These people do not have an investigator role.

Data analysts/programmers do not have an investigator role and thus declaration of interests (DOI) for these people is not needed.

2. DATA SOURCES

This study was conducted using routinely collected data from 6 databases in 6 European countries (5 EU countries and United Kingdom). All databases were previously mapped to the OMOP CDM.

1. IQVIA Disease Analyzer Germany (IQVIA DA Germany), Germany
2. Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària (SIDIAP), Spain
3. Clinical Data Warehouse of Bordeaux University Hospital (CDWBordeaux), France
4. Clinical Practice Research Datalink (CPRD) GOLD, United Kingdom (UK)
5. Estonian Biobank (EBB), Estonia

Detailed information on data source is described in Table 2.1.

Table 2.1Description of databases used for this study and ability to answer objectives.

Country	Name of Database	Health Care setting (e.g. primary care, specialist care, hospital care)	Type of Data (EHR, claims, registries)	Number of active subjects	Calendar period covered by each data source.	Ability to answer study objectives
DE	IQVIA DA Germany	Primary care and outpatient specialist care	EHR	8.5 million	31/12/2022	2 to 6
ES	SIDIAP	Primary care with hospital linkage	EHR	5.8 million	31/12/2022	1 to 6
FR	CDWBordeaux	Secondary care (in and outpatients)	EHR	1.9 million	10/04/2023	2 to 6
UK	CPRD GOLD	Primary care	EHR	3.1 million	04/07/2022	1 to 6
EE	EBB	Primary care and secondary care	Biobank cohort.	200,000	31/12/2021	1 to 6

DE = Germany, ES = Spain, FR = France, NL = The Netherlands, UK = United Kingdom, EE= Estonia, SIDIAP = Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària, DA = Disease Analyzer, CDWBordeaux = Clinical Data Warehouse of Bordeaux University Hospital, CPRD = Clinical Practice Research Datalink, EBB = Estonian Biobank.

3. ABSTRACT

Title

DARWIN EU® - Natural history of dermatomyositis (DM) and polymyositis (PM) in adults and paediatric populations

Rationale and Background

Idiopathic inflammatory myopathies (IIM) are rare and diverse autoimmune disorders characterized by muscle inflammation, weakness, and extra-muscular manifestations affecting organs like skin, lungs, heart, and joints [1, 2]. The subgroups include dermatomyositis, anti-synthetase syndrome, immune-mediated necrotizing myopathy, inclusion body myositis, polymyositis, and overlap myositis [1]. Despite their rarity, understanding the epidemiology of these disorders is essential to identify patterns and determinants.

Currently, there are no approved specific therapies for dermatomyositis (DM) and polymyositis (PM) based on randomized controlled trials. These diseases are challenging because of their associated morbidity and

mortality [3]. Classification criteria developed by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) help identify major IIM subgroups. Diagnostic tools involve elevated muscle-derived enzymes in serum, antinuclear antibodies, muscle biopsy, electromyography, and MRI [1, 4].

The pathogenesis, treatment responses, and organ involvement vary among IIM subtypes, necessitating a deeper understanding of molecular pathways and auto-antigens [1, 5]. Glucocorticoids are commonly used as first-line treatment, often combined with immunosuppressive agents like methotrexate, azathioprine, and others [2, 6]. Rituximab shows promise in refractory cases [7, 8]. Although TNF's role is implicated, anti-TNF treatments' efficacy is limited [1].

Paediatric cases require special consideration. Juvenile idiopathic inflammatory myopathies affect children and young individuals, involving muscles, skin, and other organs. Differences exist between juvenile and adult forms in terms of pathogenesis, autoantibody profiles, and treatment responses. Consensus guidelines help guide diagnosis and management [9].

In conclusion, idiopathic inflammatory myopathies encompass a spectrum of rare autoimmune disorders affecting muscles and various organs. Understanding their epidemiology, classification, diagnostic criteria, and treatment approaches is essential for improving patient outcomes and tailoring treatments, especially in paediatric cases.

Research question and Objectives

The overall objective of this study was to describe and characterise dermatomyositis (DM), polymyositis (PM) and their juvenile forms (JDM and JPM), in terms of prevalence, natural history of the disease, disease severity, and treatment patterns.

The specific objectives of this study were:

1. To estimate the yearly prevalence of DM and PM in adult (18+ years) and paediatric populations (less than 2 years, 2 to less than 6 years, 6 to less than 12 years, 12 to less than 18 years) overall and by sex.
2. To characterise patients and describe age at disease onset, for DM, PM, JDM and JPM.
3. To describe the occurrence in adults and children of biomarker measurements (e.g. creatinine kinase, tests for myositis auto-antibodies - INF-b levels, INF type I gene signature) before, at the time of, and after a diagnosis of DM, PM, JDM and JPM.
4. To describe the occurrence of clinical manifestations (muscle inflammation, muscle weakness, connective tissue disease overlap, presence of calcinosis in children) before, at the time of, and after a diagnosis of DM, PM, JDM and JPM.
5. To describe disease severity including organ involvement (skin, joints, lung, heart, GI tract) before, at the time of, and after a diagnosis of DM, PM, JDM and JPM.
6. To describe treatment administered (including combinations and sequences) after a diagnosis of DM, PM, JDM and JPM

All results were reported by database, overall, and by study periods (2006-2012, 2013-2019, and 2020-2022), and stratified by age and sex when possible.

Research Methods

Study design

Cohort study. We included cohorts of first diagnosed DM, PM, JDM, JPM and new user cohorts of their treatments (for objective 6).

Population

The source population included all individuals eligible in the database between 01/01/2006 and end of the available date in each database. For objective 1, all patients active in the database at the start of every calendar year were included. For objectives 2-5, two cohorts were characterised, one with a 90-day prior history requirement from diagnosis date, and one without this requirement. For objective 6, a washout period of 365 days at the treatment ingredient level was applied to capture new users of DM, PM, JDM and JPM treatment.

Variables

DM, PM, JDM and JPM were assessed as first occurrence of the codes specified in Appendix 1. Additional age criteria, <18 years old at time of first diagnosis was applied for JDM and JPM and 18 years old and above the time of first diagnosis for DM and PM. Co-morbidities and co-medications were used for large-scale patient characterisation, identified as concept/code and descendants. A list of pre-specified co-morbidities, measurements, clinical manifestations, and severity markers was also characterised and is included in Appendix2. Treatments of DM, PM, JDM, JPM were identified using the codes included in Appendix 1.

Data sources

1. IQVIA Disease Analyzer Germany (IQVIA DA Germany), Germany
2. Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària (SIDIAP), Spain
3. Clinical Data Warehouse of Bordeaux University Hospital (CDW Bordeaux), France
4. Clinical Practice Research Datalink (CPRD) GOLD, United Kingdom (UK)
5. Estonian Biobank (EBB), Estonia

Sample size

No sample size was calculated as this was a descriptive Disease Epidemiology Study where we were interested in the characteristics of all DM, PM, JDM and JPM patients.

Data analyses

Period and point prevalence of each outcome of interest (DM, PM, JDM, JPM), with every individual deemed to have the diagnosis from first occurrence until end of follow-up calculated on an annual basis (as of the 1st January for each year for point and over all year for period), estimated overall and stratified by age and sex.

Age and sex at time of DM, PM, JDM, JPM diagnosis (index date) was described for each of the generated study cohorts (Objective 2). Large-scale patient-level characterisation was conducted for objectives 3 to 5. Occurrence of co-morbidities, measurements, clinical manifestations, and severity markers was assessed for anytime –and up to 365 days before index date, for 364 to 91, for 90 to 31, and for 30 to 1 day before index date, and at index date. We also reported them for 1 to 90, 91 to 180, 181 to 365 days, 366 to 1095, 1096 to 1825 days, and 1826 days to any time post index date.

The number and percentage of patients receiving each of a pre-specified list of DM, PM, JDM and JPM treatments (see Appendix 1) and treatment combinations were described at index date, 1 to 90, 91 to 180, 181 to 365 days, 366 to 1095, 1096 to 1825 days, and 1826 days to any time post index date. Additionally, sunburst plots and Sankey diagrams were used to describe treatment patterns and sequences over time (objective 6).

For all continuous variables, mean, standard deviation, median, and interquartile range were reported. For all categorical analyses, number and percentages were reported. A minimum cell count of 5 was used when reporting results, with any smaller counts reported as "<5". All analyses were reported by country/database, overall and stratified by age groups and sex when possible (minimum cell count reached).

Results

We identified 3,969 DM patients, 2,541 PM patients, 333 JDM patients and 32 JPM patients. Most of the patients for all the conditions were women, around 60-70% in most cases, with a median age of 50-60 years old across data sources for DM and PM. JDM median age of diagnosis across data sources was around 9-13 years old.

Period complete prevalence of DM and PM in adults (>18 years old) increased or was stable over time in all databases. Prevalence of DM was slightly higher than PM for all databases and ranged from 7 per 100,000 in SIDIAP to 40 per 100,000in EBB at the end of the study. Prevalence for PM at the end of the study ranged from 0.5 per million in SIDIAP to 3 per million in EBB. Looking at juvenile forms, JPM was very rare, with prevalences of less than 0.05 per million children in primary care databases. JDM was slightly more frequent but still with lower incidence than adult forms, with prevalence estimates at the end of the study period ranging from 0.2 per million in CPRD (0.3 per million in IQVIA Germany) to 1 per million in Bordeaux. Most of these cases of JDM occurred in patients aged 13 to 18.

In most databases, biomarkers such as CRP, ESR and AST showed higher testing in the months before and after diagnosis of DM and PM. Testing of specific auto-antibodies can be seen in hospital databases. As for clinical manifestations, the highest was the occurrence of muscle pain; 14% and 15% for DM and PM, respectively. For JDM and JPM, the number of individuals with clinical manifestations and complications was less than 5.

Adult DM and PM showed similar patterns in treatment use. The most used drug class one month before cohort entry were Glucocorticoids. Their use increased notably in the 3 months after the index date and decreased afterwards. Use of disease-modifying anti-rheumatic drugs (DMARDS)was low before index but increased in the months following diagnosis and for up to 3 years after. Some use of biologics and immunoglobulins was seen in databases with hospital information, especially in the 3 months to 3 years after diagnosis.

Results of the point prevalence and of further stratifications can be found in the Shiny app: https://data-dev.darwin-eu.org/P2-C1-007-DermatomyositisPolymyositis/

Conclusion

Our prevalence estimates for PM and DM are consistent with previous studies, ranging between2 to 10 per 100,000 people in other studies using population-based data sources. Consistent with previous research, we see a rise in the prevalence of PM and DM in all databases, which could be potentially attributed to improved diagnosis and data recording but needs further research. The observed disease manifestations for both diseases align with the latest clinical criteria recognised by European and American guidelines (EULAR/ACR). These include muscle weakness/pain, dysphagia, and interstitial lung disease. Testing in contributing databases aligns with diagnostic criteria in these guidelines, including inflammation markers, liver and muscle enzymes, and specific autoantibodies observed only in hospital and biobank datasets. Treatments prescribed in European real-world data for PM/DM follow recent recommendations, including glucocorticoids, DMARDs, and infrequent use of immunoglobulins and biologics.

4. LIST OF ABBREVIATIONS

Acronyms/terms	Description
ACR	American College of Rheumatology
ADM	Amyopathic dermatomyositis
ATC	Anatomical Therapeutic Chemical Classification System
CDM	Common Data Model
CDWBordeaux	Clinical Data Warehouse of Bordeaux University Hospital
COPD	Chronic obstructive pulmonary disease
CPRD	Clinical Practice Research Datalink
DA	Disease Analyzer
DARWIN EU®	Data Analysis and Real World Interrogation Network
DM	Dermatomyositis
DMARD	disease-modifying antirheumatic drug
csDMARD	conventional synthetic disease-modifying antirheumatic drug
DOI	Declaration Of Interests
EBB	Estonian BioBank
EHR	Electronic Health Records
EMA	European Medicines Agency
EULAR	European League Against Rheumatism
GERD	Gastro-esophageal reflux disease
GP	General Practitioner
IBM	Inclusion body myositis
IIM	Idiopathic inflammatory myopathies
IMASIS	Institut Municipal Assistència Sanitària Information System
JDM	Juvenile Dermatomyositis
JPM	Juvenile Polymyositis

LOINC	Logical Observation Identifiers Names and Codes
OMOP	Observational Medical Outcomes Partnership
PM	Polymyositis
PCT	Primary Care Teams
RxNorm	Medical prescription normalized
SIDIAP	Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària
SNOMED	Systematized Nomenclature of Medicine

5. AMENDMENTS AND UPDATES

Number	Date	Section of studyprotocol	Amendment orupdate	Reason
NA				

6. MILESTONES

STUDY SPECIFIC DELIVERABLE	TIMELINE (planned)	TIMELINES (actual)
Final Study Protocol	09/2023	09/2023
Creation of Analytical code	09/2023	09/2023
Execution of Analytical Code on the data	10/2023	10/2023
Interim Study Report (if applicable)	31/10/2023	31/10/2023
Final Study Report	31/11/2023	
Revised study report		
Draft Manuscript (if agreed on)		
Final Manuscript (if agreed on)		

7. RATIONALE AND BACKGROUND

Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of rare and chronic autoimmune disorders with clinical manifestations such as muscle inflammation, muscle weakness and extra-muscular manifestations including involvement of organs such as the skin, lung, heart, gastrointestinal tract and joints [1, 2].

Based on clinical, histopathological and serological features, IIM can be classified into several subgroups - dermatomyositis (including amyopathic dermatomyositis), anti-synthetase syndrome, immune-mediated necrotizing myopathy, inclusion body myositis, polymyositis and overlap myositis [1].

Although these conditions are believed to be very rare, the epidemiological features of IMs have been poorly studied and synthesis of the existing data regarding incidence and prevalence are lacking. Epidemiological

studies of rare diseases are essential to identify their geographical and population disparities as well as clusters and time trends and hence their possible key determinants. Such epidemiological patterns may provide useful clues towards improving our understanding of IMs [10].A wide range of estimates of incidence and prevalence as well as of risk factors for disease have been published. Globally, albeit with a majority of studies from Asia, Europe and North America, the incidence estimates range from 11 to 660 patients with newly diagnosed inflammatory myositis per 1,000,000 person-years and between 2.9 and 34 individuals per 100,000 population are suggested to have the disease. All available data suggest that PM, and DM are more common in women than in men. The incidence increases with age and the peak age of incidence is approximately50 years of age in both Europe and North America[1].

Polymyositis (PM), dermatomyositis (DM), and inclusion body myositis (IBM) are major IIM subsets [2]. Juvenile onset DM (JDM) and PM (JPM) are sub-categories of DM and PM whereas IBM only occurs in adults. JDM and JPM can also encompass juvenile patients with overlap myositis (ie, DM or PM signs and symptoms but co-existing with other autoimmune diseases such as lupus or scleroderma).

DM is defined by the presence of characteristic cutaneous manifestations (Gottron papules, "V sign", heliotrope rash among others) and myositis. While muscle and skin involvement coexist in the prototype of DM (classic DM), DM can exist without muscle disease (amyopathic DM) or overt muscle symptoms despite evidence of myositis on laboratory testing (hypomyopathic DM). Amyopathic DM and hypomyopathic DM are defined when the conditions last for≥at least6 months and are collectively termed as clinically amyopathic DM [11].

PM could be defined as a myositis phenotype with chronic muscle weakness without skin involvement and involving predominant cytotoxic T cell mechanisms [1]. However, most historical studies of PM included samples from patients now classified as Immune-Mediated Necrotizing Myopathy and antisynthetase syndrome without a rash, diseases now recognized to be pathologically distinct from each other. Thus, future studies are required to define the risk factors and mechanisms underlying muscle inflammation and damage more completely in PM[3].

Diagnosis of myositis is made when typical clinical and laboratory parameters are present and other possible causes are excluded. However, formal diagnostic criteria do not exist, and classification criteria are used for guidance instead. The most recent classification criteria developed by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) published in 2017 [12] can aid in identifying the major myositis subgroups: DM, PM, ADM, juvenile myositis and IBM[1]

Muscle-derived enzymes in serum are elevated in most patients with active muscle disease. Creatine kinase is the most sensitive marker and has diagnostic and monitoring utility. Antinuclear antibodies (identified by indirect inmunofluorescence) have also diagnostic utility. Muscle biopsy is an important tool to diagnose IIM, confirm signs of inflammation, identify signs of the different subtypes of IIM and, importantly, exclude other myopathies. Abnormal electrical activities of muscle fibres, signs of muscle oedema or immune-mediated changes in histopathological specimens can be detected by electromyography, imaging and muscle biopsy[1]. MRI is now favoured as a diagnostic tool[4]. In a systematic revision, Meyer et al found that the median time to diagnosis of overall IM varied between 3 and 6 months. A considerably delayed diagnosis was a constant feature of IBM. The mean duration of symptoms before diagnosis varied between 4.1 and 8 years.

The prognoses, treatment responses and organ manifestations vary among IIM subtypes, implicating different pathophysiological mechanisms in each subtype. A deeper understanding of the molecular pathways underlying the pathogenesis and identifying the auto-antigens of the immune reactions in these subgroups is crucial to improving outcomes [1, 5].

In terms of treatments and care management of patients with IIM, glucocorticoids are used empirically as the first-line treatment despite their various adverse effects. Glucocorticoid dose should be weaned when disease activity, considered across all domains, substantially improves, usually after around 6 weeks of treatment initiation[6]. Concomitant treatment with steroid-sparing immunosuppressive agents, including methotrexate, azathioprine, calcineurin inhibitors, mycophenolate mofetil, and cyclophosphamide, reduces successfully initial glucocorticoid doses for the remission induction, the relapse risk during glucocorticoid tapering, and adverse effects of glucocorticoids[2, 6].

Evidence does not exist to allow recommendation of specific csDMARDs as first-/ second-/third-line for adults. DMARDs should be prescribed and monitored according to existing age appropriate guidelines.

Rituximab depletes CD20 B cells that are likely to be involved in the pathogenesis of some myositis subgroups. Several open-label studies have reported safety and efficacy in patients with severe and refractory myositis [7, 8]. Although TNF has been implicated in the pathogenesis of myositis, the efficacy of anti-TNF agents (such as etanercept and infliximab) is somewhat disappointing. Currently, anti-TNF treatment is not typically recommended or considered in patients with adult myositis, although it may have a role in the treatment of calcinosis in juvenile DM [1].

In the context of paediatric extrapolation from adults in clinical drug development, it is important to understand the potential for disease similarity (or differences) between juvenile and adult forms of DM and PM, as well as between JPM and JDM: The childhood-onset or juvenile idiopathic inflammatory myopathies are a heterogenous group of rare and serious autoimmune diseases of children and young people that predominantly affect the muscles and skin but can also involve other organs, including the lungs, gut, joints, heart and central nervous system. Juvenile idiopathic inflammatory myopathies can differ from adult-onset myopathies in terms of the pathogenesis, autoantibody profile, disease phenotype and treatment response, but these differences need to be further defined. A Single Hub and access point for Paediatric Rheumatology in Europe (SHARE) initiative-based consensus guideline has set out recommendations for diagnosis [9]. Ultimately, a combination of a better understanding of disease mechanisms, biomarkers that accurately track disease activity, including subclinical disease, and definitions of outcomes that include the patient perspective is needed to deliver a personalized approach to managing myositis in children, and in the young people and adults they become.

8. RESEARCH QUESTION AND OBJECTIVES

The overall objective of this study is to describe and characterise dermatomyositis (DM), polymyositis (PM) and their juvenile forms (JDM and JPM), in terms of prevalence, natural history of the disease, disease severity, and treatment.

The specific objectives of this study are:

1. To estimate the yearly prevalence of DM and PM in adult (18+ years) and paediatric populations (0 to less than 2 years, 2 to less than 6 years, 6 to less than 12 years, 12 to less than 18 years) overall and by sex.
2. To characterise patients and describe age at disease onset, for DM, PM, JDM and JPM.
3. To describe the occurrence in adults and children of biomarker measurements (e.g. creatinine kinase, tests for myositis auto-antibodies - INF-b levels, INF type I gene signature) before, at the time, and after a diagnosis of DM, PM, JDM and JPM.
4. To describe the occurrence of clinical manifestations (muscle inflammation, muscle weakness, connective tissue disease overlap, presence of calcinosis in children) before, at the time, and after a diagnosis of DM, PM, JDM and JPM.
5. To describe disease severity including organ involvement (skin, joints, lung, heart, GI tract) before, at the time, and after a diagnosis of DM, PM, JDM and JPM.
6. To describe treatment administered (including combinations and sequences) after a diagnosis of DM, PM, JDM and JPM

All results are reported by database, overall, and by study periods (2006-2012, 2013-2020, and 2020-2022), and stratified by age and sex when possible.

Table 8.1 Primary research question and objective

Objectives:	1. To estimate the yearly prevalence of DM and PM in adult (18+ years) and paediatric populations (0 to less than 2 years, 2 to less than 6 years, 6 to less than 12 years, 12 to less than 18 years) overall and by sex. 2. To characterise patients and describe age at disease onset, for DM, PM, JDM and JPM. 3. To describe the occurrence in adults and children of biomarker measurements (e.g. creatinine kinase, tests for myositis auto-antibodies - INF-b levels, INF type I gene signature) before, at the time, and after a diagnosis of DM, PM, JDM and JPM. 4. To describe the occurrence of clinical manifestations (muscle inflammation, muscle weakness, connective tissue disease overlap, presence of calcinosis in children) before, at the time, and after a diagnosis of DM, PM, JDM and JPM.

	5. To describe disease severity including organ involvement before, at the time, and after a diagnosis of DM, PM, JDM and JPM. 6. To describe treatment administered (including combinations and sequences) after a diagnosis of DM, PM, JDM and JPM
Hypothesis:	N/A
Population ***(mention key inclusion-exclusion criteria):***	All individuals with a diagnosis of DM, PM, JDM and JPM identified in the database between 01/01/2006 and 31/12/2022 or end of the available date in each database. For objective 1, all patients active in the database at start of each available year were used to form the denominator. For objectives 2-5, two cohorts for each of the DM, PM, JDM and JPM groups were characterised, one with a 90-day prior history requirement from diagnosis date, and one without this requirement. For the treatment cohorts, a washout period of 365 days at the treatment ingredient level was applied to capture new users of DM, PM, JDM and JPM treatments (objective 6).
Exposure:	DM, PM, JDM and JPM assessed as first occurrence of the codes specified in Appendix 1 DM, PM, JDM and JPM treatments (Appendix 1): • Hydroxychloroquine, chloroquine • Systemic glucocorticoids (prednisone, methylprednisolone) • Methotrexate • Azathioprine • Calcineurin inhibitors (tacrolimus, cyclosporine) • Mycophenolate • Cyclophosphamide • Immunoglobulins DMARDs: Rituximab (anti-CD20), etanercept (anti-TNF), infliximab (anti-TNF), abatacept (anti-CTLA-4)
Comparator:	N/A
Outcome:	N/A
Time ***(when follow up begins and ends):***	For objectives 1 to 5, follow-up started from date of first DM, PM, JDM or JPM diagnosis until the earliest of the following: 1) loss to follow-up, 2) end of data availability, or 3) date of death. For objective 6, follow-up started from date of first DM, PM, JDM and JPM treatment after DM, PM, JDM and JPM diagnosis until the earliest of the following: 1) loss to follow-up, 2) end of data availability, or 3) date of death.

Setting:	Inpatient, outpatient, and biobank setting from 5 databases in 5 European countries.
Main measure of effect:	Prevalence of DM, PM, JDM and JPM. Biomarker, clinical severity, and clinical manifestation occurrence after and before DM, PM, JDM and JPM diagnosis. Proportions of patients on treatment types and sequences, patient-level drug utilisation.

9. RESEARCH METHODS

9.1 Study Type and Study Design

This is**a population level descriptive epidemiology** and a **patient-level characterisation** study. A retrospective cohort study of all DM, PM, JDM and JPM cases was conducted.

Table 9.1 Description of Potential Study Types and Related Study Designs

STUDY TYPE	STUDY DESIGN
Population level descriptive epidemiology	Cohort analysis.
Patient-level characterisation	Cohort analysis.
Patient-level treatment patterns	Cohort analysis.

9.2 Study Setting and Data Sources

This study was conducted using routinely collected health data from 5 databases in 5 European countries. All databases were previously mapped to the OMOP CDM.

Data sources:

1. IQVIA Disease Analyzer Germany (IQVIA DA Germany), Germany
2. Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària (SIDIAP), Spain
3. Clinical Data Warehouse of Bordeaux University Hospital (CDWBordeaux), France
4. Clinical Practice Research Datalink (CPRD) GOLD, United Kingdom (UK)
5. Estonian Biobank (EBB), Estonia

We selected 5 out of the 10 databases availablein the Network of Data Partners ofDARWIN EU® at the time of studyinitiation. The selection of databases for this study was performed based on data reliability and relevance for the proposed research question, as well as sufficient coverage of the paediatric population. CPRD has been previously used for research on inflammatorymyopathies.[13]The selection of the databases

was carried in a feasibility stage, based on a potential number of patients with any of these conditions (see Table 9.2), while covering different health care settings and regions of Europe.

Complete hospital-based DM, PM, JDM and JPM treatment data were available in all databases except CPRD (UK) and SIDIAP (Spain). A proportion of SIDIAP database had linkage to hospital data to allow for more accurate characterisation, but data on inpatient treatments was not available. In turn, any potential outpatient therapies were captured in these primary care datasets.

Detailed information on the selected data sources and their ability to answer the study research questions are described in Table 9.33.

Table 9.2. Person count estimates (rounded to the nearest 100) of diagnoses in DAWIN EU participating data partners

Phenotype	Concept id	Concept name	CHUBX	IMASIS	EBB	SIDIAP	ACI	IQVIA LPD Belgium	IQVIA DA Germany	CPRD GOLD	IPCI	NCR
Dermatomyositis	80182	Dermatomyositis	400	<100	200	1800	200	200	3500	1000		
Dermatomyositis	4081250	Dermatomyositis sine myositis		<100		<100						
Dermatomyositis	4344161	Dermatomyositis with malignant disease			<100	<100						
Dermatomyositis	46270398	Disorder of respiratory system due to dermatomyositis					<100					
Juvenile Dermatomyositis	4005037	Childhood type dermatomyositis			<100	<100	<100		200	<100		
Polymyositis	80800	Polymyositis	300	<100	<100	600	200	<100	3500	<1000		
Polymyositis	4055369	Lung disease with polymyositis				<100	<100			<100		
Juvenile Polymyositis	42538014	Juvenile Polymyositis										

** Counts cannot be added, as concepts are not exclusive of each other (a person can be in different concepts counts)*

In Green: primary care databases selected, in red, secondary care and biobank databases selected

Table 9.3 Description of the selected Data Sources.

Country	Name of Database	Justification for Inclusion	Health Care setting	Type of Data	Number of active subjects	Data lock for the last update	Ability to answer study objectives
DE	IQVIA DA Germany	Covers primary care and outpatient specialist setting with information on DM, PM diagnoses and treatment.	Primary care and outpatient specialist care	EHR	8.5 million	31/12/2022	2 to 6
ES	SIDIAP	Covers primary care setting with a proportion with hospital linkage, data on DM, PM diagnoses and some treatments.	Primary care with hospital linkage	EHR	5.8 million	31/12/2022	1 to 6
FR	CDWBordeaux	Covers secondary care setting, database has information on DM,PM diagnosis and in-hospital treatments	Secondary care (in and outpatients)	EHR	1.9 million	10/04/2023	2 to 6
UK	CPRD GOLD	Covers primary care setting, database has information on DM,PM diagnosis and treatments	Primary care	EHR	3.1 million	04/07/2022	1 to 6
EE	EBB	Covers primary care and hospital data for a biobank cohort, containing data on DM, and PM diagnoses and treatment.	Primary care and secondary care.	Biobank cohort.	200,000	31/12/2021	2 to 6

DE = Germany, ES = Spain, FR = France, NL = The Netherlands, UK = United Kingdom, EE= Estonia, SIDIAP = Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària, DA = Disease Analyzer, CDWBordeaux = Clinical Data Warehouse of Bordeaux University Hospital, CPRD = Clinical Practice Research Datalink, EBB = Estonian Biobank.

IQVIA Disease Analyser (DA) Germany, Germany

DA Germany is collected from extracts of patient management software used by GPs and specialists practicing in ambulatory care settings.

Data coverage includes more than 34M distinct person records out of at total population of 80M (42.5%) in the country and collected from 2,734 providers. Patient visiting more than one provider are not cross identified for data protection reasons and therefore recorded as separate in the system. Dates of service include from 1992 through present. Observation time is defined by the first and last consultation dates. Germany has no mandatory GP system and patient have free choice of specialist. As a result, data are collected from visits to 28.8% General, 13.4% Orthopaedic Surgery, 11.8% Otolaryngology, 11.2% Dermatology, 7.7% Obstetrics/Gynaecology, 6.2% various Neurology and Psychiatry 7.0% Paediatric, 4.6% Urology, 3.7% Cardiology, 3.5% Gastroenterology, 1.5% Pulmonary and 0.7% Rheumatology practices. Drugs are recorded as prescriptions of marketed products. No registration or approval is required for drug utilisation studies.

Information System for Research in Primary Care (SIDIAP), Spain

SIDIAP is collected from EHR records of patients receiving primary care delivered through Primary Care Teams, consisting of GPs, nurses and non-clinical staff [14]. The Catalan Health Institute manages 328 out of 370 such Primary Care Teams with a coverage of 5.8M patients, out of 7.8M people in the Catalan population (74%). The database started to collect data in 2006. The mean follow-up is 15 years. The observation period for a patient can be the start of the database (2006), or when a person is assigned to a Catalan Health Institute primary care centre. Date of exit can be when a person is transferred-out to a primary care centre that does not pertain to the Catalan Health Institute, or date of death, or date of end of follow-up in the database. Drug information is available from prescriptions and from dispensing records in pharmacies. Drugs not prescribed in the GP setting might be underreported; and disease diagnoses made at specialist care settings are not included. Studies using SIDIAP data require previous approval by both a Scientific and an Ethics Committee.

Clinical Data Warehouse of Bordeaux University Hospital (CDWBordeaux), France

The clinical data warehouse of the Bordeaux University Hospital comprises electronic health records on more than 2 million patients with data collection starting in 2005. The hospital complex is made up of three main sites and comprises a total of 3,041 beds (2021 figures) (https://www.chu-bordeaux.fr/). The database currently holds information about the person (demographics), visits (inpatient and outpatient), conditions and procedures (billing codes), drugs (outpatient prescriptions and inpatient orders and administrations), measurements (laboratory tests and vital signs) and dates of death (in or out-hospital death).

Clinical Practice Research Datalink GOLD, United Kingdom

The Clinical Practice Research Datalink (CPRD) is a governmental, not-for-profit research service, jointly funded by the National Institute for Health and Care Research and the Medicines and Healthcare products Regulatory Agency, a part of the Department of Health, United Kingdom (UK) (https://cprd.com). CPRD GOLD [15] comprises computerized records of all clinical and referral events in primary care in addition to comprehensive demographic information and medication prescription data in a sample of UK patients (predominantly from Scotland (52% of practices) and Wales (28% of practices). The prescription records include information on the type of product, date of prescription, strength, dosage, quantity, and route of administration. Data from contributing practices are collected and processed into research databases. Quality checks on patient and practice level are applied during the initial processing. Data are available for 21 million patients, including 3.1 million currently registered patients [16]. Access to CPRD GOLD data requires approval via the Research Data Governance Process.

Estonian Biobank (EBB), Estonia

The Estonian Biobank (EBB) is a population-based biobank of the Estonian Genome Center at the University of Tartu (EGCUT. Its cohort size is currently close to 200,000 participants (“gene donors” ≥ 18 years of age), which closely reflects the age, sex and geographical distribution of the Estonian population. Estonians represent 83%, Russians 14%, and other nationalities 3% of all participants. Genomic GWAS analyses have been performed on all gene donors. The database also covers health insurance claims, digital prescriptions, discharge reports, information about incident cancer cases, and causes of death from national sources for each donor.

9.3 Study Period

The study period started from 01/01/2006 to end of available data in each of the data sources as provided in Table 9.2

9.4 Follow-up

For objectives 1 to 5, follow-up started from date of first DM, PM, JDM and JPM diagnosis until the earliest of the following: 1) loss to follow-up, 2) end of data availability, or 3) date of death.

For objective 6, follow-up started from date of first treatment occurrence of a DM, PM, JDM or JPM diagnosis treatment until the earliest of the following: 1) loss to follow-up, 2) end of data availability, or 3) date of death.

9.5 Study Population with inclusion and exclusion criteria

For objective 1, the study population included all individuals identified in the database between 01/01/20066and end of available data in each database.

For objective 2-6, the study population included all individuals with a first diagnosis of DM, PM, JDM and JPM identified in the database between 01/01/2006 and end of available data in each database.

Diagnoses were identified using condition and observation codes in the OMOP CDM that use the Systematized Nomenclature of Medicine (SNOMED) as the standard vocabulary for these. A code list is provided in appendix 1.

Additional eligibility criteria were applied for each study objective:

For objectives 2-4, two cohorts per diagnosis, one with at least 365 days of prior history available before date of new DM, PM, JDM and JPM diagnosis was applied for large-scale characterisation and another without this requirement.

9.6 Variables

9.6.1. Exposure/s

For Objective 6, DM, PM, JDM and JPM treatments were identified using RxNorm and RxNorm extension codes. These included hydroxychloroquine, chloroquine, systemic glucocorticoids (prednisone, methylprednisolone), methotrexate, azathioprine, calcineurin inhibitors (tacrolimus, cyclosporine, voclosporin), mycophenolate, cyclophosphamide, immunoglobulins, and DMARDs: rituximab (anti-CD20), etanercept (anti-TNF), infliximab (anti-TNF), abatacept (anti-CTLA-4). A list of codes to identify these treatments can be found in Appendix 1.

9.6.2. Outcome/s

For Objective 1, the outcome was a diagnosis of DM, PM, JDM and JPM as defined in Appendix 1.

For Objective 2, Age at DM, PM, JDM, JPM diagnosis was described.

For Objective 3, the outcome was the presence of a biomarker measurement code as defined by SNOMED and LOINC codes, including autoantibodies, inflammation markers, and muscular disease markers. A list of codes can be found in Appendix 2.

For Objective 4 and 5, clinical manifestations and disease severity including organ involvement were identified as defined by SNOMED codes. A list of codes can be found in Appendix 2.

9.6.3. Other covariates, including confounders, effect modifiers and other variables

The following age grouping were used: 0-2; 3-6; 7-12; 13-17; 18 and over. The sex (male/ female) of study participants was also identified. All co-morbidities and co-medications recorded prior and at index date were used for large-scale patient characterisation, identified as concept/code and descendants.

9.7 Sample size

No sample size has been calculated as this is a descriptive disease epidemiology study where we are interested in the characteristics of all DM, PM, JDM, and JPM patients.

9.8 Data transformation

Analyses were conducted separately for each database. Before study initiation, test runs of the analytics were performed on a subset of the data sources or on a simulated set of patients and quality control checks were performed. Once all the tests passed, the final package was released in the version-controlled Study Repository for execution against all the participating data sources.

The data partners locally executed the analytics against the OMOP-CDM in RStudio and reviewed and approved the by default aggregated results before returning them to the Coordination Centre. Sometimes multiple execution iterations were performed, and additional fine tuning of the code base was needed. A service desk was available during the study execution for support.

The study results of all data sources were checked after which they were made available to the team in the Digital Research Environment (DRE) and the Study Dissemination Phase can start. All results were locked and timestamped for reproducibility and transparency.

9.9 Statistical Methods

Table 9.3 describes the details of the analysis and rationale for the choices of analysis, with reference to the Complete Catalogue of Standard Analyses of DARWIN EU®.

Table 9.2Description of Study Types and Type of analysis

STUDY TYPE	STUDY CLASSIFICATION	TYPE OF ANALYSIS
Disease epidemiology - Population-level characterization	Off-the-shelf	- Prevalence of disease
Disease epidemiology - Patient-level characterization	Off-the-shelf	- Large-scale characterisation

STUDY TYPE	STUDY CLASSIFICATION	TYPE OF ANALYSIS
Drug epidemiology - Patient-level characterization	Off-the-shelf	- Patient-level treatment patterns

9.9.1 Patient privacy protection

Cell masking was applied as required by databases to prevent confidentiality issues. Cell counts lower than 5 were reported as "<5".

9.9.2 Statistical model specification and assumptions of the analytical approach considered

Software

All analyses were performed in R. "IncidencePrevalence" (https://github.com/darwin-eu/IncidencePrevalence) was used for the computation of prevalence; "TreatmentPatterns" (https://github.com/darwin-eu-dev/TreatmentPatterns) and "PatientProfiles" (https://github.com/darwin-eu-dev/PatientProfiles)were used for the patient-level characterisation of treatments including combination and sequence of therapy. The study package is available viahttps://github.com/darwin-eu-studies/P2-C1-007-DermatomyositisPolymyositis

Population-level epidemiology

For objective 1, point prevalence of each outcome of interest (DM, PM, JDM, JPM) with complete persistence (an individual is deemed to have the diagnosis from first occurrence until end of follow-up) calculated on an annual basis as of the 1st of January for each year, were estimated overall and stratified by age and sex. We also estimated period prevalence on an annual basis (between the 1st January and 31st December for each year). Period prevalence was first estimated based on participants required to contribute a minimum time at risk of only one day of the period to be included. All analyses were further stratified by sex and by paediatric and adult populations.

Drug exposure calculations

Drug eras were defined as follows: Exposure starts at date of the first prescription of each drug. For each prescription, the estimated duration of use was retrieved from the drug exposure table in the CDM. Subsequent prescriptions were combined into continuous exposed episodes (drug eras) using the following specifications:

Two drug eras were merged into one continuous drug era if the distance in days between end of the first era and start of the second era was 30 days or less. The time between the two joined eras was considered as exposed by the first era as show in in Figure 9.1.

.

Gap era joint mode	Schematics	Dose in between	Cumulative dose	Cumulative time
"first"		d_1	$d_1 \cdot (x_1 + x_{12}) + d_2 \cdot x_2$	$x_1 + x_{12} + x_2$
"second"		d_2	$d_1 \cdot x_1 + d_2 \cdot (x_2 + x_{12})$	$x_1 + x_{12} + x_2$
"zero"		0	$d_1 \cdot x_1 + d_2 \cdot x_2$	$x_1 + x_{12} + x_2$
"join"		NA	$d_1 \cdot x_1 + d_2 \cdot x_2$	$x_1 + x_2$

Figure 9.1 Gap era joint mode

If two eras overlapped, the overlap time was considered exposed by the first era (Figure 9.2). No time was added at the end of the combined drug era to account for the overlap. If two eras started at the same date, the overlapping period was considered exposed by both. We did not consider repetitive exposure.

Overlap mode	Schematics	Dose overlap
"first"		d_1
"second"		d_2
"both"		$d_1 + d_2$
"maximum"		$\max(d_1, d_2)$

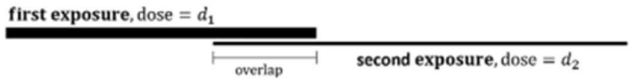


Figure 9.2 Gap era overlap mode

To construct treatment pathways, various parameters were defined in the TreatmentPatterns package (Figure 9.3).

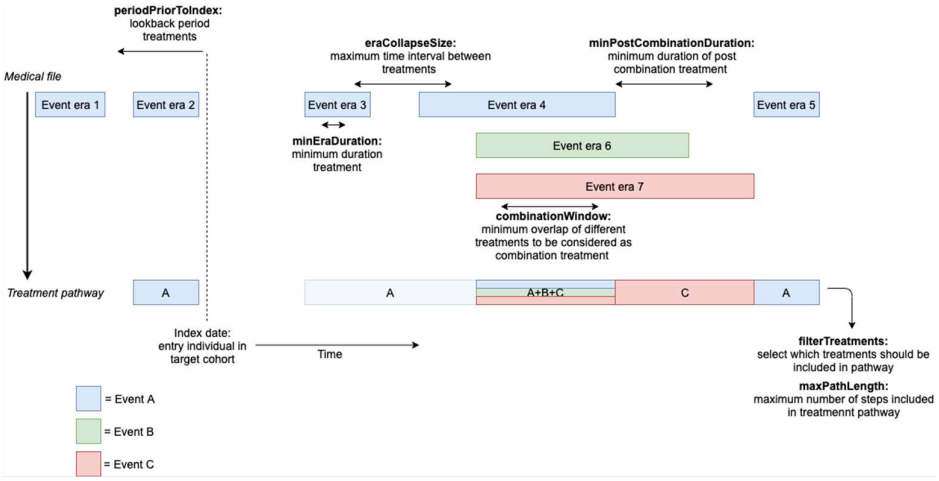


Figure 9.3 Parameters in Treatment Patterns package

The following parameters were defined in this study.

Individual pathway settings		
periodPriorToIndex	The period (number of days) prior to the index date of the target cohort from which treatments should be included	0
minEraDuration	Minimum time (days) an event era should last to be included in the analysis	0
eraCollapseSize	Maximum gap (days) within two eras of the same event cohort which would still allow the eras to be collapsed into one era	30
combinationWindow	Time (days) that two event eras need to overlap to be considered a combination treatment	30
minPostCombinationDuration	Minimum time (days) that an event era before or after a generated combination treatment should last to be included in the pathway as a separate treatment	30
filterTreatments	Select which treatments should be included in pathway first time occurrences of treatments ('First'), remove sequential repeated treatments ('Changes'), all treatments ('All')	First
maxPathLength	Maximum number of treatments included in pathway	5
Aggregate pathway settings		
minCellCount	Minimum number of persons with a specific treatment pathway for the pathway to be included in analysis	5

minCellMethod	Select to completely remove / sequentially adjust (by removing last step as often as necessary) treatment pathways below minCellCount	Adjust
groupCombinations	Select to group all non-fixed combinations in one category 'other' in the sunburst plot	TRUE/10
addNoPaths	Select to include untreated persons without treatment pathway in the sunburst plot	TRUE

For all continuous variables, mean, standard deviation, median and interquartile range were reported. For all categorical variables, number and percentages were reported. A minimum cell count of 5 was used when reporting results, with any smaller counts reported as "<5". All analyses were reported by country/database, overall and stratified by age and sex when possible (minimum cell count reached). Additionally, to capture treatments availability and changes over time, sunburst plots, Sankey diagrams were further stratified by study periods (2006-2012, 2013-2019, and 2020-2022).

9.9.3 Methods to derive parameters of interest

Index date

The index date was the date of the PM, DM, JDM and JPM diagnosis for each patient.

Age

Age at index date was calculated using January 1st of the year of birth as proxy for the actual birthday. The following age groups were used for stratification by paediatric and adult populations (0 to less than 2 years, 2 to less than 6 years, 6 to less than 12 years, 12 to less than 18 years, 18 or more years).

Characterisation of patient-level features

Large-scale patient-level characterisation was conducted for objectives 2 to 5. Age and sex at time of PM, DM, JDM and JPM diagnosis were described for each of the generated study cohorts. Medical condition and medication use history were assessed for anytime –and up to 365 days before index date, for 364 to 91, for 90 to 31, and for 30 to 1 day before index date, and at index date. We also reported them for 1 to 90, 91 to 180, 181 to 365 days, 366 to 1095, 1096 to 1825 days, and 1826 days to any time post index date. Occurrence of biomarker measurements, clinical manifestations codes, and disease severity codes specified as described in the outcomes section were also measured in these timeframes. All patient level characterisation were presented in baseline characteristics tables.

9.9.4 Methods planned to obtain point estimates with confidence intervals of measures of occurrence

Period and point prevalence were calculated as shown above. Confidence intervals were only calculated for period and point prevalence using the Wilson score interval method.

9.9.5 Methods to control for potential sources of bias

No method was used to control for sources of bias.

9.9.6 Missing data assumptions

For this study, subjects with no available age or sex were excluded from the analysis. Our estimated characteristics implicitly assume missing data occurred completely at random. For prevalence, subjects lost-to-follow-up or whose observation period ended before the end of the study period had part of their follow-up missing. They contributed to the analysis with their time at risk up to the time of censoring, which implies the prevalence estimates assumed censoring was not informative.

9.9.7 Description of sensitivity analyses

Sensitivity analyses included a repetition of all analyses with DM,PM, JDM, and JPM cohorts with no restriction on the previous visibility time window.

9.9.8 Evidence synthesis

Results from analyses described in section 9are presented separately for each database and no meta-analysis of results is conducted.

9.10 Deviations from the protocol

Included databases and analyses:

It was not possible to report treatment patterns, with sequences and combinations of drugs due to small sample size. It was also not possible to present further age stratifications amongst <18 and of calendar time due to the low count number.

10. DATA MANAGEMENT

Data management

All databases have previously mapped their data to the OMOP common data model. This enabled the use of standardised analytics and tools across the network since the structure of the data and the terminology system is harmonised. The OMOP CDM was developed and maintained by the Observational Health Data Sciences and Informatics (OHDSI) initiative and is described in detail on the wiki page of the CDM: https://ohdsi.github.io/CommonDataModel and in The Book of OHDSI: http://book.ohdsi.org

This analytic code for this study was written in R. Each data partner executed the study code against their database containing patient-level data and then returned the results set which only contained aggregated data. The results from each of the contributing data sites were then be combined in tables and figures for this study report.

Data storage and protection

For this study, participants from various EU member states and from the UK processed personal data from individuals which was collected in national/regional electronic health record databases. Due to the sensitive nature of this personal medical data, it is important to be fully aware of ethical and regulatory aspects and to strive to take all reasonable measures to ensure compliance with ethical and regulatory issues on privacy.

All databases used in this study were already used for pharmaco-epidemiological research and have a well-developed mechanism to ensure that European and local regulations dealing with ethical use of the data and adequate privacy control are adhered to. In agreement with these regulations, rather than combining person level data and performing only a central analysis, local analyses were run, which generated non-identifiable aggregate summary results. All and any results with n<5 participants were suppressed using cell suppression to minimise risk of reidentification.

The output files were stored in the DARWIN EU Data transfer zone. These output files did not contain any data that allow identification of subjects included in the study. The DTZ implemented further security measures in order to ensure a high level of stored data protection to comply with the local implementation of the General Data Protection Regulation (GDPR) (EU) 679/20161 in the various member states.

11. QUALITY CONTROL

General database quality control

A number of open-source quality control mechanisms for the OMOP CDM have been developed (see Chapter 15 of The Book of OHDSI http://book.ohdsi.org/DataQuality.html). In particular, it was expected that data partners would have run the OHDSI Data Quality **Dashboard** tool (https://github.com/OHDSI/DataQualityDashboard). This tool provided numerous checks relating to the conformance, completeness and plausibility of the mapped data. Conformance focused on checks that describe the compliance of the representation of data against internal or external formatting, relational, or computational definitions, completeness in the sense of data quality was solely focused on quantifying

missingness, or the absence of data, while plausibility seeks to determine the believability or truthfulness of data values. Each of these categories had one or more subcategories and were evaluated in two contexts: validation and verification. Validation related to how well data aligned with external benchmarks with expectations derived from known true standards, while verification related to how well data conformed to local knowledge, metadata descriptions, and system assumptions. Additionally, two more tools were used to control the quality of data during the onboarding. **Achilles** for database characterisation, running 293 analyses against the data. This output is not shared with the DARWIN-EU® CC as it reveals granular information of the data. It is expected that the data partners review the Achilles output internally. Secondly, **CdmOnboarding** generates a Word report with the most important database characteristics, providing insight in the readiness of the database to use for network studies. The output is shared with and inspected by the DARWIN-EU® CC.

Study specific quality control

When defining DM, PM, JDM, and JPM, a systematic search of possible codes for inclusion were identified using CodelistGenerator R package (https://github.com/darwin-eu/CodelistGenerator). This software allows the user to define a search strategy and using this then queries the vocabulary tables of the OMOP CDM so as to find potentially relevant codes. The codes returned were reviewed by two clinical epidemiologists to consider their relevance. In addition, we ran cohort diagnostics to assess the use of different codes across the databases contributing to the study and identify any codes potentially omitted in error. This allowed for a consideration of the validity of the study cohort of patients in each of the databases and inform decisions around whether multiple definitions are required.

When defining drug cohorts, non-systemic products were excluded from the list of included codes summarised on the ingredient level. A pharmacist reviewed the codes for the treatments.

The study code was based on two R packages currently being developed to (1) characterise demographic and clinical characteristics, (2) characterise treatment patterns. These packages include numerous automated unit tests to ensure the validity of the codes, alongside software peer review and user testing. The R package was made publicly available via GitHub.

12. RESULTS

Results are presented in this section, including population-level analyses reporting inclusion criteria and the prevalence of DM, PM, JDM, and JPM in Section 12.1. Secondly, in 12.2 we present the demographic characteristics of the participants in terms of demographics, biomarker and clinical manifestation occurrences and treatments.

We selected the most relevant results for this report. However, all results are available in an interactive web-application ("Rshiny app") at https://data-dev.darwin-eu.org/P2-C1-007-DermatomyositisPolymyositis/

12.1 Population level analyses

12.1.1 Number of participants

The starting number of people in each database varied between 209,457 for EBB to 41,974,403 for IQVIA Germany (see Table 12.1). From this total, no one had missing age, and we excluded participants who were missing information about sex: 28,542 participants in IQVIA Germany and 1,221 in the CDW Bordeaux database. Individuals who had no observation time available during the study period were also excluded, and this applied to 1,832,089 individuals from the IQVIA Germany database, 3,382,072 participants from CPRD Gold and 204,735 people from CDW Bordeaux.

We also excluded individuals who lacked observation time after applying age and prior observation criteria. In the pediatric analyses, adults were excluded, this exclusion ranged from 168,622 (EBB) to 33,279,710 (IQVIA Germany). Four out of five of these databases had individuals without any observation during the database interval, and these were also excluded, ranging from 17,975 (CPW Bordeaux) to 93,665 (IQVIA Germany). The final sample for the pediatric population therefore consisted of 6,740,397 individuals for IQVIA Germany, 520,463 individuals for CDW Bordeaux, 3,692,615 individuals for CPRD Gold, 40,835 for EBB and 35,259 for SIDIAP.

For the adult analyses, the number of individuals excluded for lacking observation time after applying age and prior observation criteria (patients that were less than 18 years old during the study period or that did not fulfil previous observation criteria) ranged from 99 (EBB) to 5,945,654 (IQVIA Germany). We also excluded individuals lacking observations during the database interval; this was zero for EBB but ranged between 57,100 for CDW Bordeaux to 506,135 for IQVIA Germany for the other databases. This led to a final sample of 33,661,983 participants for IQVIA Germany, 1,642,532 for CDW Bordeaux, 191,534 participants for CPRD Gold, 209,358 for EBB and 6,840,335 for SIDIAP.

Table 12.1Number of participants and attrition in each source population during the study period

		IQVIA_Germany_DA		CDWBordeaux		CPRDGold		EBB		SIDIAP	
Age group	**reason**	**N**	**excluded**	**N**	**excluded**	**N**	**excluded**	**N**	**excluded**	**N**	**excluded**
	Starting population	41,974,403		2,371,226		17,216,081		209,457		8,265,343	
	Missing year of birth	41,974,403		2,371,226		17,216,081		209,457		8,265,343	
	Missing sex	41,945,861	28,542	2,370,005	1,221	17,216,081		209,457		8,265,343	
	No observation time available in study period	40,113,772	1,832,089	2,164,638	204,735	13,834,009	3,382,072	209,457		8,265,343	
Paediatric	**No observation time available after applying age, prior observation**	6,834,062	33,279,710	538,438	1,626,194	3,752,581	10,081,428	40,835	168,622	2,257,179	6,008,164
Paediatric	**Not observed during the complete database interval**	6,740,397	93,665	520,463	17,975	3,692,615	59,966	40,835		2,221,920	35,259
Adult	**No observation time available after applying age, prior observation**	34,168,118	5,945,654	1,699,632	465,000	11,124,597	2,709,412	209,358	99	6,924,228	1,341,115
Adult	**Not observed during the complete database interval**	33,661,983	506,135	1,642,532	57,100	10,933,063	191,534	209,358		6,840,335	83,893

12.1.2 Period prevalence over time

Figure 12.1shows period prevalence of Dermatomyositis and Polymyositis in primary care settings for people aged 18years or older from 2006 to 2022. Figure 12.2shows complete period prevalence of diagnoses in the paediatric population (less than 18 years old). First, we present the period prevalence in Primary Care databases (CPRD and SIDIAP) and after that the prevalence in outpatient settings and in the biobank linked data (CDW Bordeaux, EBB, IQVIA DA Germany).

CPRD

Prevalence of Adult PM and DM was very similar in CPRD, and relatively stable over time.DM had a prevalence ranging from 4.3 (3.8 to 4.9) per 100,000 people in 2006 to 6.7 (5.8 to 7.7) in 2021 and PM prevalence increased from 5.7 (5.1 to 6.3) in 2006 to 6.4 (5.6 to 7.4) in 2021.

As for juvenile forms, JDM was more frequent than JPM with a prevalence of JDM in CPRD ranging from 1.7 per 100,000 children (1.1 to 2.4) in 2006 to 1.9 per 100,000 children (1.1 to 3.2) in 2021. Conversely the prevalence for JPM was of 0.4 (0.2 to 0.8) in 2006 and rose to 0.6 (0.3 to 1.4) in 2020, with 2021 having less than 5 cases.

SIDIAP

In SIDIAP, both adult DM and PM annual prevalence estimates increase over time, with the prevalence of DM increase much more markedly. The prevalence of DM went from 0.5 (0.4 to 0.8) cases per 100,000 in 2007 to 20.0 (18.8to 21.2) in 2021. The prevalence of PM started at 0.4 (0.3 to 0.6) cases per 100,000 in 2007 and ended in 2021 with 4.6 (4.1 to 5.3).

In SIDIAP, JPM prevalence was 0 or there were less than 5 cases, so no prevalence could be calculated. As for JDM, the prevalence went from 0.5 (0.2 to 1.2) in 2007 to 7.8 (6.3 to 9.6) in 2021.

CDW Bordeaux

Hospital/Outpatient prevalence is considerably higher, probably inherent to the setting, with an increasing trend for both diseases. Prevalence of PM starts at 3.2 (1.8 to 5.8) per 100,000 people in 2009 increasing to 24.0 (19.6 to 29.4) in 2022. Prevalence of DM starts at 5.3 (3.4 to 8.4) in 2009 and increases to 31.3 (26.3 to 37.4) in 2022.

As for the juvenile DM in Bordeaux, there were less than 5 cases until 2014, when the prevalence was 4.0 (1.9 to 8.8) per 100,000 and went up to 10.8 (6.0 to 19.4) in 2022. As for juvenile Polymyositis there were 5 cases or less during the whole study period.

EBB

The prevalence of adult DM was greater than that of adult PM in EBB, and both diseases exhibited an upward trend over time. DM had a prevalence of 16.6 (11.5 to 24.0) per 100,000 people in 2006, which increased to 52 (43 to 62.8) in the year 2021. PM prevalence rose from 7.7 (4.5 to 13.2) in 2006 to 34 (26.9 to 43.0) in 2022.

As for juvenile forms, both forms had counts of less than 5 cases, so no prevalence estimates are presented.

IQVIA GERMANY DA

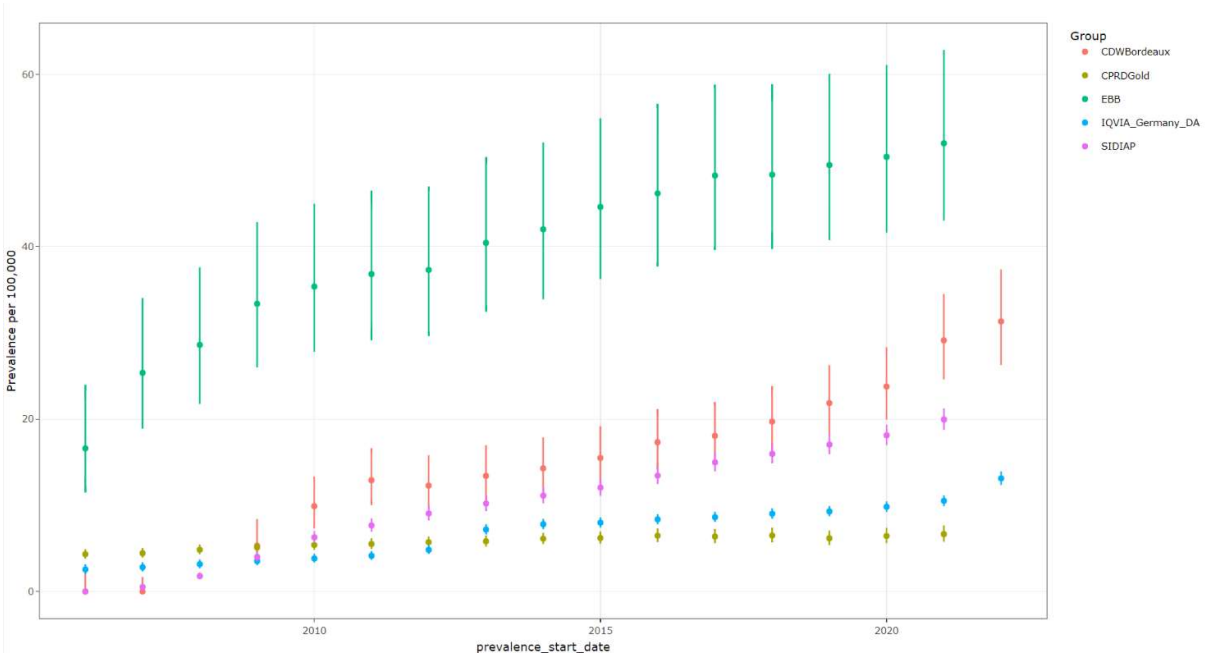
IQVIA GERMANY DA showed a similar prevalence of adult PM and DM, with both conditions experiencing an increase over time. DM had a prevalence ranging from 2.6 (2.1 to 3.2) per 100,000 people in 2006 to 13.1 (12.4 to 13.9) in 2022 and PM prevalence increased from 2.6 (2.1 to 3.2) in 2006 to 10.1 (9.5 to 10.8) in 2022.

Prevalence estimates are not available for JPM as it had counts of less than 5 cases. For JDM the prevalence also increased, from 1.6 (0.8 to 2.9) in 2006 to 3.3 (2.4 to 4.4) in 2022.

Adult forms

Figure 12.1Period prevalence of Adult Dermatomyositis and Polymyositis in primary care and outpatient settings, year (2006-2022)

Adult Dermatomyositis



Adult Polymyositis

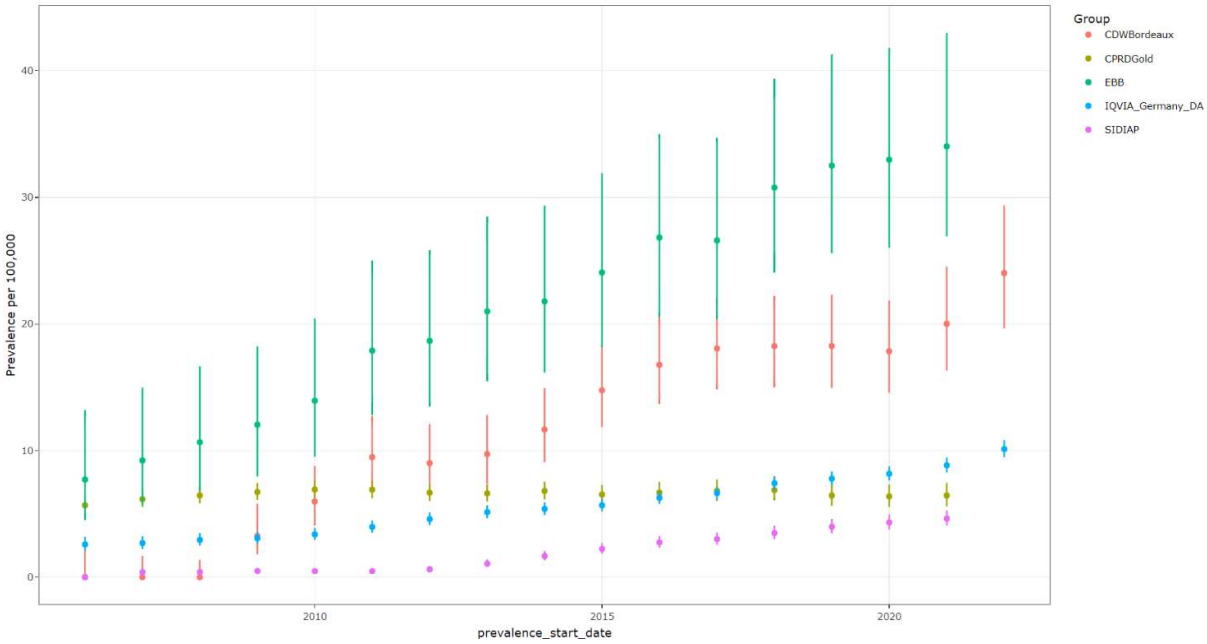
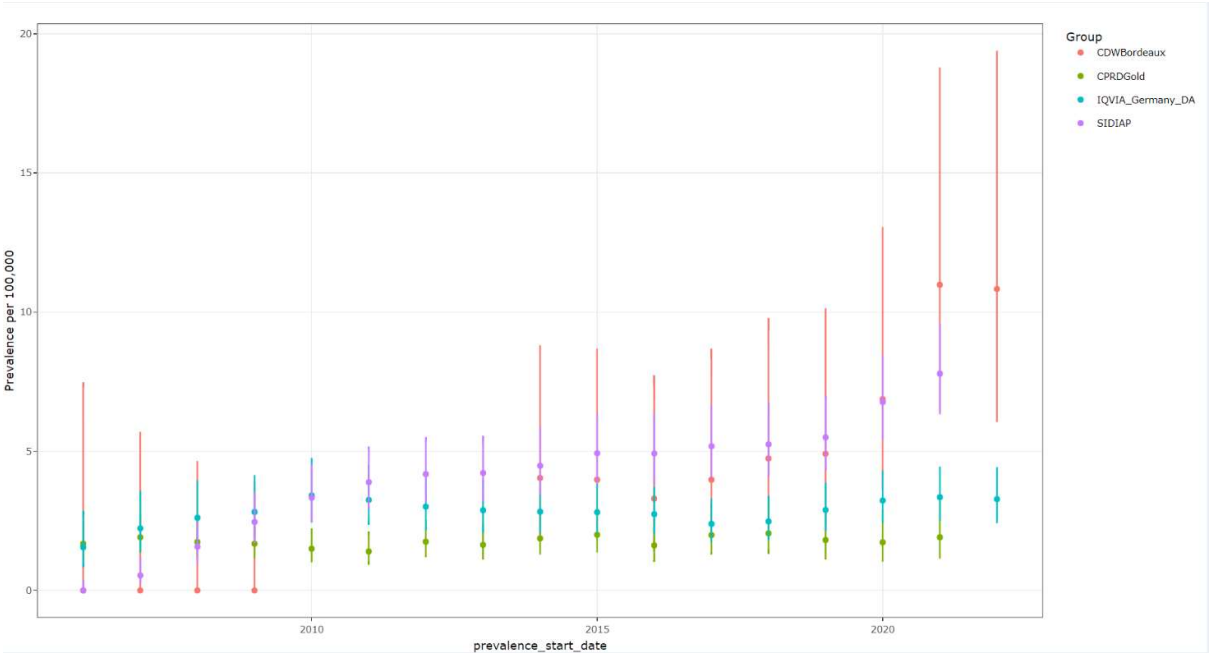


Figure 12.2 Period prevalence of Juvenile Polymyositis and Dermatomyositis in primary care settings care and outpatient, by year (2006-2022)

Juvenile Dermatomyositis



Juvenile Polymyositis

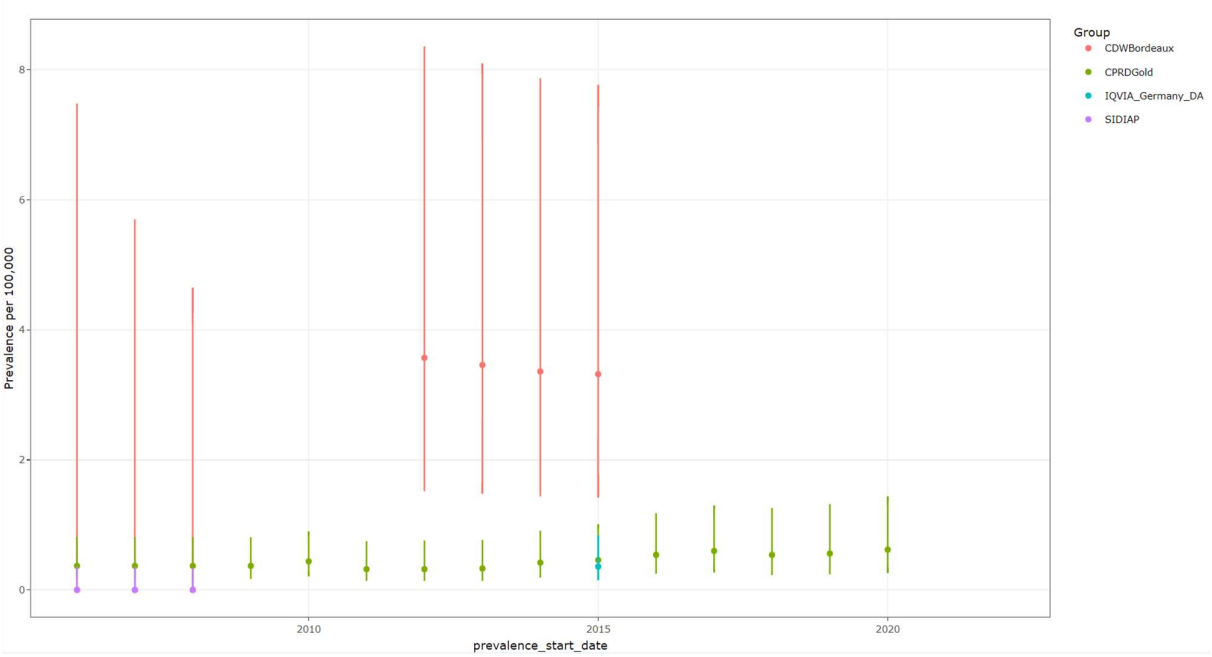


Table 12.2 ***Period prevalence per 100,000 people 18 years old or more of Adult Dermatomyositis and Polymyositis 2006-2023***

		CDW Bordeaux			CPRD Gold			EBB			IQVIA Germany DA			SIDIAP		
	year	cases	N	Prevalence (95%CI)	cases	N	Prevalence (95%CI)	cases	N	Prevalence (95%CI)	cases	N	Prevalence (95%CI)	cases	N	Prevalence (95%CI)
PM	2006	<5	172,311		324	5,707,463	5.7 (5.1 to 6.3)	13	168,622	7.7 (4.5 to 13.2)	87	3,360,617	2.6 (2.1 to 3.2)	<5	4,605,045	
PM	2007	<5	226,678		357	5,796,340	6.2 (5.6 to 6.8)	16	173,463	9.2 (5.7 to 15)	109	4,043,870	2.7 (2.2 to 3.2)	19	4,747,668	0.4 (0.3 to 0.6)
PM	2008	<5	281,245		374	5,791,849	6.5 (5.8 to 7.2)	19	178,247	10.7 (6.8 to 16.6)	138	4,672,168	3 (2.5 to 3.5)	20	4,865,153	0.4 (0.3 to 0.6)
PM	2009	11	338,939	3.2 (1.8 to 5.8)	392	5,823,696	6.7 (6.1 to 7.4)	22	182,733	12 (8 to 18.2)	164	5,327,247	3.1 (2.6 to 3.6)	24	4,939,797	0.5 (0.3 to 0.7)
PM	2010	26	434,558	6 (4.1 to 8.8)	403	5,820,081	6.9 (6.3 to 7.6)	26	186,551	13.9 (9.5 to 20.4)	199	5,884,311	3.4 (2.9 to 3.9)	24	4,981,975	0.5 (0.3 to 0.7)
PM	2011	44	464,244	9.5 (7.1 to 12.7)	395	5,720,080	6.9 (6.3 to 7.6)	34	190,064	17.9 (12.8 to 25)	260	6,550,140	4 (3.5 to 4.5)	24	4,980,764	0.5 (0.3 to 0.7)
PM	2012	44	488,361	9 (6.7 to 12.1)	376	5,636,378	6.7 (6 to 7.4)	36	192,941	18.7 (13.5 to 25.8)	329	7,172,001	4.6 (4.1 to 5.1)	31	4,965,825	0.6 (0.4 to 0.9)
PM	2013	50	514,349	9.7 (7.4 to 12.8)	369	5,574,720	6.6 (6 to 7.3)	41	195,290	21 (15.5 to 28.5)	400	7,774,642	5.1 (4.7 to 5.7)	52	4,876,499	1.1 (0.8 to 1.4)
PM	2014	62	531,932	11.7 (9.1 to 14.9)	361	5,302,408	6.8 (6.1 to 7.6)	43	197,465	21.8 (16.2 to 29.3)	447	8,297,045	5.4 (4.9 to 5.9)	81	4,862,129	1.7 (1.3 to 2.1)
PM	2015	80	542,012	14.8 (11.9 to 18.4)	314	4,811,795	6.5 (5.8 to 7.3)	48	199,461	24.1 (18.1 to 31.9)	497	8,749,951	5.7 (5.2 to 6.2)	108	4,842,144	2.2 (1.9 to 2.7)
PM	2016	92	548,617	16.8 (13.7 to 20.6)	275	4,117,960	6.7 (5.9 to 7.5)	54	201,364	26.8 (20.6 to 35)	589	9,387,731	6.3 (5.8 to 6.8)	133	4,831,942	2.8 (2.3 to 3.3)
PM	2017	99	548,229	18.1 (14.8 to 22)	253	3,712,245	6.8 (6 to 7.7)	54	203,055	26.6 (20.4 to 34.7)	653	9,832,408	6.6 (6.2 to 7.2)	146	4,857,178	3 (2.6 to 3.5)
PM	2018	99	542,573	18.2 (15 to 22.2)	239	3,475,349	6.9 (6.1 to 7.8)	63	204,721	30.8 (24.1 to 39.4)	734	9,894,622	7.4 (6.9 to 8)	171	4,895,352	3.5 (3 to 4.1)
PM	2019	96	525,746	18.3 (14.9 to 22.3)	217	3,366,764	6.4 (5.6 to 7.4)	67	206,130	32.5 (25.6 to 41.3)	792	10,167,077	7.8 (7.3 to 8.3)	197	4,938,004	4 (3.5 to 4.6)
PM	2020	93	521,346	17.8 (14.6 to 21.9)	202	3,164,881	6.4 (5.6 to 7.3)	68	206,228	33 (26 to 41.8)	816	9,986,125	8.2 (7.6 to 8.8)	214	4,948,835	4.3 (3.8 to 4.9)
PM	2021	92	459,841	20 (16.3 to 24.5)	188	2,914,698	6.4 (5.6 to 7.4)	70	205,761	34 (26.9 to 43)	880	9,955,260	8.8 (8.3 to 9.4)	230	4,964,785	4.6 (4.1 to 5.3)
PM	2022	95	395,622	24 (19.6 to 29.4)							838	8,278,855	10.1 (9.5 to 10.8)			
DM	2006	<5	172,311		247	5,707,463	4.3 (3.8 to 4.9)	28	168,622	16.6 (11.5 to 24)	86	3,360,617	2.6 (2.1 to 3.2)	<5	4,605,045	
DM	2007	<5	226,678		258	5,796,340	4.4 (3.9 to 5)	44	173,463	25.4 (18.9 to 34)	114	4,043,870	2.8 (2.4 to 3.4)	25	4,747,668	0.5 (0.4 to 0.8)
DM	2008	<5	281,245		281	5,791,849	4.8 (4.3 to 5.4)	51	178,247	28.6 (21.8 to 37.6)	148	4,672,168	3.2 (2.7 to 3.7)	87	4,865,153	1.8 (1.4 to 2.2)
DM	2009	18	338,939	5.3 (3.4 to 8.4)	298	5,823,696	5.1 (4.6 to 5.7)	61	182,733	33.4 (26 to 42.9)	188	5,327,247	3.5 (3.1 to 4.1)	198	4,939,797	4 (3.5 to 4.6)
DM	2010	43	434,558	9.9 (7.3 to 13.3)	314	5,820,081	5.4 (4.8 to 6)	66	186,551	35.4 (27.8 to 45)	226	5,884,311	3.8 (3.4 to 4.4)	313	4,981,975	6.3 (5.6 to 7)
DM	2011	60	464,244	12.9 (10 to 16.6)	316	5,720,080	5.5 (5 to 6.2)	70	190,064	36.8 (29.1 to 46.5)	272	6,550,140	4.2 (3.7 to 4.7)	382	4,980,764	7.7 (6.9 to 8.5)
DM	2012	60	488,361	12.3 (9.6 to 15.8)	323	5,636,378	5.7 (5.1 to 6.4)	72	192,941	37.3 (29.6 to 47)	347	7,172,001	4.8 (4.4 to 5.4)	450	4,965,825	9.1 (8.3 to 9.9)
DM	2013	69	514,349	13.4 (10.6 to 17)	325	5,574,720	5.8 (5.2 to 6.5)	79	195,290	40.5 (32.5 to 50.4)	559	7,774,642	7.2 (6.6 to 7.8)	498	4,876,499	10.2 (9.3 to 11.2)
DM	2014	76	531,932	14.3 (11.4 to 17.9)	325	5,302,408	6.1 (5.5 to 6.8)	83	197,465	42 (33.9 to 52.1)	648	8,297,045	7.8 (7.2 to 8.4)	541	4,862,129	11.1 (10.2 to 12.1)
DM	2015	84	542,012	15.5 (12.5 to 19.2)	299	4,811,795	6.2 (5.6 to 7)	89	199,461	44.6 (36.3 to 54.9)	699	8,749,951	8 (7.4 to 8.6)	584	4,842,144	12.1 (11.1 to 13.1)
DM	2016	95	548,617	17.3 (14.2 to 21.2)	267	4,117,960	6.5 (5.8 to 7.3)	93	201,364	46.2 (37.7 to 56.6)	786	9,387,731	8.4 (7.8 to 9)	650	4,831,942	13.4 (12.5 to 14.5)
DM	2017	99	548,229	18.1 (14.8 to 22)	237	3,712,245	6.4 (5.6 to 7.2)	98	203,055	48.3 (39.6 to 58.8)	849	9,832,408	8.6 (8.1 to 9.2)	728	4,857,178	15 (13.9 to 16.1)
DM	2018	107	542,573	19.7 (16.3 to 23.8)	226	3,475,349	6.5 (5.7 to 7.4)	99	204,721	48.4 (39.7 to 58.9)	893	9,894,622	9 (8.4 to 9.6)	782	4,895,352	16 (14.9 to 17.1)

DM	2019	115	525,746	21.9 (18.2 to 26.2)	208	3,366,764	6.2 (5.4 to 7.1)	102	206,130	49.5 (40.8 to 60.1)	946	10,167,077	9.3 (8.7 to 9.9)	842	4,938,004	17 (15.9 to 18.2)
DM	2020	124	521,346	23.8 (20 to 28.4)	204	3,164,881	6.4 (5.6 to 7.4)	104	206,228	50.4 (41.6 to 61.1)	982	9,986,125	9.8 (9.2 to 10.5)	897	4,948,835	18.1 (17 to 19.4)
DM	2021	134	459,841	29.1 (24.6 to 34.5)	194	2,914,698	6.7 (5.8 to 7.7)	107	205,761	52 (43 to 62.8)	1,047	9,955,260	10.5 (9.9 to 11.2)	991	4,964,785	20 (18.8 to 21.2)
DM	2022	124	395,622	31.3 (26.3 to 37.4)							1,086	8,278,855	13.1 (12.4 to 13.9)			

DM: Dermatoymyositis, PM: Polymyositis, CI: Confidence Interval

Table 12.3 ***Period prevalence per 100,000 of Juvenile Dermatomyositis and Polymyositis 2006-2023***

		CDW Bordeaux			CPRD Gold			EBB			IQVIA Germany DA			SIDIAP		
	year	cases	N	Prevalence (95%CI)	cases	N	Prevalence (95%CI)	cases	N	Prevalence (95%CI)	cases	N	Prevalence (95%CI)	cases	N	Prevalence (95%CI)
JDM	2006	<5	51,380		27	1,608,000	1.7 (1.1 to 2.4)	<5	40,835		10	643,648	1.6 (0.8 to 2.9)	0	1,057,041	0 (0 to 0.4)
JDM	2007	<5	67,354		31	1,620,002	1.9 (1.4 to 2.7)	<5	35,994		17	761,404	2.2 (1.4 to 3.6)	6	1,101,427	0.5 (0.2 to 1.2)
JDM	2008	<5	82,662		28	1,610,631	1.7 (1.2 to 2.5)	<5	31,210		22	844,058	2.6 (1.7 to 4)	18	1,146,691	1.6 (1 to 2.5)
JDM	2009	<5	98,123		27	1,608,178	1.7 (1.1 to 2.4)	<5	26,724		26	920,418	2.8 (1.9 to 4.1)	29	1,178,692	2.5 (1.7 to 3.5)
JDM	2010	<5	125,375		24	1,600,350	1.5 (1 to 2.2)	<5	22,906		34	997,242	3.4 (2.4 to 4.8)	40	1,200,605	3.3 (2.5 to 4.5)
JDM	2011	<5	134,167		22	1,570,782	1.4 (0.9 to 2.1)	<5	19,393		36	1,108,618	3.2 (2.4 to 4.5)	47	1,207,701	3.9 (2.9 to 5.2)
JDM	2012	<5	140,047		27	1,545,687	1.8 (1.2 to 2.5)	<5	16,516		36	1,196,654	3 (2.2 to 4.2)	50	1,197,232	4.2 (3.2 to 5.5)
JDM	2013	<5	144,536		25	1,522,212	1.6 (1.1 to 2.4)	<5	13,857		37	1,283,484	2.9 (2.1 to 4)	50	1,185,078	4.2 (3.2 to 5.6)
JDM	2014	6	148,670	4 (1.9 to 8.8)	27	1,443,232	1.9 (1.3 to 2.7)	<5	11,354		38	1,342,913	2.8 (2.1 to 3.9)	53	1,182,305	4.5 (3.4 to 5.9)
JDM	2015	6	150,586	4 (1.8 to 8.7)	26	1,302,338	2 (1.4 to 2.9)	<5	9,016		39	1,385,738	2.8 (2.1 to 3.9)	58	1,177,473	4.9 (3.8 to 6.4)
JDM	2016	5	151,522	3.3 (1.4 to 7.7)	18	1,111,807	1.6 (1 to 2.6)	<5	6,772		41	1,495,725	2.7 (2 to 3.7)	58	1,178,533	4.9 (3.8 to 6.4)
JDM	2017	6	150,577	4 (1.8 to 8.7)	20	1,003,339	2 (1.3 to 3.1)	<5	4,706		37	1,544,932	2.4 (1.7 to 3.3)	61	1,177,281	5.2 (4 to 6.7)
JDM	2018	7	147,672	4.7 (2.3 to 9.8)	19	926,309	2 (1.3 to 3.2)	<5	2,699		38	1,532,784	2.5 (1.8 to 3.4)	62	1,180,949	5.2 (4.1 to 6.7)

JDM	2019	7	142,546	4.9 (2.4 to 10.1)	16	885,268	1.8 (1.1 to 2.9)	<5	886		44	1,524,718	2.9 (2.1 to 3.9)	65	1,181,850	5.5 (4.3 to 7)
JDM	2020	9	131,006	6.9 (3.6 to 13.1)	14	810,708	1.7 (1 to 2.9)	<5	261		47	1,454,226	3.2 (2.4 to 4.3)	79	1,166,957	6.8 (5.4 to 8.4)
JDM	2021	13	118,356	11 (6.4 to 18.8)	14	731,210	1.9 (1.1 to 3.2)	<5	99		47	1,404,856	3.4 (2.5 to 4.4)	90	1,155,966	7.8 (6.3 to 9.6)
JDM	2022	11	101,610	10.8 (6 to 19.4)							42	1,282,244	3.3 (2.4 to 4.4)			
JPM	2006	<5	51,380		6	1,608,000	0.4 (0.2 to 0.8)	<5	40,835		<5	643,648		<5	1,057,041	
JPM	2007	<5	67,354		6	1,620,002	0.4 (0.2 to 0.8)	<5	35,994		<5	761,404		<5	1,101,427	
JPM	2008	<5	82,662		6	1,610,631	0.4 (0.2 to 0.8)	<5	31,210		<5	844,058		<5	1,146,691	
JPM	2009	<5	98,123		6	1,608,178	0.4 (0.2 to 0.8)	<5	26,724		<5	920,418		<5	1,178,692	
JPM	2010	<5	125,375		7	1,600,350	0.4 (0.2 to 0.9)	<5	22,906		<5	997,242		<5	1,200,605	
JPM	2011	<5	134,167		5	1,570,782	0.3 (0.1 to 0.8)	<5	19,393		<5	1,108,618		<5	1,207,701	
JPM	2012	5	140,047	3.6 (1.5 to 8.4)	5	1,545,687	0.3 (0.1 to 0.8)	<5	16,516		<5	1,196,654		<5	1,197,232	
JPM	2013	5	144,536	3.5 (1.5 to 8.1)	5	1,522,212	0.3 (0.1 to 0.8)	<5	13,857		<5	1,283,484		<5	1,185,078	
JPM	2014	5	148,670	3.4 (1.4 to 7.9)	6	1,443,232	0.4 (0.2 to 0.9)	<5	11,354		<5	1,342,913		<5	1,182,305	
JPM	2015	5	150,586	3.3 (1.4 to 7.8)	6	1,302,338	0.5 (0.2 to 1)	<5	9,016		5	1,385,738	0.4 (0.1 to 0.8)	<5	1,177,473	
JPM	2016	<5	151,522		6	1,111,807	0.5 (0.2 to 1.2)	<5	6,772		<5	1,495,725		<5	1,178,533	
JPM	2017	<5	150,577		6	1,003,339	0.6 (0.3 to 1.3)	<5	4,706		<5	1,544,932		<5	1,177,281	
JPM	2018	<5	147,672		5	926,309	0.5 (0.2 to 1.3)	<5	2,699		<5	1,532,784		<5	1,180,949	
JPM	2019	<5	142,546		5	885,268	0.6 (0.2 to 1.3)	<5	886		<5	1,524,718		<5	1,181,850	
JPM	2020	<5	131,006		5	810,708	0.6 (0.3 to 1.4)	<5	261		<5	1,454,226		<5	1,166,957	

JPM	**2021**	<5	118,356		<5	731,210		<5	99		<5	1,404,856		<5	1,155,966	
JPM	**2022**	<5	101,610								<5	1,282,244				

JDM: Juvenile Dermatoymyositis, JPM: Juvenile Polymyositis, CI: Confidence Interval

12.1.5 Other Analysis

Point prevalence, and period prevalence for the 0 days of previous observation cohorts were very similar to period prevalence for all analyses. Results from these prevalence estimates by gender, and further age groups for the paediatric population are available in the shiny app at https://data-dev.darwin-eu.org/P2-C1-007-DermatomyositisPolymyositis/

12.2. Patient-level characteristics

12.2.1 Participants

Table 12.4 shows the number of patients with DM, PM, JDM, and JPM in each database having at least 365 days of previous visibility in each database. The starting number of patients with DM ranged from 95 in EBB to 1863 in IQVIA Germany DA. For Adult Polymyositis, it ranged from 66 in EBB to 1519 in IQVIA Germany DA. As for the juvenile forms, number of patients were much lower, with JDM having between less than 5 patients in EBB to 143 in SIDIAP. We identified less than 5 children with JPM in EBB, 5 children in SIDIAP, and 9 children in IQVIA Germany DA, CDW Bordeaux and in CPRD Gold. The low number of participants prevented us from showing any counts or prevalences in the analyses, as they amount to less than 5.

Table 12.4 Total number of patients with each of the conditions and 365 days of visibility in each database

Database	DM	PM	JDM	JPM
IQVIA_Germany_DA	1863	1519	118	9
CDWBordeaux	230	187	19	9
CPRDGold	495	481	53	9
EBB	95	66	<5	<5
SIDIAP	1286	288	143	5

12.2.2 Demographics

Baseline Demographics

Table 12.5 to Table 12.8 show the demographics for each of the cohorts. DM, PM seem to be predominant in women in all databases, with percentage of women ranging from 71.9% for adult DM in CDW Bordeaux to 61.4% in DM for SIDIAP. Juvenile forms show similar distribution, with more than 50% female in all databases except for JDM in CDW Bordeaux (47.4%).

As for age distribution, median age was between 50 to 62 for DM and between 57 and 60 for PM. Age of diagnosis for juvenile DM forms varied from 9 in SIDIAP to 13 in CDW Bordeaux. Juvenile PM patients seemed younger but there were only few patients.

Table 12.5 Baseline characteristics of Adult Dermatomyositis population by database

Database	CDWBordeaux	CPRD GOLD	EBB	SIDIAP	IQVIA Germany
Number subjects	230	495	95	1286	1863
Number records	231	495	95	1286	1863
Sex, N (%)					
Female	166 (71.9%)	328 (66.3%)	76 (80%)	790 (61.4%)	1219 (65.4%)
Age					
median [p25 - p75]	62 [50 – 69]	58 [46 - 68.5]	50 [38 - 61.5]	51 [38 - 67]	60 [48.5 – 72]
Prior history, days					
median [p25 - p75]	1690 [822 – 3033.5]	3500 [1990.5 - 5474]	2548 [1439 - 4636]	3083 [1646.75 - 4652.25]	2202 [976.5 – 4298]
Minimum cohort start date	03/12/2008	06/01/2006	06/01/2006	01/01/2007	20/02/2006
Maximum cohort end date	02/08/2023	15/12/2022	31/12/2021	30/06/2022	01/04/2023

Table 12.6 Baseline characteristics of Adult Polymyositis population by database

Database	CDWBordeaux	CPRD GOLD	EBB	SIDIAP	IQVIA Germany
Number subjects	187	481	66	288	1519
Number records	187	481	66	288	1519
Sex, N (%)					
Female	118 (63.1%)	281 (58.4%)	47 (71.2%)	187 (64.9%)	1032 (67.9%)
Age					
median [p25 - p75]	57 [46 - 67]	60 [47 - 71]	57 [43 - 68.75]	59 [47 - 70]	60 [49 - 70]
Prior history, days					
median [p25 - p75]	1875 [897 - 3029.5]	3041 [1651 - 4892]	3836 [2590.5 - 5196]	3715.5 [2894 - 4870]	1954 [950.5 - 3632]
Minimum cohort start date	23/01/2009	13/01/2006	22/06/2006	05/03/2007	05/01/2006
Maximum cohort end date	02/08/2023	14/12/2022	31/12/2021	30/06/2022	01/04/2023

Table 12.7 Baseline characteristics of Juvenile Dermatomyositis population by database

Database	CDWBordeaux	CPRD GOLD	EBB	SIDIAP	IQVIA Germany
Number subjects	19	53	<5	143	118
Number records	19	53	<5	143	118
Sex, N (%)					
Female	9 (47.4%)	37 (69.8%)	NA	81 (56.6%)	70 (59.3%)

Database	CDWBordeaux	CPRD GOLD	EBB	SIDIAP	IQVIA Germany
Age					
median [p25 - p75]	13 [6.5 – 15.5]	10 [7 - 14]	NA	9 [5 - 14]	10 [6.25 – 14]
Age groups, N (%)					
0 to 2	<5	<5	NA	12 (8.4%)	5 (4.2%)
3 to 6	<5	10 (18.9%)	NA	34 (23.8%)	25 (21.2%)
7 to 12	<5	23 (43.4%)	NA	55 (38.5%)	45 (38.1%)
13 to 18	10 (52.6%)	18 (34%)	NA	42 (29.4%)	43 (36.4%)
Prior history, days					
median [p25 - p75]	1012 [588 - 2856.5]	2699 [1279 - 3506]	NA	1828 [1036.5 - 3488.5]	1301 [880 - 2628.5]
Minimum cohort start date	07/02/2010	12/06/2006	NA	27/04/2007	15/02/2006
Maximum cohort end date	02/08/2023	15/12/2022	NA	30/06/2022	01/04/2023

Table 12.8 Baseline characteristics of Juvenile Polymyositis population by database

Database	CDWBordeaux	CPRD GOLD	EBB	SIDIAP	IQVIA Germany
Number subjects	9	9	<5	5	9
Number records	9	9	<5	5	9
Sex, N (%)					
Female	5 (55.6%)	<5	NA	<5	7 (77.8%)
Age					
median [p25 - p75]	6 [5 - 14]	8 [7 - 11]	NA	13 [12 - 15]	12 [6 - 13]
Age groups, N (%)					
0 to 2	0 (0)	0 (0)	NA	0 (0)	0 (0)
3 to 6	5 (55.6%)	<5	NA	0 (0)	<5
7 to 12	<5	6 (66.7%)	NA	<5	<5
13 to 18	<5	<5	NA	<5	<5
Prior history, days					
median [p25 - p75]	1610 [1440 - 1782]	2721 [2499 - 3112]	NA	3681 [3143 - 3852]	1300 [539 - 2316]
Minimum cohort start date	18/12/2009	20/07/2007	NA	26/08/2009	27/01/2011
Maximum cohort end date	06/03/2023	14/12/2022	NA	30/06/2022	01/04/2023

12.2.3 Biomarker and Clinical manifestations

The occurrence of recorded biomarkers assessments and clinical manifestations is depicted in Table 12.9 to Table 12.166. Occurrence of both was measured as at least one code of biomarkers assessments or clinical manifestations within the selected time windows: anytime to 1year before index date, 1 year to 3 months before, 3 to 1 months before, 1 month before, on the same day as the index date, 3 months after, 3 to 6 months after, 6 to 12 months after, 1 to 3 years after, 3 to 5 years after, and >5 years after. We didn't present in the report those biomarkers assessments/clinical manifestations that did not occur more than 5 times per period and in at least one database, but the information is available and can be viewed in the shiny app: https://data-dev.darwin-eu.org/P2-C1-007-DermatomyositisPolymyositis/

Biomarker assessment occurrence

The occurrences of biomarker measurements over time showed significant variability among different databases and settings, as the visibility of each biomarker occurrence could differ across settings. JPM biomarkers are omitted from the text and showed only in Table 12.12 as the number of patients with this condition is very low in all databases and all counts are <5 except in CDW Bordeaux. Please note, that only the occurrence of biomarker measurements and not the results of the tests are reported here.

CPRD

In CPRD, the biomarker tests that were most frequently used in the month leading up to the diagnosis of DM were C-reactive Protein (CRP) at a rate of 17%, Erythrocyte sedimentation rate (ESR) at 15%, Creatine kinase (CK) at 13%, and aspartate aminotransferase (AST) at 5%. After the initial period, the biomarker- tests that were used showed comparable percentages, including CRP at 25%, ESR at 21%, CK at 23%, and AST at 8%. Similar ratios can be noted in both the before and after periods. For PM, the biomarker tests used in the month before were the same with similar percentages both before and after. AST, CRP, CK, and ESR testing was observed also in JDM, with a significant emphasis on the follow-up period of 1-3 years after the index date.

SIDIAP

According to SIDIAP data, the biomarker tests that saw the highest usage in the month leading to DM diagnosis were aspartate aminotransferase (AST) at 10%, Erythrocyte sedimentation rate (ESR) at 9%, C-reactive Protein (CRP) at a rate of 6%, and Cancer Ag 125 (Ca125) at 1%. After the initial period, the biomarker tests that were used showed comparable percentages, including AST at 18%, ESR at 15%, CRP at 10%, and Ca125 at 2%. The before and after periods both show higher proportions. The biomarker tests used for PM were consistent in the month before and showed similar percentages before and after. AST, CRP, and ESR were observed also in JDM, with lower percentages, 10, 5 and 6% respectively in the month leading to JDM diagnosis.

CDW Bordeaux

In Bordeaux, we see some of the biomarker tests seen in the previous databases (CRP, CK, and AST) being performed in many more patients in the months before or after a diagnosis of DM, PM or JDM, with for example more than 75% of the patients with a record of these tests in the 3 months following the diagnosis. In addition, in adult forms (DM and PM) we also see (although for less than 10% of patients for each timeframe) measurements of Lactate dehydrogenase (LDH), Antinuclear antibodies (ANA), Mi-2 Ab, PL-12 Ab, PL-17 Ab, Myoglobin, SRP Ab, and SAE Ab.

EBB

In EBB, occurrence of biomarker measurement is similar to that observed in CDW Bordeaux, with the majority of tests performed in the months before and after a PM or a DM diagnosis being CRP, ESR, CK, AST and LDH. These were followed by myoglobin, ANA, Mi-2 Ab, PL-12 Ab, PL-17 Ab, SRP Ab, and SAE Ab, that can be seen but in less than 5 people. There were less than 5 people with any biomarker test assessment amongst people with JPM or JDM.

IQVIA DA

It was observed in the IQVIA DA Germany data that a very small proportion of patients underwent testing for DM, and the available records only included information on AST, CRP, and ESR testing. For PM we observed a higher rate of CRP testing (18% in the 3 months after diagnosis), and similarly low rates of AST (7%) and ESR (1%) testing. For JDM, there are some occurrences of CRP and AST testing, but in 5 or fewer patients.

Table 12.9 Biomarker occurring before, on, and after the diagnosis of Adult Dermatomyositis on 2006-2022

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
CDWBordeaux	Antinuclear antibodies (ANA)	11 (5%)	7 (3%)	0 (0%)	5 (2%)	5 (2%)	17 (7%)	<5	<5	14 (6%)	12 (5%)	29 (13%)
	aspartate aminotransferase (AST)	141 (61%)	108 (47%)	63 (27%)	42 (18%)	128 (55%)	200 (87%)	101 (44%)	111 (48%)	144 (62%)	82 (36%)	68 (29%)
	Cancer Ag 125	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	<5	<5	<5	<5	<5	0 (0%)
	C-reactive protein	142 (61%)	106 (46%)	58 (25%)	38 (16%)	129 (56%)	203 (88%)	95 (41%)	113 (49%)	146 (63%)	83 (36%)	69 (30%)
	Creatine kinase (CK)	107 (46%)	88 (38%)	50 (22%)	42 (18%)	103 (45%)	172 (74%)	87 (38%)	95 (41%)	113 (49%)	67 (29%)	62 (27%)
	Erythrocyte sedimentation rate (ESR)	<5	<5	<5	<5	<5	<5	<5	<5	<5	0 (0%)	5 (2%)
	Lactate dehydrogenase (LDH)	12 (5%)	11 (5%)	10 (4%)	7 (3%)	10 (4%)	24 (10%)	5 (2%)	8 (3%)	20 (9%)	9 (4%)	22 (10%)
	Mi-2 antibody	6 (3%)	5 (2%)	0 (0%)	6 (3%)	5 (2%)	10 (4%)	<5	<5	8 (3%)	<5	16 (7%)
	Myoglobin	5 (2%)	9 (4%)	0 (0%)	<5	7 (3%)	7 (3%)	<5	<5	<5	<5	7 (3%)
	PL-12 antibody	6 (3%)	5 (2%)	0 (0%)	6 (3%)	5 (2%)	10 (4%)	<5	<5	8 (3%)	<5	16 (7%)
	PL-7 antibody	6 (3%)	5 (2%)	0 (0%)	6 (3%)	5 (2%)	10 (4%)	<5	<5	8 (3%)	<5	16 (7%)
	Polymyositis-scleroderma antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Ribonucleoprotein extractable nuclear antibody (ENA)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Signal Recognition Particle (SRP) antibody	6 (3%)	5 (2%)	0 (0%)	6 (3%)	5 (2%)	10 (4%)	<5	<5	8 (3%)	<5	16 (7%)
	SUMO-activating enzyme subunit 1 (SAE) antibody	6 (3%)	5 (2%)	0 (0%)	6 (3%)	5 (2%)	10 (4%)	<5	<5	8 (3%)	<5	16 (7%)
CPRD	Antinuclear antibodies (ANA)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	aspartate aminotransferase (AST)	120 (24%)	52 (11%)	36 (7%)	27 (5%)	6 (1%)	41 (8%)	42 (8%)	49 (10%)	55 (11%)	43 (9%)	33 (7%)
	Cancer Ag 125	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	C-reactive protein	197 (40%)	131 (26%)	97 (20%)	86 (17%)	23 (5%)	122 (25%)	90 (18%)	135 (27%)	182 (37%)	123 (25%)	112 (23%)
	Creatine kinase (CK)	93 (19%)	66 (13%)	49 (10%)	63 (13%)	28 (6%)	114 (23%)	72 (15%)	110 (22%)	136 (27%)	83 (17%)	69 (14%)
	Erythrocyte sedimentation rate (ESR)	219 (44%)	134 (27%)	102 (21%)	76 (15%)	19 (4%)	104 (21%)	85 (17%)	114 (23%)	162 (33%)	102 (21%)	76 (15%)
	Lactate dehydrogenase (LDH)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Myoglobin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	PL-12 antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	PL-7 antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Polymyositis-scleroderma antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Ribonucleoprotein extractable nuclear antibody (ENA)	0 (0%)	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Signal Recognition Particle (SRP) antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	SUMO-activating enzyme subunit 1 (SAE) antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
EBB	Antinuclear antibodies (ANA)	<5	<5	0 (0%)	5 (5%)	0 (0%)	<5	<5	0 (0%)	0 (0%)	<5	5 (5%)
	aspartate aminotransferase (AST)	19 (20%)	10 (11%)	7 (7%)	10 (11%)	<5	13 (14%)	11 (12%)	18 (19%)	24 (25%)	27 (28%)	47 (49%)
	Cancer Ag 125	8 (8%)	<5	<5	<5	0 (0%)	<5	<5	<5	8 (8%)	8 (8%)	13 (14%)

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
	C-reactive protein	58 (61%)	41 (43%)	29 (31%)	32 (34%)	18 (19%)	46 (48%)	32 (34%)	45 (47%)	71 (75%)	68 (72%)	64 (67%)
	Creatine kinase (CK)	16 (17%)	<5	6 (6%)	15 (16%)	<5	14 (15%)	6 (6%)	12 (13%)	13 (14%)	15 (16%)	33 (35%)
	Erythrocyte sedimentation rate (ESR)	38 (40%)	21 (22%)	18 (19%)	17 (18%)	9 (9%)	23 (24%)	18 (19%)	25 (26%)	40 (42%)	42 (44%)	48 (51%)
	Lactate dehydrogenase (LDH)	8 (8%)	<5	<5	7 (7%)	<5	9 (9%)	6 (6%)	10 (11%)	9 (9%)	17 (18%)	21 (22%)
	Mi-2 antibody	<5	0 (0%)	0 (0%)	<5	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5
	Myoglobin	<5	<5	<5	<5	<5	7 (7%)	<5	6 (6%)	8 (8%)	7 (7%)	13 (14%)
	PL-12 antibody	<5	0 (0%)	0 (0%)	<5	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5
	PL-7 antibody	<5	0 (0%)	0 (0%)	<5	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5
	Polymyositis-scleroderma antibody	<5	<5	0 (0%)	<5	0 (0%)	<5	<5	0 (0%)	0 (0%)	<5	5 (5%)
	Ribonucleoprotein extractable nuclear antibody (ENA)	<5	<5	<5	<5	0 (0%)	<5	<5	0 (0%)	0 (0%)	<5	5 (5%)
	Signal Recognition Particle (SRP) antibody	<5	0 (0%)	0 (0%)	<5	0 (0%)	<5	0 (0%)	0 (0%)	<5	0 (0%)	<5
	SUMO-activating enzyme subunit 1 (SAE) antibody	<5	0 (0%)	0 (0%)	<5	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5
SIDIAP	Antinuclear antibodies (ANA)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	aspartate aminotransferase (AST)	712 (55%)	291 (23%)	153 (12%)	128 (10%)	15 (1%)	230 (18%)	186 (14%)	251 (20%)	426 (33%)	326 (25%)	361 (28%)
SIDIAP	Cancer Ag 125	42 (3%)	14 (1%)	15 (1%)	14 (1%)	<5	25 (2%)	6 (0%)	25 (2%)	44 (3%)	24 (2%)	25 (2%)
SIDIAP	C-reactive protein	319 (25%)	149 (12%)	96 (7%)	80 (6%)	11 (1%)	131 (10%)	89 (7%)	130 (10%)	251 (20%)	186 (14%)	254 (20%)
SIDIAP	Creatine kinase (CK)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Erythrocyte sedimentation rate (ESR)	571 (44%)	204 (16%)	123 (10%)	112 (9%)	11 (1%)	193 (15%)	125 (10%)	166 (13%)	318 (25%)	245 (19%)	287 (22%)
SIDIAP	Lactate dehydrogenase (LDH)	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	<5	<5	0 (0%)	<5	0 (0%)	0 (0%)
SIDIAP	Myoglobin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	PL-12 antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	PL-7 antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Polymyositis-scleroderma antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Ribonucleoprotein extractable nuclear antibody (ENA)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Signal Recognition Particle (SRP) antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	SUMO-activating enzyme subunit 1 (SAE) antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA	Antinuclear antibodies (ANA)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA	aspartate aminotransferase (AST)	213 (11%)	134 (7%)	48 (3%)	54 (3%)	47 (3%)	145 (8%)	90 (5%)	125 (7%)	193 (10%)	128 (7%)	120 (6%)
IQVIA	Cancer Ag 125	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
	C-reactive protein	174 (9%)	120 (6%)	58 (3%)	66 (4%)	51 (3%)	130 (7%)	89 (5%)	102 (5%)	156 (8%)	114 (6%)	128 (7%)
	Creatine kinase (CK)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Erythrocyte sedimentation rate (ESR)	32 (2%)	<5	<5	<5	<5	10 (1%)	<5	<5	<5	<5	<5
	Lactate dehydrogenase (LDH)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Myoglobin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	PL-12 antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	PL-7 antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Polymyositis-scleroderma antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Ribonucleoprotein extractable nuclear antibody (ENA)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Signal Recognition Particle (SRP) antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	SUMO-activating enzyme subunit 1 (SAE) antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 12.10 Biomarker occurring before, on, an after the diagnosis of Adult Polymyositis on 2006-2022

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
CDWBordeaux	Antinuclear antibodies (ANA)	5 (3%)	6 (3%)	<5	12 (6%)	<5	14 (7%)	<5	<5	6 (3%)	7 (4%)	18 (10%)
	aspartate aminotransferase (AST)	108 (58%)	91 (49%)	50 (27%)	36 (19%)	83 (44%)	152 (81%)	80 (43%)	78 (42%)	107 (57%)	60 (32%)	55 (29%)
	Cancer Ag 125	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5	0 (0%)
	C-reactive protein	110 (59%)	93 (50%)	52 (28%)	38 (20%)	86 (46%)	159 (85%)	85 (45%)	75 (40%)	107 (57%)	69 (37%)	56 (30%)
	Creatine kinase (CK)	87 (47%)	79 (42%)	41 (22%)	31 (17%)	56 (30%)	135 (72%)	64 (34%)	65 (35%)	86 (46%)	55 (29%)	47 (25%)
	Erythrocyte sedimentation rate (ESR)	<5	<5	<5	<5	<5	<5	0 (0%)	<5	<5	<5	<5
	Lactate dehydrogenase (LDH)	7 (4%)	10 (5%)	5 (3%)	<5	6 (3%)	14 (7%)	<5	5 (3%)	14 (7%)	12 (6%)	16 (9%)
	Mi-2 antibody	<5	6 (3%)	<5	10 (5%)	<5	9 (5%)	<5	0 (0%)	0 (0%)	<5	13 (7%)
	Myoglobin	5 (3%)	<5	<5	5 (3%)	<5	5 (3%)	0 (0%)	0 (0%)	<5	<5	<5
	PL-12 antibody	<5	6 (3%)	<5	10 (5%)	<5	9 (5%)	<5	0 (0%)	0 (0%)	<5	13 (7%)
	PL-7 antibody	<5	6 (3%)	<5	10 (5%)	<5	9 (5%)	<5	0 (0%)	0 (0%)	<5	13 (7%)
	Signal Recognition Particle (SRP) antibody	<5	6 (3%)	<5	10 (5%)	<5	9 (5%)	<5	0 (0%)	0 (0%)	<5	13 (7%)

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
	SUMO-activating enzyme subunit 1 (SAE) antibody	<5	6 (3%)	<5	10 (5%)	<5	9 (5%)	<5	0 (0%)	0 (0%)	<5	13 (7%)
CPRD	Antinuclear antibodies (ANA)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CPRD	aspartate aminotransferase (AST)	123 (26%)	53 (11%)	25 (5%)	28 (6%)	<5	39 (8%)	34 (7%)	35 (7%)	51 (11%)	35 (7%)	35 (7%)
CPRD	Cancer Ag 125	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CPRD	C-reactive protein	194 (40%)	136 (28%)	84 (17%)	75 (16%)	19 (4%)	133 (28%)	98 (20%)	115 (24%)	187 (39%)	137 (28%)	123 (26%)
CPRD	Creatine kinase (CK)	134 (28%)	97 (20%)	66 (14%)	78 (16%)	27 (6%)	137 (28%)	94 (20%)	117 (24%)	168 (35%)	97 (20%)	79 (16%)
CPRD	Erythrocyte sedimentation rate (ESR)	214 (44%)	138 (29%)	97 (20%)	74 (15%)	20 (4%)	135 (28%)	109 (23%)	110 (23%)	161 (33%)	112 (23%)	95 (20%)
CPRD	Lactate dehydrogenase (LDH)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CPRD	Myoglobin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CPRD	PL-12 antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CPRD	PL-7 antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CPRD	Signal Recognition Particle (SRP) antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CPRD	SUMO-activating enzyme subunit 1 (SAE) antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
EBB	Antinuclear antibodies (ANA)	<5	<5	<5	<5	0 (0%)	<5	<5	<5	<5	<5	6 (9%)
EBB	aspartate aminotransferase (AST)	19 (29%)	16 (24%)	10 (15%)	17 (26%)	11 (17%)	26 (39%)	16 (24%)	21 (32%)	27 (41%)	18 (27%)	26 (39%)
EBB	Cancer Ag 125	<5	5 (8%)	<5	8 (12%)	<5	8 (12%)	0 (0%)	<5	7 (11%)	7 (11%)	5 (8%)
EBB	C-reactive protein	53 (80%)	38 (58%)	26 (39%)	41 (62%)	17 (26%)	41 (62%)	34 (52%)	39 (59%)	47 (71%)	43 (65%)	35 (53%)
EBB	Creatine kinase (CK)	21 (32%)	13 (20%)	6 (9%)	18 (27%)	15 (23%)	30 (45%)	14 (21%)	18 (27%)	20 (30%)	12 (18%)	20 (30%)
EBB	Erythrocyte sedimentation rate (ESR)	32 (48%)	20 (30%)	10 (15%)	27 (41%)	12 (18%)	29 (44%)	20 (30%)	23 (35%)	36 (55%)	29 (44%)	24 (36%)
EBB	Lactate dehydrogenase (LDH)	13 (20%)	6 (9%)	5 (8%)	11 (17%)	5 (8%)	19 (29%)	8 (12%)	15 (23%)	13 (20%)	16 (24%)	13 (20%)
EBB	Mi-2 antibody	0 (0%)	<5	0 (0%)	<5	0 (0%)	<5	0 (0%)	<5	<5	<5	<5
EBB	Myoglobin	<5	5 (8%)	<5	9 (14%)	6 (9%)	16 (24%)	8 (12%)	7 (11%)	10 (15%)	7 (11%)	6 (9%)
EBB	PL-12 antibody	0 (0%)	<5	0 (0%)	<5	0 (0%)	<5	0 (0%)	<5	<5	<5	<5
EBB	PL-7 antibody	0 (0%)	<5	0 (0%)	<5	0 (0%)	<5	0 (0%)	<5	<5	<5	<5
EBB	Signal Recognition Particle (SRP) antibody	0 (0%)	<5	0 (0%)	<5	0 (0%)	<5	0 (0%)	<5	<5	<5	<5
EBB	SUMO-activating enzyme subunit 1 (SAE) antibody	0 (0%)	<5	0 (0%)	<5	0 (0%)	<5	0 (0%)	<5	<5	<5	<5
SIDIAP	Antinuclear antibodies (ANA)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	aspartate aminotransferase (AST)	191 (66%)	91 (32%)	40 (14%)	48 (17%)	<5	76 (26%)	61 (21%)	85 (30%)	117 (41%)	96 (33%)	86 (30%)
SIDIAP	Cancer Ag 125	10 (3%)	<5	<5	<5	<5	<5	<5	<5	10 (3%)	9 (3%)	11 (4%)

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
	C-reactive protein	118 (41%)	61 (21%)	37 (13%)	40 (14%)	5 (2%)	73 (25%)	47 (16%)	63 (22%)	96 (33%)	62 (22%)	66 (23%)
	Creatine kinase (CK)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Erythrocyte sedimentation rate (ESR)	170 (59%)	73 (25%)	40 (14%)	52 (18%)	7 (2%)	75 (26%)	53 (18%)	72 (25%)	111 (39%)	69 (24%)	64 (22%)
	Lactate dehydrogenase (LDH)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Myoglobin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	PL-12 antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	PL-7 antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Signal Recognition Particle (SRP) antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	SUMO-activating enzyme subunit 1 (SAE) antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	Antinuclear antibodies (ANA)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	aspartate aminotransferase (AST)	151 (10%)	99 (7%)	54 (4%)	57 (4%)	44 (3%)	111 (7%)	64 (4%)	101 (7%)	174 (11%)	142 (9%)	130 (9%)
IQVIA DA GERMANY	Cancer Ag 125	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	C-reactive protein	258 (17%)	159 (10%)	89 (6%)	74 (5%)	188 (12%)	269 (18%)	106 (7%)	162 (11%)	246 (16%)	201 (13%)	173 (11%)
IQVIA DA GERMANY	Creatine kinase (CK)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	Erythrocyte sedimentation rate (ESR)	18 (1%)	12 (1%)	<5	<5	<5	10 (1%)	<5	<5	8 (1%)	8 (1%)	<5
IQVIA DA GERMANY	Lactate dehydrogenase (LDH)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	Myoglobin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	PL-12 antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	PL-7 antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	Signal Recognition Particle (SRP) antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	SUMO-activating enzyme subunit 1 (SAE) antibody	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 12.11 Biomarker occurring before, on, an after the diagnosis of Juvenile Dermatomyositis on 2006-2022

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
CDWBordeaux	aspartate aminotransferase (AST)	9 (47%)	6 (32%)	<5	<5	12 (63%)	16 (84%)	<5	10 (53%)	10 (53%)	<5	<5
	C-reactive protein	12 (63%)	6 (32%)	<5	<5	12 (63%)	15 (79%)	5 (26%)	9 (47%)	9 (47%)	<5	<5
	Creatine kinase (CK)	9 (47%)	6 (32%)	5 (26%)	<5	13 (68%)	17 (89%)	5 (26%)	8 (42%)	7 (37%)	<5	<5
	Erythrocyte sedimentation rate (ESR)	<5	0 (0%)	0 (0%)	0 (0%)	<5	<5	<5	<5	<5	<5	0 (0%)
CPRD	aspartate aminotransferase (AST)	<5	<5	0 (0%)	0 (0%)	0 (0%)	<5	<5	5 (9%)	10 (19%)	5 (9%)	6 (11%)
	C-reactive protein	<5	13 (25%)	7 (13%)	5 (9%)	0 (0%)	9 (17%)	10 (19%)	14 (26%)	23 (43%)	15 (28%)	12 (23%)
	Creatine kinase (CK)	<5	<5	<5	5 (9%)	0 (0%)	6 (11%)	8 (15%)	8 (15%)	15 (28%)	5 (9%)	8 (15%)
	Erythrocyte sedimentation rate (ESR)	<5	9 (17%)	<5	6 (11%)	<5	7 (13%)	7 (13%)	13 (25%)	19 (36%)	12 (23%)	11 (21%)
SIDIAP	aspartate aminotransferase (AST)	15 (10%)	5 (4%)	9 (6%)	14 (10%)	<5	9 (6%)	6 (4%)	12 (8%)	19 (13%)	14 (10%)	29 (20%)
	C-reactive protein	6 (4%)	5 (4%)	6 (4%)	7 (5%)	0 (0%)	5 (4%)	5 (4%)	6 (4%)	11 (8%)	5 (4%)	19 (13%)
	Creatine kinase (CK)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Erythrocyte sedimentation rate (ESR)	10 (7%)	10 (7%)	9 (6%)	9 (6%)	<5	8 (6%)	6 (4%)	8 (6%)	16 (11%)	13 (9%)	18 (13%)
IQVIA DA	aspartate aminotransferase (AST)	<5	<5	<5	<5	<5	6 (5%)	<5	<5	<5	6 (5%)	10 (8%)
	C-reactive protein	<5	<5	0 (0%)	<5	<5	6 (5%)	<5	<5	<5	<5	5 (4%)
	Creatine kinase (CK)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Erythrocyte sedimentation rate (ESR)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 12.12 Biomarker occurring before, on, an after the diagnosis of Juvenile Polymyositis on 2006-2022

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
CDWBordeaux	C-reactive protein	<5	<5	0 (0%)	0 (0%)	<5	6 (67%)	<5	0 (0%)	<5	<5	<5
	Creatine kinase (CK)	<5	<5	0 (0%)	0 (0%)	6 (67%)	8 (89%)	0 (0%)	<5	<5	<5	0 (0%)
CPRD	C-reactive protein	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Creatine kinase (CK)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	C-reactive protein	<5	0 (0%)	0 (0%)	0 (0%)	<5	<5	0 (0%)	<5	<5	<5	<5
	Creatine kinase (CK)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	C-reactive protein	<5	<5	<5	0 (0%)	0 (0%)	<5	<5	<5	<5	<5	0 (0%)
	Creatine kinase (CK)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Clinical manifestations and comorbidities occurrence

The occurrences of clinical manifestations and comorbidities over time was very low for all databases and settings, with clinical manifestations seemingly only well recorded for CDW Bordeaux. The highest proportions of these at index were for muscle pain (14% in DM, 15% in PM), interstitial lung disease (8% in DM, 6% in PM), dysphagia (7% in DM, 11% in PM), Raynaud's (3% in DM, 4% in PM), and thrombosis (2% in DM, 4% in PM).

For JDM and JPM, all clinical manifestations and comorbidities entries had either 0 or <5 occurrences so no tables were presented, except for SIDIAP, where 12 (8%) JDM individuals had other musculoskeletal disorders occurring anytime to 1 year before, 8 (6%) occurring 1 to 3 years after index date, and 9 (6%) occurring more than5 years after.

Table 12.13 Clinical manifestation and comorbidities occurring before, on, and after the diagnosis of Adult Dermatomyositis on 2006-2022

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
CDWBordeaux	Diastolic dysfunction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Dysphagia	10 (4%)	10 (4%)	<5	<5	17 (7%)	27 (12%)	6 (3%)	10 (4%)	13 (6%)	10 (4%)	12 (5%)
	Erythematous rash	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Gottron's papules	<5	<5	<5	<5	8 (3%)	16 (7%)	5 (2%)	6 (3%)	5 (2%)	<5	<5
	Interstitial drug disease	17 (7%)	9 (4%)	6 (3%)	6 (3%)	18 (8%)	22 (10%)	9 (4%)	10 (4%)	17 (7%)	11 (5%)	12 (5%)
	Degenerative musculoskeletal disease	13 (6%)	10 (4%)	<5	<5	25 (11%)	25 (11%)	10 (4%)	13 (6%)	22 (10%)	13 (6%)	19 (8%)
	Lung disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Malignant disease	0 (0%)	<5	<5	<5	0 (0%)	<5	<5	<5	<5	0 (0%)	<5
	Muscle pain	23 (10%)	21 (9%)	7 (3%)	6 (3%)	32 (14%)	36 (16%)	18 (8%)	18 (8%)	31 (13%)	20 (9%)	16 (7%)
	Muscle weakness	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Other musculoskeletal disorders	5 (2%)	6 (3%)	NA	NA	7 (3%)	8 (3%)	<5	<5	11 (5%)	9 (4%)	12 (5%)
	Raynaud's	6 (3%)	<5	<5	NA	6 (3%)	6 (3%)	<5	<5	6 (3%)	7 (3%)	6 (3%)
	Thromboembolism	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Thrombosis	8 (3%)	<5	<5	0 (0%)	5 (2%)	8 (3%)	<5	8 (3%)	6 (3%)	5 (2%)	7 (3%)
CPRD	Diastolic dysfunction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5
	Dysphagia	18 (4%)	<5	<5	6 (1%)	<5	12 (2%)	<5	<5	5 (1%)	<5	<5
	Erythematous rash	0 (0%)	0 (0%)	<5	<5	0 (0%)	0 (0%)	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)
	Gottron's papules	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Interstitial drug disease	5 (1%)	<5	<5	<5	<5	7 (1%)	<5	<5	<5	5 (1%)	<5
	Degenerative musculoskeletal disease	70 (14%)	13 (3%)	<5	<5	<5	11 (2%)	8 (2%)	13 (3%)	24 (5%)	15 (3%)	27 (5%)
	Lung disease	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Malignant disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Muscle pain	28 (6%)	12 (2%)	<5	10 (2%)	<5	6 (1%)	<5	5 (1%)	13 (3%)	6 (1%)	7 (1%)
	Muscle weakness	13 (3%)	7 (1%)	<5	<5	<5	<5	0 (0%)	<5	<5	<5	<5
	Other musculoskeletal disorders	95 (19%)	9 (2%)	0 (0%)	<5	0 (0%)	6 (1%)	<5	7 (1%)	19 (4%)	13 (3%)	9 (2%)
	Raynaud's	<5	<5	0 (0%)	0 (0%)	<5	<5	0 (0%)	0 (0%)	<5	0 (0%)	<5
	Thromboembolism	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5
	Thrombosis	17 (3%)	5 (1%)	<5	0 (0%)	0 (0%)	0 (0%)	6 (1%)	<5	7 (1%)	<5	6 (1%)
EBB	Diastolic dysfunction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Dysphagia	0 (0%)	<5	0 (0%)	0 (0%)	<5	<5	0 (0%)	0 (0%)	<5	0 (0%)	<5
	Erythematous rash	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Gottron's papules	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Interstitial drug disease	<5	<5	<5	<5	<5	<5	<5	<5	<5	<5	<5

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
	Degenerative musculoskeletal disease	30 (32%)	12 (13%)	5 (5%)	<5	<5	5 (5%)	5 (5%)	11 (12%)	13 (14%)	15 (16%)	31 (33%)
	Lung disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Malignant disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Muscle pain	10 (11%)	<5	0 (0%)	0 (0%)	<5	6 (6%)	<5	<5	<5	<5	6 (6%)
	Muscle weakness	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Other musculoskeletal disorders	27 (28%)	12 (13%)	<5	<5	<5	<5	7 (7%)	12 (13%)	22 (23%)	11 (12%)	28 (29%)
	Raynaud's	<5	0 (0%)	<5	0 (0%)	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	<5	<5
	Thromboembolism	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Thrombosis	9 (9%)	<5	<5	<5	<5	<5	<5	<5	<5	<5	5 (5%)
SIDIAP	Diastolic dysfunction	<5	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	<5	0 (0%)	6 (0%)	<5	6 (0%)
SIDIAP	Dysphagia	15 (1%)	<5	<5	<5	<5	6 (0%)	<5	<5	<5	<5	22 (2%)
SIDIAP	Erythematous rash	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Gottron's papules	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Interstitial drug disease	11 (1%)	<5	0 (0%)	<5	<5	7 (1%)	<5	<5	<5	5 (0%)	8 (1%)
SIDIAP	Degenerative musculoskeletal disease	177 (14%)	30 (2%)	<5	6 (0%)	9 (1%)	20 (2%)	6 (0%)	13 (1%)	40 (3%)	37 (3%)	51 (4%)
SIDIAP	Lung disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Malignant disease	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Muscle pain	23 (2%)	7 (1%)	5 (0%)	5 (0%)	<5	<5	<5	7 (1%)	12 (1%)	9 (1%)	15 (1%)
SIDIAP	Muscle weakness	<5	<5	0 (0%)	<5	<5	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Other musculoskeletal disorders	234 (18%)	49 (4%)	17 (1%)	<5	6 (0%)	25 (2%)	8 (1%)	33 (3%)	81 (6%)	49 (4%)	95 (7%)
SIDIAP	Raynaud's	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Thromboembolism	7 (1%)	<5	<5	0 (0%)	<5	6 (0%)	<5	<5	<5	<5	<5
SIDIAP	Thrombosis	27 (2%)	10 (1%)	<5	<5	5 (0%)	13 (1%)	6 (0%)	8 (1%)	13 (1%)	10 (1%)	16 (1%)
IQVIA DA GERMANY	Diastolic dysfunction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	Dysphagia	48 (3%)	15 (1%)	<5	5 (0%)	7 (0%)	13 (1%)	7 (0%)	11 (1%)	20 (1%)	17 (1%)	24 (1%)
IQVIA DA GERMANY	Erythematous rash	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	Gottron's papules	<5	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	Interstitial drug disease	6 (0%)	<5	<5	<5	<5	5 (0%)	<5	<5	5 (0%)	<5	<5
IQVIA DA GERMANY	Degenerative musculoskeletal disease	414 (22%)	132 (7%)	38 (2%)	27 (1%)	45 (2%)	108 (6%)	52 (3%)	95 (5%)	160 (9%)	115 (6%)	136 (7%)
IQVIA DA GERMANY	Lung disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	Malignant disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	Muscle pain	57 (3%)	14 (1%)	<5	9 (0%)	14 (1%)	26 (1%)	5 (0%)	7 (0%)	26 (1%)	12 (1%)	15 (1%)
IQVIA DA GERMANY	Muscle weakness	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	Other musculoskeletal disorders	332 (18%)	99 (5%)	35 (2%)	12 (1%)	34 (2%)	70 (4%)	47 (3%)	61 (3%)	137 (7%)	91 (5%)	119 (6%)
IQVIA DA GERMANY	Raynaud's	5 (0%)	<5	0 (0%)	0 (0%)	<5	<5	<5	<5	<5	<5	<5

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
	Thromboembolism	<5	0 (0%)	0 (0%)	<5	0 (0%)	0 (0%)	<5	<5	<5	0 (0%)	0 (0%)
	Thrombosis	61 (3%)	17 (1%)	7 (0%)	5 (0%)	6 (0%)	17 (1%)	17 (1%)	19 (1%)	34 (2%)	27 (1%)	20 (1%)

Table 12.14 Clinical manifestation and comorbidities occurring before, on, an after the diagnosis of Adult Polymyositis on 2006-2022

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
CDWBordeaux	Antisynthetase syndrome	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Diastolic dysfunction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Dysphagia	13 (7%)	12 (6%)	8 (4%)	5 (3%)	21 (11%)	25 (13%)	11 (6%)	12 (6%)	17 (9%)	12 (6%)	20 (11%)
	Erythematous rash	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Gottron's papules	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Interstitial drug disease	8 (4%)	6 (3%)	<5	<5	12 (6%)	20 (11%)	6 (3%)	6 (3%)	9 (5%)	8 (4%)	8 (4%)
	Degenerative musculoskeletal disease	11 (6%)	13 (7%)	8 (4%)	<5	15 (8%)	25 (13%)	9 (5%)	19 (10%)	26 (14%)	13 (7%)	18 (10%)
	Lung disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Malignant disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Muscle pain	19 (10%)	20 (11%)	6 (3%)	6 (3%)	28 (15%)	37 (20%)	14 (7%)	13 (7%)	19 (10%)	9 (5%)	14 (7%)
	Muscle weakness	0 (0%)	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Other musculoskeletal disorders	5 (3%)	0 (0%)	0 (0%)	0 (0%)	<5	<5	<5	7 (4%)	8 (4%)	<5	9 (5%)
	Raynaud's	7 (4%)	6 (3%)	<5	<5	7 (4%)	10 (5%)	5 (3%)	7 (4%)	12 (6%)	10 (5%)	8 (4%)
	Thromboembolism	<5	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5
	Thrombosis	7 (4%)	6 (3%)	0 (0%)	<5	7 (4%)	13 (7%)	<5	<5	11 (6%)	<5	9 (5%)
CPRD	Antisynthetase syndrome	<5	<5	<5	<5	<5	5 (1%)	<5	<5	0 (0%)	<5	0 (0%)
	Diastolic dysfunction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Dysphagia	15 (3%)	5 (1%)	<5	<5	<5	<5	<5	0 (0%)	6 (1%)	5 (1%)	8 (2%)
	Erythematous rash	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Gottron's papules	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Interstitial drug disease	8 (2%)	8 (2%)	<5	<5	<5	9 (2%)	<5	<5	<5	<5	<5
	Degenerative musculoskeletal disease	81 (17%)	20 (4%)	8 (2%)	<5	<5	10 (2%)	11 (2%)	7 (1%)	33 (7%)	21 (4%)	32 (7%)
	Lung disease	<5	0 (0%)	0 (0%)	0 (0%)	9 (2%)	11 (2%)	0 (0%)	0 (0%)	<5	0 (0%)	<5
	Malignant disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Muscle pain	37 (8%)	13 (3%)	14 (3%)	11 (2%)	<5	10 (2%)	<5	8 (2%)	13 (3%)	10 (2%)	10 (2%)
	Muscle weakness	20 (4%)	11 (2%)	7 (1%)	6 (1%)	0 (0%)	6 (1%)	<5	<5	10 (2%)	6 (1%)	<5

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
	Other musculoskeletal disorders	79 (16%)	10 (2%)	<5	0 (0%)	<5	10 (2%)	<5	8 (2%)	20 (4%)	12 (2%)	21 (4%)
	Raynaud's	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Thromboembolism	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Thrombosis	22 (5%)	<5	<5	<5	0 (0%)	<5	0 (0%)	6 (1%)	6 (1%)	<5	5 (1%)
EBB	Antisynthetase syndrome	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
EBB	Diastolic dysfunction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
EBB	Dysphagia	<5	<5	0 (0%)	0 (0%)	0 (0%)	<5	<5	0 (0%)	<5	0 (0%)	<5
EBB	Erythematous rash	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
EBB	Gottron's papules	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
EBB	Interstitial drug disease	<5	<5	<5	<5	<5	<5	<5	<5	<5	<5	<5
EBB	Degenerative musculoskeletal disease	30 (45%)	7 (11%)	7 (11%)	<5	<5	10 (15%)	5 (8%)	10 (15%)	16 (24%)	9 (14%)	17 (26%)
EBB	Lung disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
EBB	Malignant disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
EBB	Muscle pain	8 (12%)	<5	<5	<5	0 (0%)	<5	<5	<5	<5	5 (8%)	<5
EBB	Muscle weakness	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
EBB	Other musculoskeletal disorders	31 (47%)	10 (15%)	<5	<5	<5	9 (14%)	5 (8%)	5 (8%)	11 (17%)	12 (18%)	20 (30%)
EBB	Raynaud's	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
EBB	Thromboembolism	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
EBB	Thrombosis	11 (17%)	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5	<5	<5	<5
SIDIAP	Antisynthetase syndrome	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Diastolic dysfunction	<5	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5	0 (0%)	<5	0 (0%)	<5
SIDIAP	Dysphagia	<5	<5	0 (0%)	<5	<5	<5	<5	<5	5 (2%)	<5	<5
SIDIAP	Erythematous rash	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Gottron's papules	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Interstitial drug disease	<5	0 (0%)	<5	0 (0%)	0 (0%)	<5	0 (0%)	<5	<5	<5	6 (2%)
SIDIAP	Degenerative musculoskeletal disease	52 (18%)	10 (3%)	<5	0 (0%)	<5	9 (3%)	<5	<5	14 (5%)	11 (4%)	6 (2%)
SIDIAP	Lung disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Malignant disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Muscle pain	13 (5%)	7 (2%)	<5	5 (2%)	<5	<5	0 (0%)	<5	<5	<5	<5
SIDIAP	Muscle weakness	0 (0%)	0 (0%)	0 (0%)	<5	0 (0%)	0 (0%)	0 (0%)	<5	<5	0 (0%)	<5
SIDIAP	Other musculoskeletal disorders	61 (21%)	10 (3%)	<5	<5	<5	8 (3%)	<5	10 (3%)	20 (7%)	14 (5%)	20 (7%)
SIDIAP	Raynaud's	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Thromboembolism	<5	0 (0%)	0 (0%)	0 (0%)	<5	<5	0 (0%)	0 (0%)	0 (0%)	<5	0 (0%)
SIDIAP	Thrombosis	9 (3%)	<5	<5	0 (0%)	<5	<5	<5	<5	<5	6 (2%)	<5
–	Antisynthetase syndrome	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
Diastolic dysfunction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dysphagia	17 (1%)	7 (0%)	<5	<5	<5	7 (0%)	<5	<5	11 (1%)	6 (0%)	8 (1%)
Erythematous rash	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Gottron's papules	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Interstitial drug disease	11 (1%)	7 (0%)	<5	<5	7 (0%)	7 (0%)	<5	<5	8 (1%)	7 (0%)	<5
Degenerative musculoskeletal disease	389 (26%)	113 (7%)	52 (3%)	36 (2%)	83 (5%)	125 (8%)	61 (4%)	88 (6%)	179 (12%)	121 (8%)	116 (8%)
Lung disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Malignant disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Muscle pain	120 (8%)	32 (2%)	10 (1%)	14 (1%)	102 (7%)	94 (6%)	9 (1%)	18 (1%)	28 (2%)	12 (1%)	19 (1%)
Muscle weakness	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other musculoskeletal disorders	303 (20%)	84 (6%)	34 (2%)	23 (2%)	40 (3%)	73 (5%)	37 (2%)	54 (4%)	112 (7%)	76 (5%)	74 (5%)
Raynaud's	<5	<5	0 (0%)	0 (0%)	<5	5 (0%)	<5	<5	6 (0%)	<5	<5
Thromboembolism	<5	<5	<5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5	<5	<5	<5
Thrombosis	61 (4%)	19 (1%)	11 (1%)	<5	9 (1%)	17 (1%)	7 (0%)	17 (1%)	23 (2%)	23 (2%)	28 (2%)

Table 12.15 Clinical manifestation and comorbidities occurring before, on, an after the diagnosis of Juvenile Dermatomyositis on 2006-2022

Results not shown as the number of cases is0 or less than 5 .

Table 12.16 Clinical manifestation and comorbidities occurring before, on, an after the diagnosis of Juvenile Polymyositis on 2006-2022

Results not shown as the number of cases is 0 or less than5.

12.2.4 Treatment patterns

Treatments used differed between databases and health care settings. In databases where there is only primary care prescription information, like CPRD, EBB and SIDIAP we were able to only see some DMARDs and corticoids, while in databases with hospital drug information we were able to see other treatments. Due to the low number of patients, treatment patters including combinations and sequences were not informative and are not presented.

Treatments used over time

Glucocorticoids

For adult DM, 1 month before entry to the cohort, the most used drug class were Glucocorticoids (GCs), with secondary care databases showing lower prevalence, 6% in CDW Bordeaux and 7% in IQVIA Germany, than primary care,25% in CPRD, 9% in EBB and 14% in SIDIAP. This percentage increases in the 3 months after, to 49% of patients using GCs in CDW Bordeaux, 53% in CPRD,33% in EBB, 22% in SIDIAP, and 17% in IQVIA DA Germany. After that, the use of corticoids tends to decrease overall. For adult PM the trend is similar but with a slightly higher prevalence of GCs users, with a peak of use of GCs 3 months after entry to the cohort (58% CDW Bordeaux to 29% in IQVIA Germany). As for JDM, the use of GCs is variable among databases, with low use or no use in hospital data and around 10% in primary care data before index date; but a noticeable increase in primary care data in the 3 months after followed by a progressive decline thereafter.

DMARDS

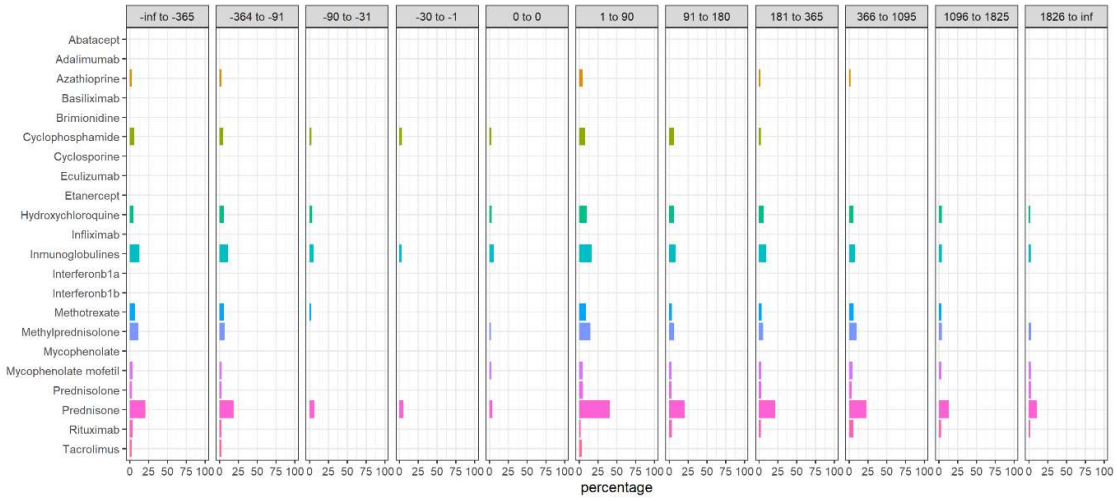
As for DMARDS, mostly for methotrexate and hydroxychloroquine, its use was low before index date both in DM and PM (from 3% in CDW Bordeaux in DM patients to 15% in SIDIAP in PM patients). This use increased greatly in the month after diagnosis and stayed that way for up to 3 years after, ranging from 42% in CPRD DM cohort to 8% in IQVIA DA Germany also for DM. Use of DMARDs was similarly high in JDM after index, with only Methotrexate used in these patients.

Others

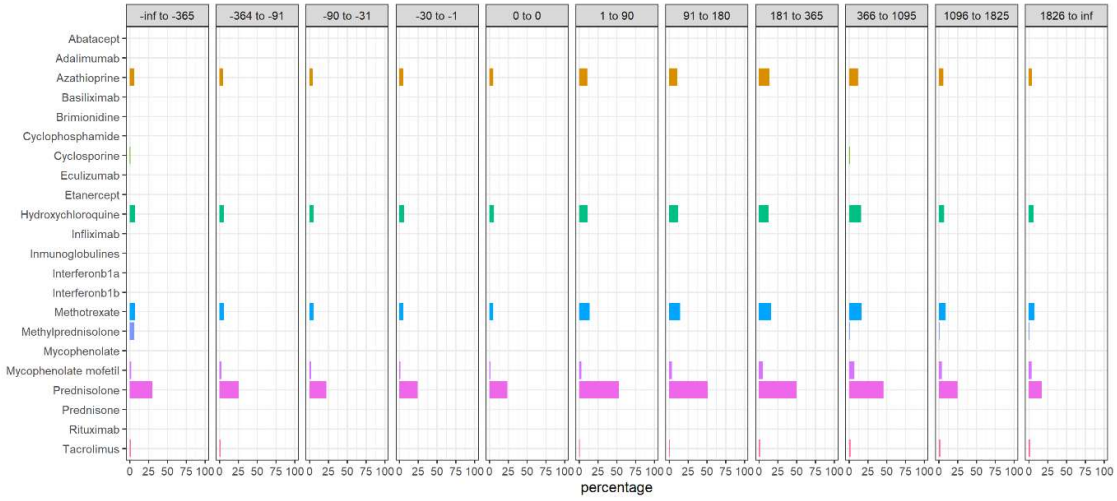
Biologics use was only seen in more than 5 DM patients in CDW Bordeaux, with most of the use occurring in the 3 to 6 months after diagnosis (4%) and 1 to 3 years after diagnosis (7%). Immunoglobulin use was low before index date (3%) and increased and peaked in the 3 months after with a 16% use. Some biologics and immunoglobulins were seen in JDM, but in all cases in less than in 5 people.

Figure 12.3 Treatments received before, on, an after the diagnosis of Adult Dermatomyositis on 2006-2022 by selected treatments and groups.

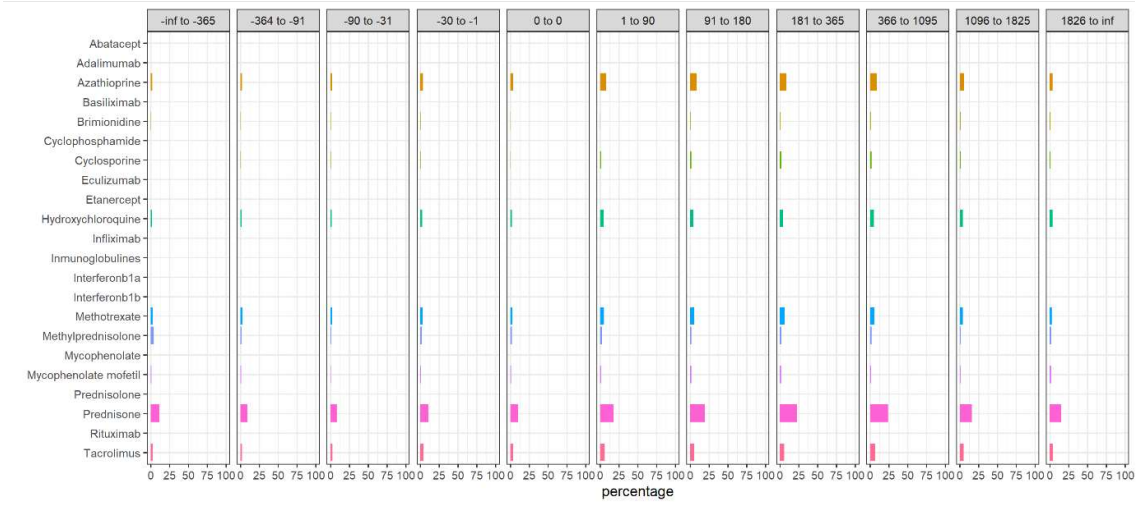
CDWBordeaux



CPRD Gold



SIDIAP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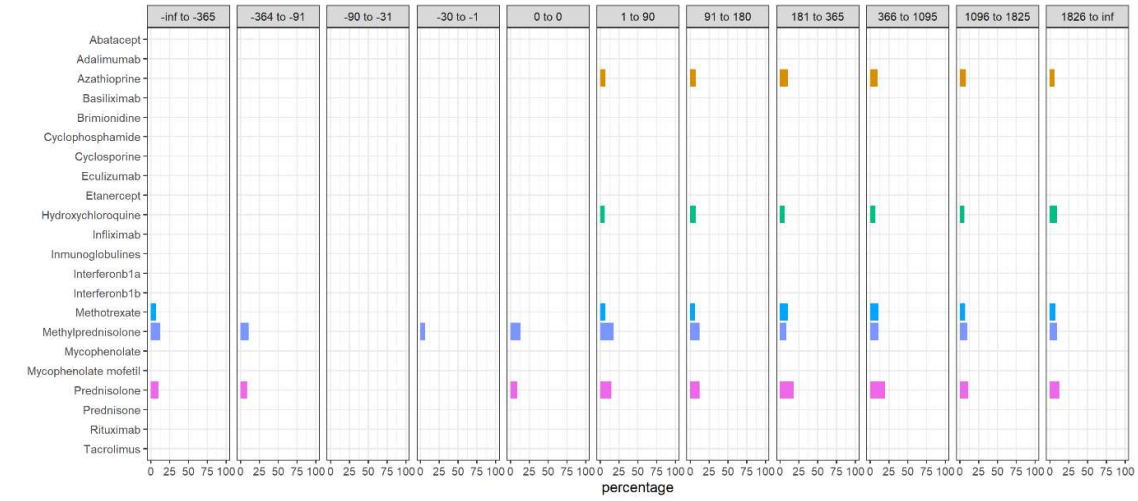
1 to 90
91 to 180
181 to 365
366 to 1095
1096 to 1825
1826 to inf
Abatacept
Adalimumab
Azathioprine
Basiliximab
Brimionidine
Cyclophosphamide
Cyclosporine
Eculizumab
Etanercept
Hydroxychloroquine
Infliximab
Inmunoglobulines
Interferonb1a
Interferonb1b
Methotrexate
Methylprednisolone
Mycophenolate
Mycophenolate mofetil
Prednisolone
Prednisone
Rituximab
Tacrolimus
0 25 50 75 100
percentage

EBB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-90 to -31
-30 to -1
0 to 0
1 to 90
91 to 180
181 to 365
366 to 1095
1096 to 1825
1826 to inf
Abatacept
Adalimumab
Azathioprine
Basiliximab
Brimionidine
Cyclophosphamide
Cyclosporine
Eculizumab
Etanercept
Hydroxychloroquine
Infliximab
Inmunoglobulines
Interferonb1a
Interferonb1b
Methotrexate
Methylprednisolone
Mycophenolate
Mycophenolate mofetil
Prednisolone
Prednisone
Rituximab
Tacrolimus
0 25 50 75 100
percentage

IQVIA DA GERMANY

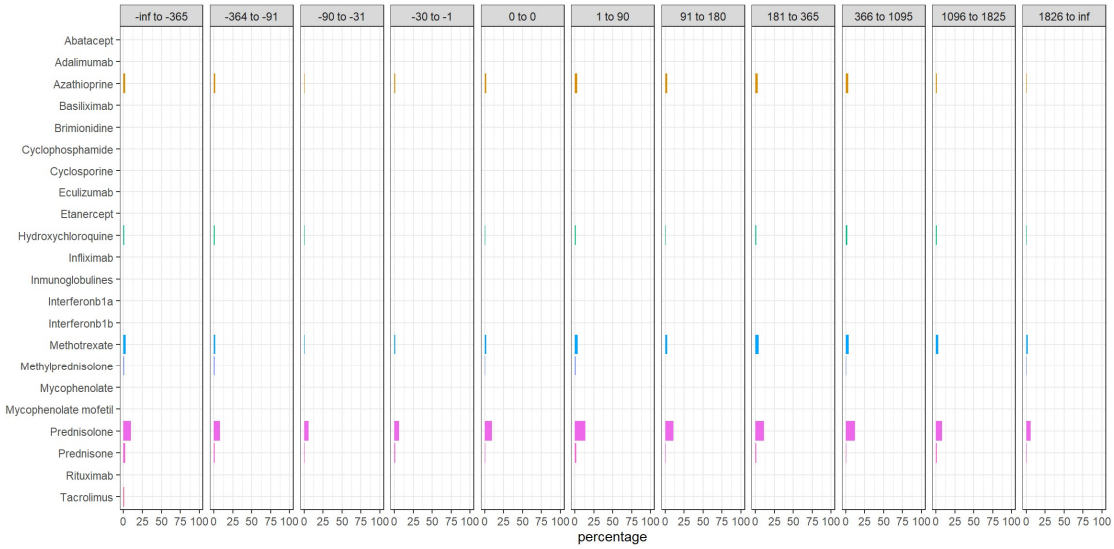
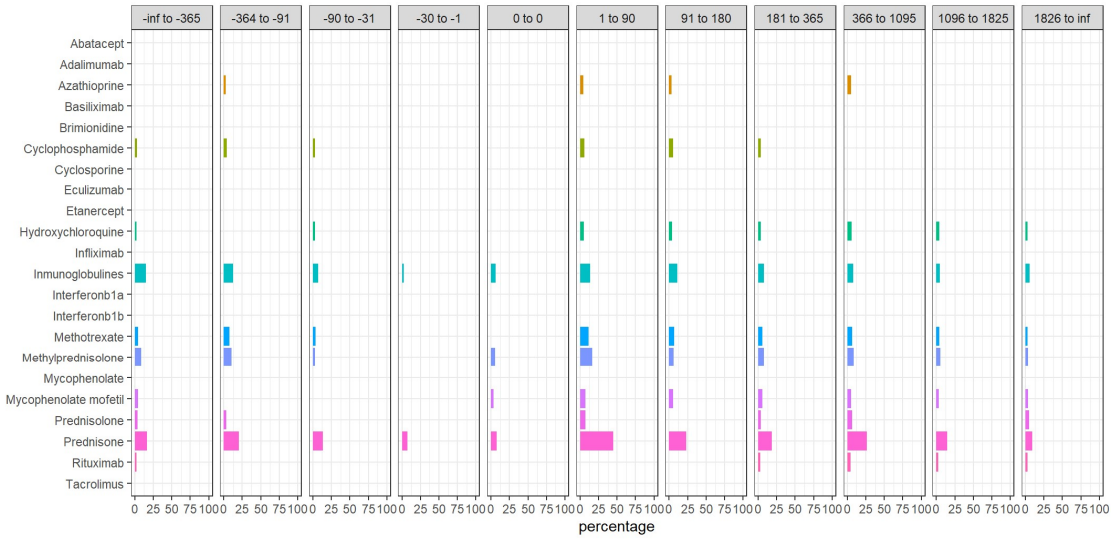
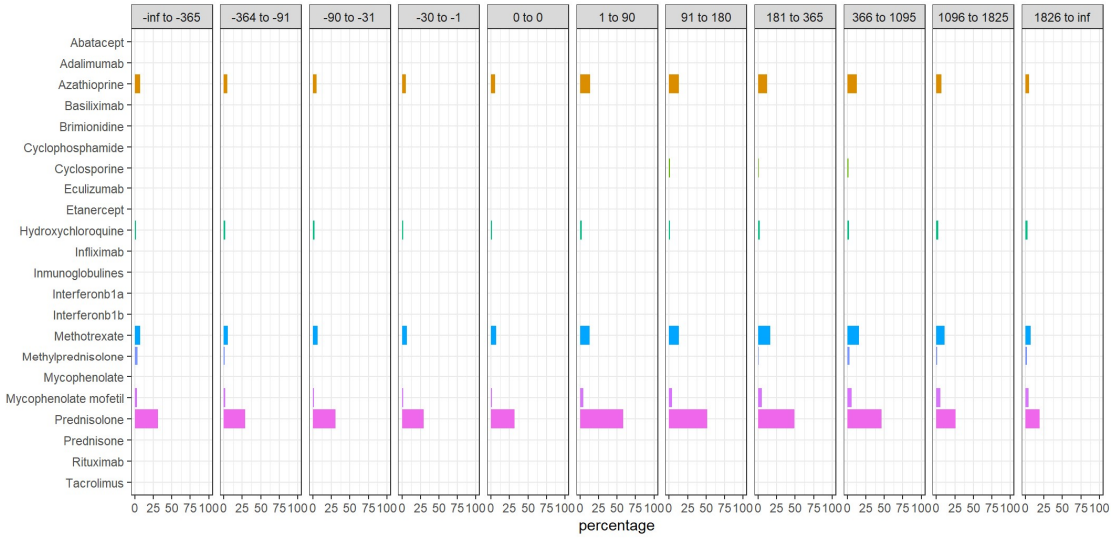


Figure 12.4 Prevalence of treatments received before, on, an after the diagnosis of Adult Polymyositis on 2006-2022 by selected treatments and groups.

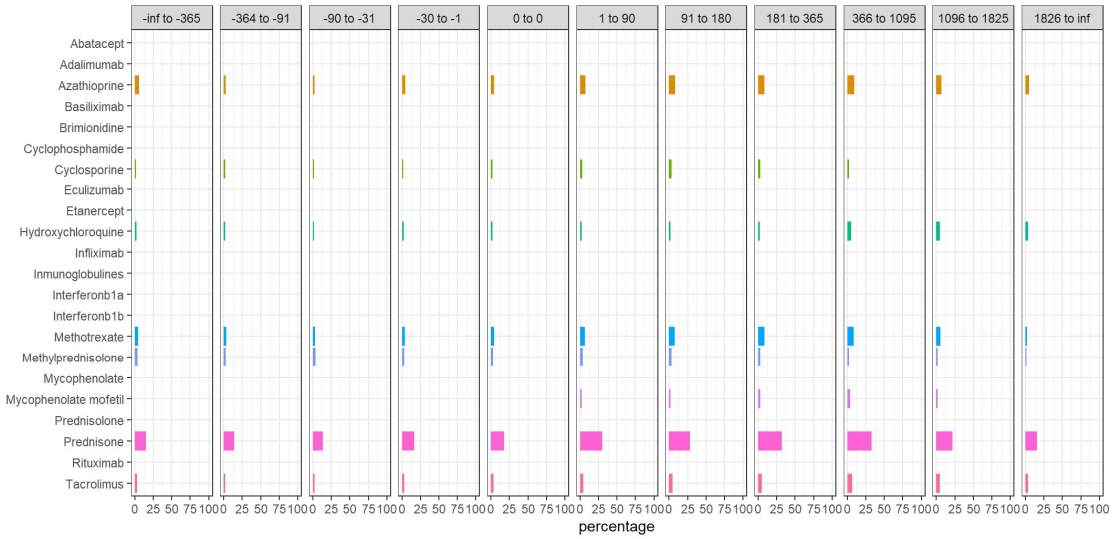
CDWBordeaux



CPRD Gold



SIDIAP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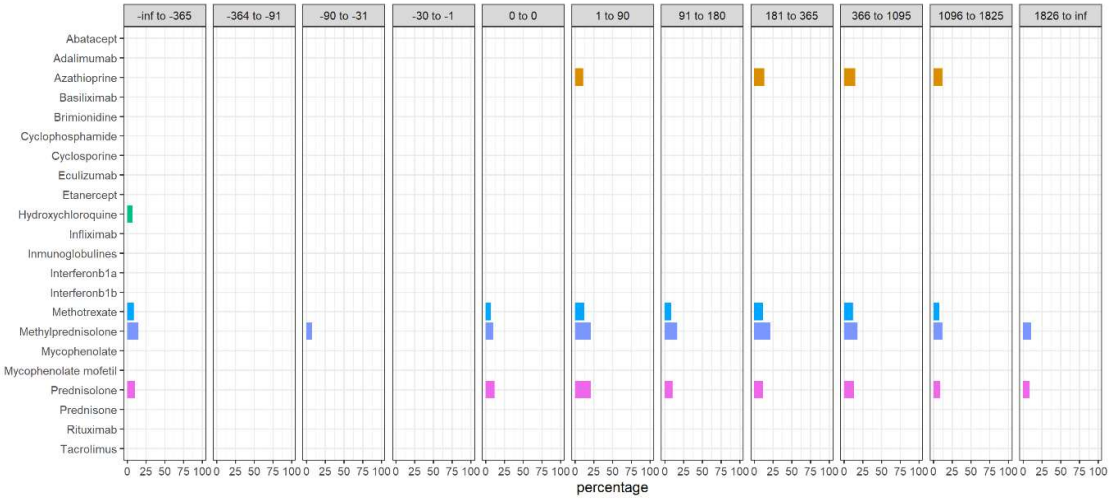
-90 to -31
-30 to -1
0 to 0
1 to 90
91 to 180
181 to 365
366 to 1095
1096 to 1825
1826 to inf
Abatacept
Adalimumab
Azathioprine
Basiliximab
Brimionidine
Cyclophosphamide
Cyclosporine
Eculizumab
Etanercept
Hydroxychloroquine
Infliximab
Inmunoglobulines
Interferonb1a
Interferonb1b
Methotrexate
Methylprednisolone
Mycophenolate
Mycophenolate mofetil
Prednisolone
Prednisone
Rituximab
Tacrolimus
0 25 50 75 100
percentage

EBB


-inf to -365
-364 to -91
-90 to -31
-30 to -1
0 to 0
1 to 90
91 to 180
181 to 365
366 to 1095
1096 to 1825
1826 to inf
Abatacept
Adalimumab
Azathioprine
Basiliximab
Brimionidine
Cyclophosphamide
Cyclosporine
Eculizumab
Etanercept
Hydroxychloroquine
Infliximab
Inmunoglobulines
Interferonb1a
Interferonb1b
Methotrexate
Methylprednisolone
Mycophenolate
Mycophenolate mofetil
Prednisolone
Prednisone
Rituximab
Tacrolimus
0 25 50 75 100
percentage

IQVIA DA GERMANY

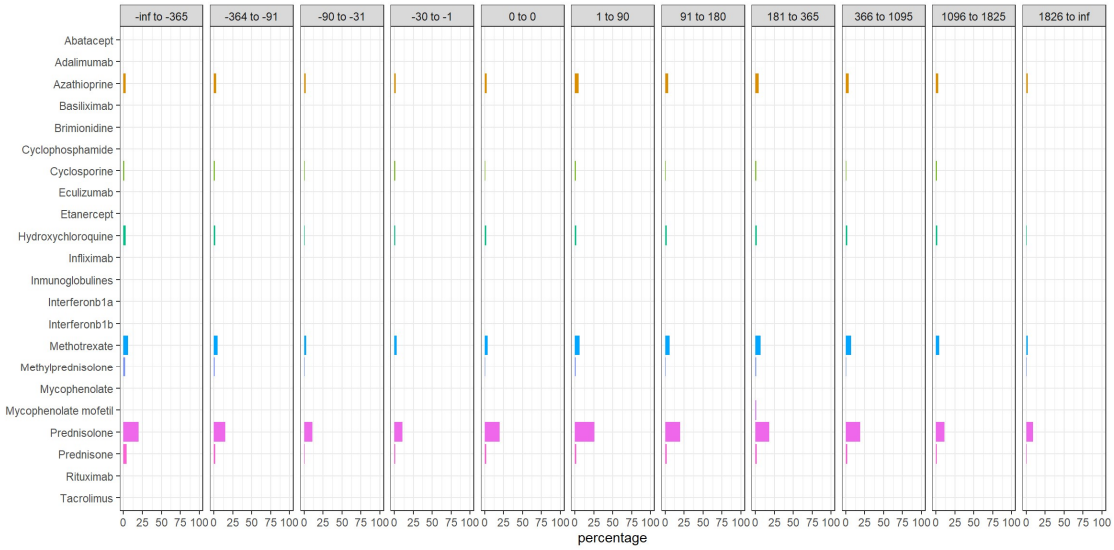


Table 12.17 Treatment class received before, on, an after the diagnosis of Adult Dermatomyositis on 2006-2022 by selected treatments and groups.

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
CDWBordeaux	Antineoplastics	15 (6%)	11 (5%)	6 (3%)	8 (3%)	6 (3%)	19 (8%)	15 (6%)	6 (3%)	<5 (NA%)	0 (0%)	<5 (NA%)
	Biologics	11 (5%)	6 (3%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	5 (2%)	9 (4%)	6 (3%)	16 (7%)	7 (3%)	6 (3%)
	Dmards	37 (16%)	30 (13%)	16 (7%)	8 (3%)	17 (7%)	61 (26%)	33 (14%)	31 (13%)	36 (16%)	25 (11%)	17 (7%)
	Glucocorticoids	59 (26%)	52 (23%)	21 (9%)	15 (6%)	16 (7%)	113 (49%)	64 (28%)	63 (27%)	70 (30%)	38 (16%)	31 (13%)
	Immunoglobulins	30 (13%)	26 (11%)	13 (6%)	7 (3%)	13 (6%)	38 (16%)	20 (9%)	23 (10%)	20 (9%)	9 (4%)	6 (3%)
	Others	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CPRD	Antineoplastics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5 (NA%)	<5 (NA%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Biologics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	0 (0%)	0 (0%)
	Dmards	86 (17%)	83 (17%)	75 (15%)	76 (15%)	80 (16%)	177 (36%)	188 (38%)	203 (41%)	210 (42%)	117 (24%)	88 (18%)
	Glucocorticoids	179 (36%)	134 (27%)	116 (23%)	123 (25%)	120 (24%)	264 (53%)	261 (53%)	257 (52%)	234 (47%)	126 (25%)	93 (19%)
	Immunoglobulins	<5 (NA%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	0 (0%)
	Others	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	0 (0%)
EBB	Antineoplastics	<5 (NA%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Biologics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5 (NA%)
	Dmards	11 (12%)	9 (9%)	8 (8%)	6 (6%)	10 (11%)	20 (21%)	18 (19%)	23 (24%)	23 (24%)	19 (20%)	19 (20%)
	Glucocorticoids	24 (25%)	19 (20%)	7 (7%)	9 (9%)	21 (22%)	31 (33%)	24 (25%)	26 (27%)	32 (34%)	24 (25%)	26 (27%)
	Immunoglobulins	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Others	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Antineoplastics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5 (NA%)	<5 (NA%)	<5 (NA%)
	Biologics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Dmards	95 (7%)	91 (7%)	106 (8%)	159 (12%)	165 (13%)	282 (22%)	282 (22%)	287 (22%)	290 (23%)	211 (16%)	172 (13%)
	Glucocorticoids	255 (20%)	163 (13%)	137 (11%)	182 (14%)	183 (14%)	287 (22%)	289 (22%)	330 (26%)	359 (28%)	248 (19%)	246 (19%)
	Immunoglobulins	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Others	7 (1%)	5 (0%)	5 (0%)	6 (0%)	5 (0%)	6 (0%)	5 (0%)	8 (1%)	13 (1%)	9 (1%)	11 (1%)
IQVIA DA GERMANY	Antineoplastics	<5 (NA%)	<5 (NA%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5 (NA%)	0 (0%)
	Biologics	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	5 (0%)	<5 (NA%)	5 (0%)	<5 (NA%)	<5 (NA%)
	Dmards	109 (6%)	96 (5%)	69 (4%)	55 (3%)	106 (6%)	162 (9%)	134 (7%)	148 (8%)	155 (8%)	91 (5%)	68 (4%)
	Glucocorticoids	256 (14%)	184 (10%)	130 (7%)	134 (7%)	234 (13%)	320 (17%)	233 (13%)	240 (13%)	261 (14%)	172 (9%)	140 (8%)
	Immunoglobulins	<5 (NA%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5 (NA%)	<5 (NA%)	0 (0%)	<5 (NA%)	0 (0%)	0 (0%)
	Others	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)

Table 12.18 Treatment class received before, on, an after the diagnosis of Adult Polymyositis on 2006-2022 by selected treatments and groups.

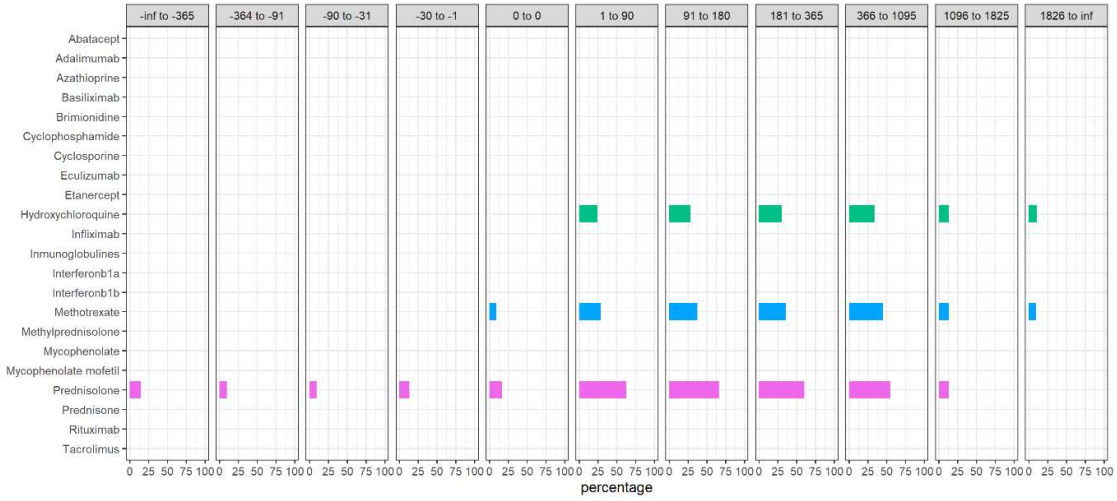
	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
CDWBordeaux	Antineoplastics	6 (3%)	7 (4%)	5 (3%)	<5 (NA%)	<5 (NA%)	11 (6%)	10 (5%)	6 (3%)	<5 (NA%)	<5 (NA%)	0 (0%)
	Biologics	7 (4%)	5 (3%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	6 (3%)	5 (3%)	7 (4%)	12 (6%)	9 (5%)	7 (4%)
	Dmards	23 (12%)	24 (13%)	18 (10%)	8 (4%)	16 (9%)	51 (27%)	32 (17%)	29 (16%)	40 (21%)	19 (10%)	18 (10%)
	Glucocorticoids	42 (22%)	46 (25%)	29 (16%)	15 (8%)	27 (14%)	108 (58%)	54 (29%)	51 (27%)	64 (34%)	36 (19%)	27 (14%)
	Immunoglobulins	28 (15%)	23 (12%)	13 (7%)	5 (3%)	12 (6%)	26 (14%)	21 (11%)	14 (7%)	15 (8%)	9 (5%)	11 (6%)
	Others	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5 (NA%)
CPRD	Antineoplastics	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)
	Biologics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	0 (0%)	0 (0%)	<5 (NA%)
	Dmards	71 (15%)	65 (14%)	67 (14%)	67 (14%)	68 (14%)	145 (30%)	143 (30%)	155 (32%)	156 (32%)	112 (23%)	76 (16%)
	Glucocorticoids	172 (36%)	145 (30%)	148 (31%)	141 (29%)	153 (32%)	282 (59%)	254 (53%)	239 (50%)	230 (48%)	130 (27%)	95 (20%)
	Immunoglobulins	<5 (NA%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5 (NA%)	0 (0%)	<5 (NA%)	<5 (NA%)	0 (0%)	0 (0%)
	Others	<5 (NA%)	<5 (NA%)	<5 (NA%)	0 (0%)	0 (0%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	0 (0%)
EBB	Antineoplastics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Biologics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5 (NA%)	0 (0%)	0 (0%)	0 (0%)
	Dmards	10 (15%)	6 (9%)	0 (0%)	<5 (NA%)	9 (14%)	16 (24%)	11 (17%)	16 (24%)	18 (27%)	13 (20%)	8 (12%)
	Glucocorticoids	20 (30%)	8 (12%)	7 (11%)	7 (11%)	15 (23%)	26 (39%)	20 (30%)	23 (35%)	22 (33%)	15 (23%)	14 (21%)
	Immunoglobulins	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Others	<5 (NA%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SIDIAP	Antineoplastics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Biologics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Dmards	36 (12%)	31 (11%)	32 (11%)	44 (15%)	45 (16%)	64 (22%)	66 (23%)	74 (26%)	81 (28%)	59 (20%)	40 (14%)
	Glucocorticoids	71 (25%)	60 (21%)	55 (19%)	61 (21%)	63 (22%)	99 (34%)	92 (32%)	104 (36%)	111 (39%)	70 (24%)	51 (18%)
	Immunoglobulins	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Others	<5 (NA%)	0 (0%)	0 (0%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)
IQVIA DA GERMANY	Antineoplastics	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	0 (0%)	<5 (NA%)	0 (0%)	<5 (NA%)	<5 (NA%)	0 (0%)	0 (0%)
	Biologics	13 (1%)	11 (1%)	9 (1%)	10 (1%)	9 (1%)	14 (1%)	13 (1%)	14 (1%)	13 (1%)	9 (1%)	6 (0%)
	Dmards	166 (11%)	140 (9%)	109 (7%)	98 (6%)	145 (10%)	206 (14%)	183 (12%)	202 (13%)	202 (13%)	118 (8%)	70 (5%)
	Glucocorticoids	372 (24%)	261 (17%)	208 (14%)	199 (13%)	339 (22%)	438 (29%)	351 (23%)	305 (20%)	339 (22%)	199 (13%)	163 (11%)
	Immunoglobulins	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	6 (0%)	5 (0%)	<5 (NA%)	<5 (NA%)	<5 (NA%)
	Others	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Figure 12.5 Treatments received before, on, an after the diagnosis of Juvenile Dermatomyositis on 2006-2022 by selected treatments and groups.

Bordeaux CDW

Results not shown as the number of cases is 0 or less than5.

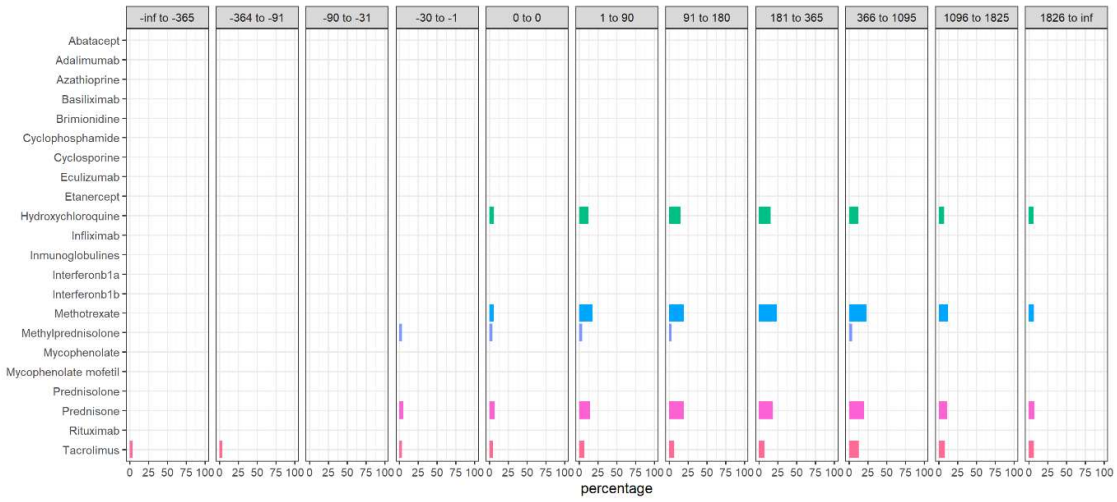
CPRD Gold



EBB

Results not shown as the number of cases is 0 or less than5 .

SIDIAP



IQVIA DA

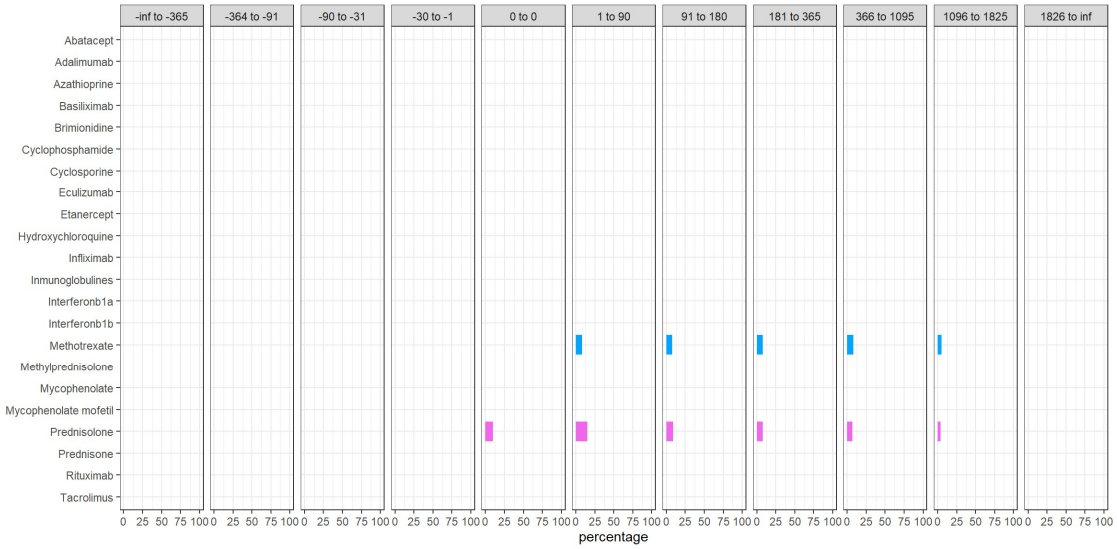


Figure 12.6 Prevalence of treatments received before, on, an after the diagnosis of Juvenile Polymyositis on 2006-2022 by selected treatments and groups.

Results not shown as the number of cases is 0 or less than5.

Table 12.19 Treatments received before, on, an after the diagnosis of Juvenile Dermatomyositis on 2006-2022 by selected treatments and groups.

	outcome	anytime to 1y before	1 year to 3 months before	3 to 1 months before	1 month before	index date	3 months after	3 to 6 months after	6 to 12 months after	1 to 3 years after	3 to 5 years after	>5 years after
CDWBordeaux	Antineoplastics	<5 (NA%)	<5 (NA%)	<5 (NA%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Biologics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Dmards	<5 (NA%)	<5 (NA%)	0 (0%)	<5 (NA%)	<5 (NA%)	5 (26%)	0 (0%)	<5 (NA%)	<5 (NA%)	0 (0%)	<5 (NA%)
	Glucocorticoids	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	0 (0%)	0 (0%)	0 (0%)
	Immunoglobulins	0 (0%)	<5 (NA%)	<5 (NA%)	0 (0%)	0 (0%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	0 (0%)
	Others	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CPRD	Antineoplastics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Biologics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Dmards	5 (9%)	7 (13%)	7 (13%)	7 (13%)	9 (17%)	21 (40%)	28 (53%)	28 (53%)	32 (60%)	15 (28%)	11 (21%)
	Glucocorticoids	9 (17%)	5 (9%)	5 (9%)	7 (13%)	9 (17%)	33 (62%)	35 (66%)	34 (64%)	30 (57%)	7 (13%)	<5 (NA%)
	Immunoglobulins	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5 (NA%)	0 (0%)	<5 (NA%)
	Others	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
EBB	Antineoplastics	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)
	Biologics	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)
	Dmards	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)
	Glucocorticoids	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)
	Immunoglobulins	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)
	Others	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)
SIDIAP	Antineoplastics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Biologics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Dmards	6 (4%)	6 (4%)	<5 (NA%)	10 (7%)	17 (12%)	33 (23%)	36 (25%)	39 (27%)	40 (28%)	22 (15%)	14 (10%)
	Glucocorticoids	7 (5%)	5 (4%)	6 (4%)	14 (10%)	19 (13%)	29 (20%)	34 (24%)	32 (22%)	35 (24%)	21 (15%)	15 (10%)
	Immunoglobulins	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Others	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IQVIA DA GERMANY	Antineoplastics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5 (NA%)	0 (0%)
	Biologics	0 (0%)	0 (0%)	0 (0%)	0 (0%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Dmards	5 (4%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	7 (6%)	14 (12%)	12 (10%)	13 (11%)	12 (10%)	8 (7%)	5 (4%)
	Glucocorticoids	9 (8%)	<5 (NA%)	<5 (NA%)	<5 (NA%)	14 (12%)	20 (17%)	12 (10%)	11 (9%)	11 (9%)	8 (7%)	5 (4%)
	Immunoglobulins	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Others	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 12.20 Treatments received before, on, an after the diagnosis of Juvenile Polymyositis on 2006-2022 by selected treatments and groups.
Results not shown as the number of cases is 0 or less than5.

12.2.5 Other Analysis

Results from sensitivity analyses using patients with 0 days of lookback period available, and a large-scale characterisation where we assessed use of all drugs, conditions, and measurements occurring in each database in all time windows, are available in the Shiny Web-application: https://data-dev.darwin-eu.org/P2-C1-007-DermatomyositisPolymyositis/.

13 MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

In agreement with the guideline on good pharmacovigilance practice (EMA/873138/2011), there was no requirement for expedited reporting of adverse drug reactions as only secondary data was used.

14 DISCUSSION

14.1 Summary of key results

Trends of prevalence of Adult DM & PM

The prevalence of DM and PM in adults aged 18 and above showed either an increase or stable trend over time in all databases. The study revealed that the prevalence of DM was slightly greater than that of PM across all databases, ranging from 20 per 100,000 people in SIDIAP to 52 in EBB by the end of the study. Across the different datasets, the prevalence of PM at the conclusion of the study varied, ranging from 5 per 100,000 people in SIDIAP to 34 in EBB.

Juvenile forms of JPM (Juvenile Polymyositis) were extremely rare, with incidence rates of less than 0.05 per million children in primary care databases. JDM (Juvenile Dermatomyositis), on the other hand, was slightly more frequent but still rarer than its adult counterpart. Prevalence at the end of the study period varied across databases, ranging from 2 per 100,000 people in CPRD GOLD and 3 in IQVIA Germany, to 11 per 100,000 people in Bordeaux. It is worth noting that the majority of these cases of JDM occurred in patients aged 13 to 18.

We identified 3,969 DM patients, 2,541 PM patients, 333 JDM patients and 32 JPM patients. Most of the patients for all of the conditions were women, around 60-70% in most cases, with a median age of 50-60 for DM and PM. JDM median age of diagnosis was around 9-13 years old.

Summary of biomarker assessments

Occurrence of biomarkers testing showed great variability across the different databases, as the recording of these biomarkers could differ in different settings. In most databases, biomarkers such as CRP, ESR and AST showed higher testing in the months before and after diagnosis of DM and PM. CDW Bordeaux had the highest proportions of CRP testing, for example being recorded on index date in 56% of adult DM in CDW Bordeaux vs. 5% in CPRD.

For JDM and JPM, the same biomarkers were observed but with much lower percentages, except in CDW Bordeaux where quite high percentages of CRP, AST and CK testing were recorded on index date (respectively 63, 63 and 68%).

Summary of clinical manifestations and complications

For clinical manifestations and complications, occurrence over time was low in all databases except for CDW Bordeaux which had well-recorded occurrences of these manifestations and complications. The highest was the occurrence of muscle pain; 14% in adult DM and 15% in adult PM on index date, slightly increasing to 16% and 20% respectively three months after diagnosis. For JDM and JPM, all clinical manifestations and complications were less than 5. Only SIDIAP had reported >5 occurrences, e.g., 8% had other musculoskeletal disorders.

Summary of treatments

Similar to other trends and occurrences, treatment usage differed depending on the setting of each database. Primary care databases, such as CPRD and SIDIAP, as well as EBB captured mostly DMARDs and corticoids; and we were able to see other treatments in databases with hospital information.

Adult DM and PM showed similar trends in treatment use across all databases. The most frequently used drug class one month before cohort entry were Glucocorticoids, with primary care databases showing higher usage. Their use increased notably in the 3 months after index date and decreases afterwards. CPRD had the highest Glucocorticoids use before and after index (from 25% 1 month before to 53% after 3 months) in adult DM. When it comes to JDM, the utilization of GCs varied across databases, with minimal or non-existent usage in hospital data prior to the index date, and approximately 10% usage in primary care data. GC use subsequently rose in the three months following diagnosis, to then gradually decline later on.

DMARDS use was low before index date but increased greatly in the months following diagnosis and for up to 3 years after, with CPRD having the highest proportion of use after index date (starting from 16% on index date and reaching 42% 1-3 years after index in DM).In JDM patients, the use of DMARDs was similarly high after the index date, with only Methotrexate being used.

14.2 Limitations of the research methods

The measurements of biomarkers, drugs, and symptoms over a period of time exhibited considerable variation across various databases and settings, as the detectability of each occurrence of a biomarker could differ depending on the setting. As it happens, drugs and tests usually administered in hospital were not visible in primary care settings affecting CPRD, and SIDIAP. This limitation calls for cautious interpretation of the outcomes, considering the not occurrence of clinical manifestations, biomarkers, and drugs not a proof of absence of it the impact of which is to potentially underestimate the number of outcomes. In addition, only biomarker testing occurrence, but not the results were extracted from the databases. As biomarker tests are done for various reasons (e.g. confirm/exclude a diagnosis,

monitor disease activity or organ function), the conclusions that can be drawn based on this data are limited.

Phenotyping of outcomes was concept based, and, although great care was taken to include all potential concept codes of interest, some may be missing, as no validity checks were performed. Phenotyping of DM, PM, JDM, and JPM was cohort based, and followed standard quality checks. Some of the potential codes included under ICD-10 may be unspecific to PM, such as M60.80-90 that correspond to PM in databases using ICD10 as source.

Primary care databases, CPRD and SIDIAP, have a more representative observed population and may be more accurate for prevalence, whereas secondary care databases such as CDW Bordeaux and EBB may have a higher-than-expected prevalence than in the general population because they concentrate specialised care for PM and DM patients. However, primary care databases are not linked to hospital data and may underestimate the prevalence if the diagnosis is not fed back to primary care records. Prevalence of these rare diseases can also be seen to artificially increase if the start of the database visibility is close to the start of the study period, and prevalent patients with years history of disease appear as new when they come in contact with the health services.

14.3 Results in context

Socio-demographics and prevalence

Adult DM and PM appeared to be diagnosed most often between the ages of 40 to 70 years old, slightly older than reported in previous seminal studies from the 1990s[17], but well aligned with more recent European studies [18].In line with these previous studies, we saw a clear predominance of women among people affected by both DM and PM in all the contributing databases.

Regarding prevalence, our most recent estimates ranged between 2 and 10 per 100,000 people in databases with a representative denominator (primary care and outpatient data), in line with previously observed estimates of 5 to 10 cases 100,000 in large US-based studies[17]. More recent data using updated diagnostic criteria have found prevalence estimates of 13/100,000 in the US[19] , 2.3 to 4/100,000 in Korea[20] , and 6 to 10/100,000 in Norway[18] .Prevalence was about 3-fold higher in our data obtained from a hospital database from Bordeaux, likely because this is a known centre of excellence capturing patients that are not from their catchment geographic area. Prevalence could also be underestimated in primary care databases.

A recent systematic review on the epidemiology of inflammatory myopathies[10] has shown increasing temporal trends in the incidence and prevalence of DM and PM, in line with our findings. These have been previously attributed to improved diagnostic tools and recording practices and awareness, but more research is needed to elucidate the reasons behind the observed secular trends.

Biomarker testing, manifestations, and complications

Our findings from primary care and outpatient data show the expected measurements of unspecific biomarkers of inflammation (ESR, CRP) and muscle enzymes (e.g., CK), with more specialised

laboratory measurements (e.g. auto-antibodies, LDH, liver function enzymes) mostly seen in biobank and hospital data. This is in line with our expectation, and with clinical criteria for diagnosis [12].The clinical manifestations at diagnosis were also in line with current clinical criteria, including muscle pain or weakness, dysphagia, and interstitial lung disease. The recording of these appeared more often in hospital vs other contributing databases, likely due to a combination of better completeness in specialized care as well as potentially more severe disease being seen in specialized hospital services.

Treatments

The most observed treatments after diagnosis were systemic glucocorticoids, followed by glucocorticoid sparing DMARDs (mostly methotrexate, hydroxychloroquine, but also azathioprine), and very little use of biologics or immunoglobulins. This is all in line with recent recommendations [21] and published evidence [22].Similar treatments and treatment patterns were observed in juvenile vs adult presentations.

15 CONCLUSION

This is the largest and only international European study on the prevalence of JM or DM to date. Our estimates of prevalence of JM and DM are in line with previous studies that range 3 to 40 per 100,000 people for data sources with a population-based denominator.[1] Similar to previous studies, we observe an increase in the prevalence of both JM and DM in all the contributing databases, which could be due to improved diagnosis and recording, but deserves further research.[1]

The observed clinical manifestations are in line with the most recent clinical criteria recognised by European and American (EULAR/ACR) guidelines, and include muscle weakness/pain, dysphagia, and interstitial lung disease. Testing observed in the contributing databases is also in line with diagnostic criteria in these guidelines, and include inflammation markers, liver and muscle enzymes, and specific autoantibodies, observe only in hospital and biobank datasets.

Finally, the treatments prescribed or dispensed in European real-world data following a diagnosis of PM/DM are also in line with recent recommendations and published evidence, and include systemic glucocorticoids, DMARDs, and very low frequency of use of immunoglobulins and biologic therapies.

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Appendix 1: Definition of DM, PM, JDM and JPM Diagnosis, Clinical Manifestations & Complications, Biomarkers and Treatments

Code list for DM, PM, JDM, JPM.

phenotype	concept name	concept id	vocabulary
DM Codes occurrence in 18+ yo	Disorder of respiratory system due to dermatomyositis	46270398	SNOMED
	Dermatomyositis	80182	SNOMED
	Dermatomyositis sine myositis	4081250	SNOMED
	Idiopathic dermatomyositis	4084268	SNOMED
	Dilated cardiomyopathy due to dermatomyositis	4262911	SNOMED
	Poikilodermatomyositis	4314120	SNOMED
	Adult onset dermatomyositis	4270868	SNOMED
JDM Codes occurrence in <18 yo	Disorder of respiratory system due to dermatomyositis	46270398	SNOMED
	Dermatomyositis	80182	SNOMED
	Dermatomyositis sine myositis	4081250	SNOMED
	Idiopathic dermatomyositis	4084268	SNOMED
	Dilated cardiomyopathy due to dermatomyositis	4262911	SNOMED
	Juvenile dermatomyositis co-occurrent with respiratory involvement	37395588	SNOMED
	Poikilodermatomyositis	4314120	SNOMED
	Childhood type dermatomyositis	4005037	SNOMED
PM Codes occurrence in 18+ yo	Idiopathic polymyositis	4084780	SNOMED
	Polymyositis	80800	SNOMED
	Lung disease with polymyositis	4055369	SNOMED
	Polymyositis associated with autoimmune disease	4346977	SNOMED
	Adult onset dermatomyositis	4270868	SNOMED
JPM Codes occurrence in <18 yo	Idiopathic polymyositis	4084780	SNOMED
	Polymyositis	80800	SNOMED
	Lung disease with polymyositis	4055369	SNOMED
	Polymyositis associated with autoimmune disease	4346977	SNOMED
	Juvenile polymyositis	42538014	SNOMED

Code list for PM, DM, JDM, JPM treatments

phenotype	concept name	concept id	vocabulary
Abatacept	abatacept	1186087	RxNorm
Adalimumab	adalimumab	1119119	RxNorm
Azathioprine	azathioprine	19014878	RxNorm
Basiliximab	basiliximab	19038440	RxNorm
Brimionidine	brimonidine	915542	RxNorm
Cyclophosphamide	cyclophosphamide	1310317	RxNorm
Cyclosporine	cyclosporine	19010482	RxNorm
Eculizumab	eculizumab	19080458	RxNorm
Etanercept	etanercept	1151789	RxNorm
Hydroxychloroquine	hydroxychloroquine	1777087	RxNorm
Infliximab	infliximab	937368	RxNorm
Inmunoglobulines	immunoglobulin G	19117912	RxNorm
Interferonb1a	peginterferon beta-1a	45775146	RxNorm
	interferon beta-1a	722424	RxNorm
Interferonb1b	interferon beta-1b	713196	RxNorm
Methotrexate	methotrexate	1305058	RxNorm
Methylprednisolone	lidocaine / methylprednisolone Injectable Product	36218430	RxNorm
	Methylprednisolone Extended Release Oral Tablet	41111375	RxNorm Extension
	methylprednisolone Injectable Product	36221047	RxNorm
	Methylprednisolone Oral Capsule	40923904	RxNorm Extension
	methylprednisolone Oral Product	36221049	RxNorm
	Methylprednisolone Oral Solution	43697439	RxNorm Extension
	Methylprednisolone Oral Suspension	21158588	RxNorm Extension
	methylprednisolone Pill	36221050	RxNorm
	Methylprednisolone Prefilled Syringe	42479078	RxNorm Extension
Mycophenolate mofetil	mycophenolate mofetil	19003999	RxNorm
Mycophenolate	mycophenolate	19068900	RxNorm
Prednisolone	prednisolone Disintegrating Oral Product	36245769	RxNorm
	prednisolone Effervescent Oral Tablet	43168161	RxNorm Extension
	prednisolone Extended Release Oral Tablet	40986252	RxNorm Extension
	prednisolone Injectable Product	36220909	RxNorm
	prednisolone Injection	42970587	RxNorm Extension
	prednisolone Oral Capsule	41236314	RxNorm Extension
	prednisolone Oral Liquid Product	36220911	RxNorm
	prednisolone Oral Powder	35149489	RxNorm Extension
	prednisolone Oral Product	36220912	RxNorm
	prednisolone Pill	36211785	RxNorm
	prednisolone Prefilled Syringe	42482154	RxNorm Extension
Prednisone	prednisone Pill	36223456	RxNorm
	prednisone Oral Liquid Product	36223454	RxNorm
	prednisone Oral Product	36223455	RxNorm
	Prednisone Extended Release Oral Tablet	42482157	RxNorm Extension
Rituximab	rituximab	1314273	RxNorm
Tacrolimus	tacrolimus	950637	RxNorm

Appendix 2: Definition of Clinical Manifestations, Complications, and Biomarkers

Code list for Clinical Manifestations, Complications and Biomarkers will be attached as csv files, due to the large number of codes.