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Original article

Pain profile and opioid medication use in patients with idiopathic inflammatory myopathies

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Abstract

Objectives. Pain is commonly reported in people living with myositis. This study assesses the presence of pain in the subtypes of myositis as well as the frequency of opioid and non-opioid pain medication use.

Methods. A survey was developed and distributed by Myositis Support and Understanding, a patient-led advocacy organization, to members of its group. Multivariate logistic regression analysis and chi-squared tests were performed.

Results. A total of 468 participants completed the survey. A total of 423 participants (DM $n = 183$, PM $n = 109$ and IBM $n = 131$) were included, based on reported diagnosis, for final analysis. Some 91.5% of myositis participants reported current or past pain, with 99% attributing their pain to myositis. There was a lower likelihood of pain in participants aged >60 years [odds ratio (OR) 0.2, 95% confidence interval (CI) 0.1, 0.6, $P = 0.003$]. The percentage of participants reporting pain was statistically different based on myositis type (DM 97.2%, IBM 80.9% and PM 94.5%, $P < 0.001$), with a higher likelihood of pain in DM compared with IBM (OR 3.7, 95% CI 1.3, 10.2, $P = 0.011$). There was a lower likelihood of pain in participants aged >60 years (OR 0.2, 95% CI 0.1, 0.6, $P = 0.003$). Of the 387 participants reporting pain, 335 reported using pain medications (69% prescribed opioids). Male sex, age >60 years and myositis subtype were not associated with likelihood of non-opioid use.

Conclusion. Pain is a commonly reported symptom in myositis with variable treatment strategies, including opioid medications. This study highlights the importance of addressing pain as part of myositis treatment as well as the need for future studies understanding treatment effectiveness.

Key words: myositis, pain, opioids, idiopathic inflammatory myopathy, DM, PM, IBM

CLINICAL SCIENCE

Rheumatology key messages

- Pain is common in myositis with the majority receiving opioid medications for treatment.
- DM had increased likelihood and >60 years age had lower likelihood of pain.
- Male sex and myositis subtype were not associated with likelihood of non-opioid use.

Introduction

Idiopathic inflammatory myopathies (myositis) are a rare set of systemic inflammatory diseases that primarily affect muscle and often lead to severe impairments in quality of life [1, 2]. Myositis consists of five major categories of disease: PM, DM, immune-mediated necrotizing myopathy, antisynthetase syndrome and IBM [2]. While the primary symptom is most often weakness, extra-muscular manifestations are regularly seen, including cutaneous, cardiac and pulmonary involvement [1, 2]. Pain is a prominent contributor to reduced quality of life [3, 4].

Pain is an underreported and underappreciated symptom of myositis [5]. Pain has been identified as a core patient-reported outcome when assessing life impact due to myositis [6]. As part of an international OMERACT myositis study to identify important domains, patients,

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healthcare providers and caregivers ranked pain highly as a domain of the disease, in addition to fatigue, levels of physical activity, and muscle, skin and lung symptoms [7]. In another study evaluating physical function and quality of life for myositis patients, bodily pain was shown to correlate with worse physical functioning and quality of life [4]. Despite the importance of pain as a domain of myositis, it is generally agreed that the prevalence of pain in myositis is unclear and pain management is often heterogeneous. In contrast, in other MCTDs, pain and its impact are better explored. In these conditions and in myositis, pain treatment is inadequate and requires greater attention to help address impact on physical functioning and quality of life [4, 8, 9]. Pain is multifactorial in MCTDs with central and peripheral origins related to inflammation and residual damage from previous inflammatory insults [10]. With diseases like RA and SpA, pain is a prominent component and better addressed than in conditions like DM or IBM [9–14]. Despite treatment in RA with DMARDs and symptomatic pain medications like NSAIDs, patients continue to experience pain [11, 12]. This is thought to be due to central pain dysregulation [12, 13]. In SLE, nearly 25% of patients complain of pain and report a worsened quality of life [15, 16]. Furthermore, SLE patients report that pain is a symptom that health professionals often do not sufficiently address [17–19]. Myositis is no different in that pain is a major contributor to disability [4].

Given the need for a better understanding of pain in myositis, Myositis Support and Understanding (MSU), a non-profit, patient-led advocacy organization for myositis, prioritized understanding and addressing pain in myositis. Leadership and members of MSU identified pain as a key domain that needed further exploration, which served as the motivation for the survey. MSU then led the creation of the survey items to capture their concerns in the recognition and treatment of pain in myositis. This survey was then sent to members, as reported below. This is especially relevant because, in addition to immunotherapy, multiple treatment options exist for multifactorial pain (e.g. exercise, tricyclic antidepressants) [20]. Therefore, in this study, we sought to better understand the prevalence of pain in myositis, as well as treatment strategies using a cross-sectional survey administered by MSU.

Methods

Data source

This study was determined to be Institutional Review Board (IRB)-exempt by our IRB. An anonymous survey (Supplementary Data S1, available at *Rheumatology* online) developed by MSU to reflect the lived experiences of people living with myositis was created to assess the prevalence of pain and treatment strategies for participants. The survey was then distributed to members of MSU. In total, 468 participants responded using a de-identified Google Form between May and June 2019. Participants aged 18 years or older with a confirmed diagnosis of inflammatory myopathy were included. Exclusion criteria were reported diagnoses of JDM, MCTD, necrotizing autoimmune myopathy or orbital myositis.

Demographic and diagnostic information were collected for each participant including age, sex, specific myositis diagnosis and time since myositis diagnosis. Each participant was asked if they had current or past pain, and if that pain was believed to be secondary to myositis. Participants with pain were then subsequently asked to report if they took pain medications (opioid *vs* non-opioid), as well as the specific names of each medication. For statistical analysis, non-opioid pain medications were grouped as acetaminophen/paracetamol, NSAIDs, neuropathic medications (e.g. amitriptyline, gabapentin and pregabalin), steroids and herbal medications (medical marijuana, herbal supplements, etc.).

Statistical analysis

Descriptive statistics for demographic, treatment characteristics, pain profile and pain medications were calculated. Chi-squared tests and multivariate logistic regression analysis were performed to assess the association between myositis type, age >60 years and sex, and current or past pain and use of any pain medication. Similar analysis was also performed to assess the association between demographic characteristics and myositis type on use of opioid or non-opioid medications. Age 60 years was selected as it provided a natural inflection point of age in the dataset. Significance was set at $P < 0.05$. Stata software, version 14 (StataCorp, College Station, TX) was used for all statistical analyses.

Results

A total of 423 participants were included in the final analysis (Table 1): 183 participants with DM, 131 participants with IBM and 109 participants with PM. Most participants in our study were female (74.6%), and 43.3% of participants were >60 years of age, although age and sex distributions varied by myositis type ($P < 0.001$). The plurality of participants had been diagnosed with myositis between 1 and 5 years prior to survey completion.

Pain profile

Out of the total cohort, 387 participants (91.5%) reported current or past pain. Among those with pain, 99% attributed their pain to myositis (Table 1). Using bivariate analysis (Fig. 1), the percentage of participants reporting pain was statistically different based on myositis type (DM 97.2%, IBM 80.9% and PM 94.5%, $P < 0.001$), age distribution ($P < 0.001$) and sex ($P < 0.002$). There was no significant association between pain reported and duration of myositis. To account for potential confounding, multivariate regression logistic analysis was then utilized to identify independent predictors. Based on this analysis, there was a higher likelihood of pain in participants

Table 1 Demographic, pain profile and pain medications by myositis type

	All patients	DM	IBM	PM	
	N = 423	*N* (% of total) = 183 (43.3)	*N* (% of total) = 131 (31.0)	*N* (% of total) = 109 (25.7)	*P*-value
Demographic information					
Age [*N* (%)]					**$P < 0.001$**
20–30 years	12 (2.8)	5 (2.7)	0 (0)	7 (6.4)	
30–40 years	43 (10.2)	30 (16.4)	0 (0)	13 (11.9)	
40–50 years	75 (17.7)	47 (25.7)	7 (5.3)	21 (19.3)	
50–60 years	110 (26.0)	58 (31.7)	20 (15.3)	32 (29.4)	
60–70 years	109 (25.8)	35 (19.1)	49 (37.4)	25 (22.9)	
70–80 years	63 (14.9)	8 (4.4)	44 (33.6)	11 (10.1)	
>80 years	11 (2.6)	0 (0)	11 (8.4)	0 (0)	
Male [*N* (%)]	107 (25.4)	17 (9.4)	70 (53.4)	20 (18.4)	**$P < 0.001$**
Time since myositis diagnosis [*N* (%)]					$P = 0.176$
<1 year	60 (14.2)	31 (16.9)	16 (12.2)	13 (11.9)	
1–5 years	169 (40.0)	73 (39.9)	52 (39.7)	44 (40.4)	
5–10 years	94 (22.2)	39 (21.3)	37 (28.2)	18 (16.5)	
10–15 years	50 (11.8)	18 (9.8)	14 (10.7)	18 (16.5)	
15–20 years	29 (6.9)	10 (5.5)	11 (8.4)	8 (7.3)	
20–25 years	7 (1.6)	4 (2.2)	0 (0)	3 (2.8)	
>25 years	13 (3.3)	8 (4.4)	1 (0.8)	5 (4.6)	
Pain profile					
Current or past pain [*N* (%)]	387 (91.5)	178 (97.2)	106 (80.9)	103 (94.5)	**$P < 0.001$**
Pain secondary to myositis [*N* (% of patients with pain)]	383 (99.0)	178 (100)	103 (97.2)	102 (99.0)	$P = 0.074$
Pain medications					
Any pain medication [*N* (% of patients with pain)]	335 (86.6)	152 (85.4)	88 (83.0)	95 (92.2)	$P = 0.122$
Non-opioid pain medication [*N* (% of patients taking pain medication)]	311 (92.8)	147 (96.7)	82 (93.2)	82 (86.3)	$P = 0.445$
Opioid pain medication [*N* (% of patients taking pain medication)]	231 (69.0)	104 (68.4)	55 (62.5)	72 (75.8)	$P = 0.051$

Bold values $P < 0.001$ denotes statistical significance.

with DM compared with IBM [odds ratio (OR) 3.7, 95% CI 1.3, 10.2, $P = 0.011$]. There was a lower likelihood of pain in participants >60 years of age (OR 0.2, 95% CI 0.1, 0.6, $P = 0.003$, Table 2).

Pain medications

Of the 387 participants with pain, 335 participants reported using pain medication: 92.8% were utilized non-opioid medications and 69.0% were prescribed opioid medications. Use of any pain medication was similar was similar across myositis types (Tables 1 and 2). Several non-opioids were utilized by participants including NSAIDs (59%), acetaminophen (45%), neuropathic medications (20%), herbal medications (8%) and steroids (3%) (Fig. 2). Male sex, age >60 years and myositis type were not associated with likelihood of non-opioid use (Table 3). In terms of opioid use, of the myositis subtypes, PM was associated with increased likelihood of opioid pain medication use compared with IBM (OR 2.0, 95% CI 1.04, 3.8, $P = 0.038$; Table 3).

Older age and sex were not associated with opioid use in this cohort.

Discussion

Myositis is a rare condition that is primarily managed by rheumatologists, neurologists and neuromuscular physicians. To our knowledge, this is the first and largest data set to show the prevalence of pain in myositis as well as predictors of pain and medication use in patients with myositis. Nearly all participants experienced pain that they attributed to myositis. The results underline the importance of treating physicians inquiring about and treating the pain these patients experience. The heterogeneity of pain medication use also merits future research into determining analgesic protocols or treatment plans for these patients.

Treatment varied greatly between participants. Anticonvulsant and antidepressant drugs were used in

FIG. 1 Association of pain with (**A**) myositis subtype, (**B**) age, (**C**) sex and (**D**) time since myositis diagnosis. $^{**}P = 0.002$, $^{***}P < 0.001$

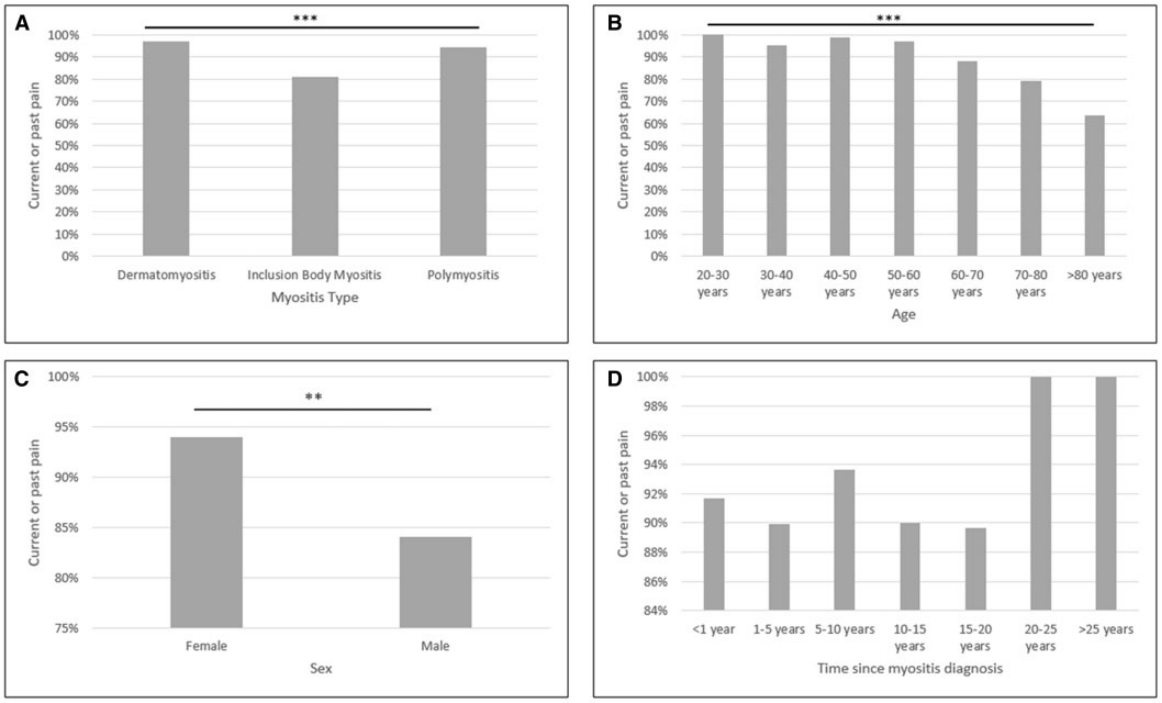

TABLE 2 Multivariable logistic regression models assessing associations with pain and use of any pain medication

	Current or past pain		Any pain medication	
Characteristic	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**
Myositis type				
IBM	–	–	–	–
DM	3.7 (1.3, 10.2)	0.011	1.0 (0.4, 2.2)	0.957
PM	2.1 (0.7, 6.7)	0.188	2.0 (0.8, 5.2)	0.165
Age >60 years	0.2 (0.1, 0.6)	0.003	0.7 (0.4, 1.4)	0.280
Male	0.8 (0.4, 1.7)	0.542	0.9 (0.4, 2.0)	0.831

addition to opioids. The survey was not designed to investigate the utility of various drugs. Importantly, opioids were commonly used, and associated most strongly with a diagnosis of PM. Opioid use in autoimmune conditions is not uncommon. For example, in SLE, one study found that nearly 33% of its cohort were prescribed opioids [21]. Musculoskeletal pain is complex and arises from multiple different pathophysiological mechanisms, grossly localizing to muscles, joints and/or bone [22, 23], with pain in myositis likely resulting from multifactorial aetiologies. Like in MCTDs, pain in myositis is likely related to acute inflammation, chronic damage from inflammation and biomechanical abnormalities that arise due to weakness and deconditioning. Exercise has been used as an intervention to improve pain and fatigue in myositis, and is thought to have impact on both [20].

Limitations of these data include the fact that this was a survey study and we were unable to confirm participant-reported data with health records. Misdiagnosis in myositis is common and it is possible that participants who responded to the survey did not have an accurate diagnosis. There is also the potential for recall and selection bias, as participants who have been or are in pain were more likely to respond to the survey. However, given our large sample size relative to prior studies of this patient population, our results are likely balanced against potential diagnostic uncertainty and recall bias. In addition, our demographic data were consistent with published epidemiologic profiles for inflammatory myopathy, suggesting appropriate sampling of this population [24–28]. Most IBM participants were men and >60 years old, as opposed to DM/PM respondents who were

Fig. 2 Distribution of non-opioid medications utilized by patients by myositis type

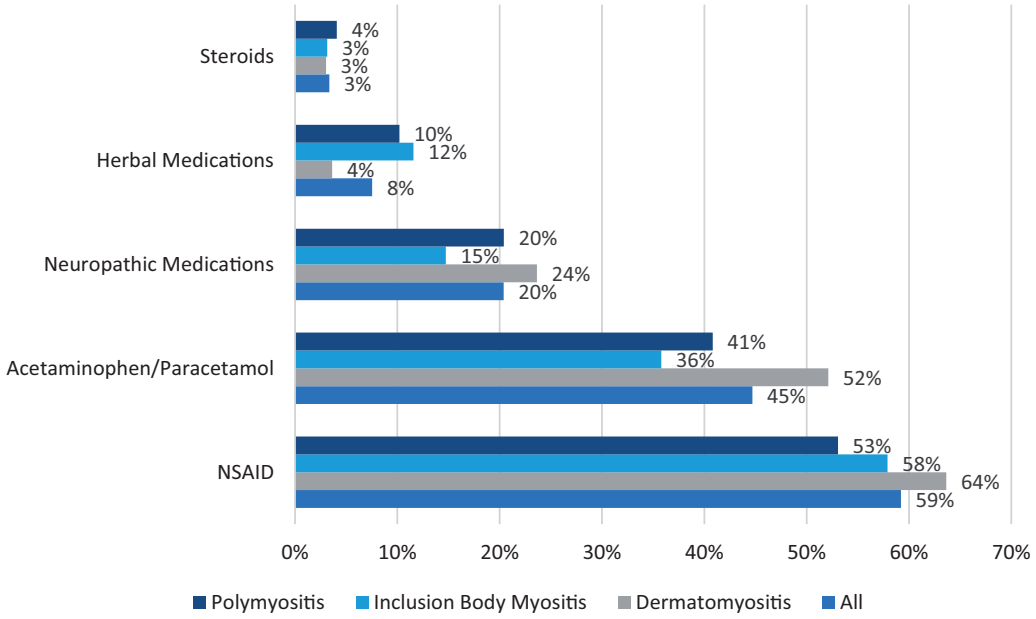

Table 3 Multivariable logistic regression models assessing associations with use of non-opioid and opioid pain medication

	Non-opioid pain medication		Opioid pain medication	
Characteristic	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Myositis type				
IBM	–	–	–	–
DM	1.1 (0.4, 3.2)	0.825	1.2 (0.7, 2.2)	0.523
PM	0.7 (0.3, 1.9)	0.491	2.0 (1.04, 3.8)	0.038
Age >60 years	1.2 (0.5, 2.7)	0.679	1.0 (0.6, 1.7)	0.854
Male	0.5 (0.3, 1.2)	0.118	0.9 (0.5, 1.6)	0.784

women and younger. This study is limited by its cross-sectional design, but it can help to enable future prospective studies to better understand pain characteristics and their impact in patients with myositis.

Conclusion

Pain is an underreported feature of myositis. It is a consistently identified domain among patients and requires recognition from healthcare providers. Younger participants and those with DM are more likely to experience pain, but a diagnosis of PM is more highly associated with use of opioids. Treatment strategies are not uniform and likely require multiple modalities of therapy to alleviate pain. Continued collaboration with patients and their caregivers can help facilitate research in this area. Future studies should prospectively investigate pain in myositis, its impact on quality of life, and the most effective treatment options.

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Data availability statement

Data can be shared by request to the authors.

Supplementary data

Supplementary data are available at *Rheumatology* online.

References

1 Carstens PO, Schmidt J. Diagnosis, pathogenesis and treatment of myositis: recent advances. Clin Exp Immunol 2014;175:349–58.

2 Dalakas MC. Inflammatory muscle diseases. N Engl J Med 2015;372:1734–47.

3 Baig S, Paik JJ. Inflammatory muscle disease - an update. Best Pract Res Clin Rheumatol 2020;34: 101484.

4 Ponyi A, Borgulya G, Constantin T *et al.* Functional outcome and quality of life in adult patients with idiopathic inflammatory myositis. Rheumatology (Oxford) 2005;44:83–8.

5 Carstens PO, Schmidt J. Diagnosis, pathogenesis and treatment of myositis: recent advances. Clin Exp Immunol 2014;175:349–58.

6 Regardt M, Mecoli CA, Park JK *et al.* OMERACT 2018 modified patient-reported outcome domain core set in the life impact area for adult idiopathic inflammatory myopathies. J Rheumatol 2019;46:1351–4.

7 Mecoli CA, Park JK, Alexanderson H *et al.* Perceptions of patients, caregivers, and healthcare providers of idiopathic inflammatory myopathies: an international OMERACT study. J Rheumatol 2019;46:106–11.

8 Chaigne B, Scirè CA, Talarico R *et al.* Mixed connective tissue disease: state of the art on clinical practice guidelines. RMD Open 2018;4:e000783.

9 Oldroyd A, Dixon W, Chinoy H, Howells K. Patient insights on living with idiopathic inflammatory myopathy and the limitations of disease activity measurement methods - a qualitative study. BMC Rheumatol 2020;4:47.

10 Atzeni F, Masala IF, Salaffi F *et al.* Pain in systemic inflammatory rheumatic diseases. Best Pract Res Clin Rheumatol 2015;29:42–52.

11 Kazis LE, Meenan RF, Anderson JJ. Pain in the rheumatic diseases. Investigation of a key health status component. Arthritis Rheum 1983;26:1017–22.

12 Sarzi-Puttini P, Salaffi F, Di Franco M *et al.* Pain in rheumatoid arthritis: a critical review. Reumatismo 2014; 66:18–27.

13 McWilliams DF, Walsh DA. Pain mechanisms in rheumatoid arthritis. Clin Exp Rheumatol 2017;35(Suppl 107):94–101.

14 Atzeni F, Boccassini L, Di Franco M *et al.* Chronic widespread pain in spondyloarthritis. Reumatismo 2014; 66:28–32.

15 Waldheim E, Ajeganova S, Bergman S, Frostegård J, Welin E. Variation in pain related to systemic lupus erythematosus (SLE): a 7-year follow-up study. Clin Rheumatol 2018;37:1825–34.

16 McElhone K, Abbott J, Teh LS. A review of health related quality of life in systemic lupus erythematosus. Lupus 2006;15:633–43.

17 Moses N, Wiggers J, Nicholas C, Cockburn J. Prevalence and correlates of perceived unmet needs of people with systemic lupus erythematosus. Patient Educ Couns 2005;57:30–8.

18 Moses N, Wiggers J, Nicholas C. Persistence of unmet need for care among people with systemic lupus erythematosus. Qual Life Res 2008;17:867–76.

19 Danoff-Burg S, Friedberg F. Unmet needs of patients with systemic lupus erythematosus. Behav Med 2009;35: 5–13.

20 Misse RG, Borges IBP, Dos Santos AM, Gupta L, Shinjo SK. Effect of exercise training on fatigue and pain in patients with systemic autoimmune myopathies: a systematic review. Autoimmun Rev 2021;20:102897.

21 Somers EC, Lee J, Hassett AL *et al.* Prescription opioid use in patients with and without systemic lupus erythematosus - Michigan lupus epidemiology and surveillance program, 2014-2015. MMWR Morb Mortal Wkly Rep 2019;68:819–24.

22 Maruotti N, Cantatore FP, Crivellato E, Vacca A, Ribatti D. Macrophages in rheumatoid arthritis. Histol Histopathol 2007;22:581–6.

23 Sherwood TW, Lee KG, Gormley MG, Askwith CC. Heteromeric acid-sensing ion channels (ASICs) composed of ASIC2b and ASIC1a display novel channel properties and contribute to acidosis-induced neuronal death. J Neurosci 2011;31:9723–34.

24 Molberg Ø, Dobloug C. Epidemiology of sporadic inclusion body myositis. Curr Opin Rheumatol 2016;28: 657–60.

25 Kronzer VL, Kimbrough BA, Crowson CS *et al.* Incidence, prevalence, and mortality of dermatomyositis: a population-based cohort study. Arthritis Care Res (Hoboken) 2021. doi:10.1002/acr.24786.

26 Paltiel AD, Ingvarsson E, Lee DK *et al.* Demographic and clinical features of inclusion body myositis in North America. Muscle Nerve 2015;52:527–33.

27 Shelly S, Mielke MM, Mandrekar J, Milone M *et al.* Epidemiology and natural history of inclusion body myositis: a 40-year population-based study. Neurology 2021;96:e2653–61.

28 Prieto S, Grau JM. The geoepidemiology of autoimmune muscle disease. Autoimmun Rev 2010;9:A330–4.