Rheumatology, 2023, **62**, 2797–2805
https://doi.org/10.1093/rheumatology/keac713
Advance access publication 13 January 2023
Original article

British Society for Rheumatology RHEUMATOLOGY OXFORD

Clinical science

An international survey of current management practices for polymyalgia rheumatica by general practitioners and rheumatologists

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Received: 21 October 2022. **Accepted:** 13 December 2022
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Abstract

Objectives: To explore current management practices for PMR by general practitioners (GPs) and rheumatologists including implications for clinical trial recruitment.

Methods: An English language questionnaire was constructed by a working group of rheumatologists and GPs from six countries. The questionnaire focused on: 1: Respondent characteristics; 2: Referral practices; 3: Treatment with glucocorticoids; 4: Diagnostics; 5: Comorbidities; and 6: Barriers to research. The questionnaire was distributed to rheumatologists and GPs worldwide via members of the International PMR/Giant Cell Arteritis Study Group.

Results: In total, 394 GPs and 937 rheumatologists responded to the survey. GPs referred a median of 25% of their suspected PMR patients for diagnosis and 50% of these were returned to their GP for management. In general, 39% of rheumatologists evaluated patients with suspected PMR >2 weeks after referral, and a median of 50% of patients had started prednisolone before rheumatologist evaluation. Direct comparison of initial treatment showed that the percentage prescribing >25 mg prednisolone daily for patients was 30% for GPs and 12% for rheumatologists. Diagnostic imaging was rarely used. More than half (56%) of rheumatologists experienced difficulties recruiting people with PMR to clinical trials.

Conclusion: This large international survey indicates that a large proportion of people with PMR are not referred for diagnosis, and that the proportion of treatment-naive patients declined with increasing time from referral to assessment. Strategies are needed to change referral and management of people with PMR, to improve clinical practice and facilitate recruitment to clinical trials.

Keywords: PMR, guideline, glucocorticoid, diagnostic, treatment, research

Rheumatology key messages

- Only 25% of people with new PMR were referred for diagnosis limiting recruitment to trials.
- The proportion of treatment-naive patients declined with increasing time from referral to evaluation.
- A significant number of people with new PMR received prednisolone doses higher than recommended.

Introduction

PMR is the most common systemic rheumatic disease of older adults and largely treated with glucocorticoids. The European Alliance of Associations for Rheumatology (EULAR)/ACR treatment guideline recommends initial prednisolone doses from 12.5–25 mg and continuation of treatment for at least one year, but it is unknown if the guideline is followed [1]. A large variation in clinical practice among both general practitioners (GPs) and rheumatologists has been reported in studies from the United Kingdom [2, 3]. In addition, high-quality evidence is lacking to support routine concomitant glucocorticoid sparing treatment with methotrexate, and given the limitations to use this drug in older adults with restricted renal function, new treatment options are needed for people with PMR. With the current expansion in PMR research, there is an increasing need for recruitment to PMR trials.

PMR is often managed entirely in primary care settings, whereas clinical trials are usually conducted in institutions of specialist care [4, 5]. Another barrier to research could be the time to rheumatology evaluation and initiation of glucocorticoid treatment prior to initial rheumatologist evaluation [6]. It is unknown how widespread these challenges are worldwide.

Diagnostic uncertainty in PMR exists. Existing classification criteria for PMR are intended for capturing patients with this disease, but do incorporate the key elements of diagnosis [7]. It is well known that misdiagnosis is common even in rheumatological practice [8]. Moreover, studies from the United Kingdom indicate that GPs as well as rheumatologists do not always rule out differential diagnoses [3, 9]. However, this issue has not been studied systematically.

The increased risk of comorbidities such as osteoporosis, cardiovascular disease and diabetes in PMR may be related to use of glucocorticoids, but possibly also to inflammation caused by the disease itself [10–13]. Comorbidities should be screened for and managed accordingly [1, 14]. However,

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studies from the United Kingdom indicated that systematic screening for comorbidities are not performed [2–4]. It is unknown if this is a worldwide problem in people with PMR.

In this study, we investigated current management practices for PMR by general practitioners and rheumatologists including implications for clinical trial recruitment.

Methods

Study design

A working group from the International PMR/GCA Study Group, consisting of rheumatologists and GPs from Denmark, the Netherlands, the United Kingdom, Austria, Australia, and Colombia drafted an English-language questionnaire [15]. The survey was refined using iterative feedback via email and during online meetings in June, August and October 2021. The questionnaire included 78 questions for rheumatologists and 71 questions for GPs focusing on six main areas: 1: Respondent characteristics; 2: Referrals of people with PMR; 3: Treatment with prednisolone; 4: Diagnostics used to confirm the diagnosis and investigate differential diagnosis; 5: Management of comorbidities; and 6: Barriers to research (see Supplementary Data S1 and S2 for full questionnaire, available at *Rheumatology* online). The questions were mainly multiple-choice format, but single-choice format was also used (Supplementary Material, available at *Rheumatology* online).

To be eligible for the study, respondents had to be medical doctors managing people with PMR, and GPs should also attend patients with any medical problem (generalist). The questionnaires were distributed to rheumatologists and GPs worldwide via members of the International PMR/GCA Study Group, using the snowball principle. Answers were collected anonymously via an online survey tool (REDcap), from 2 November 2021 to 27 January 2022 [16]. Eight reminders including updates about the overall number of respondents were sent to involved members of the PMR/GCA Study Group during this period.

Ethical considerations

The questionnaire for rheumatologists and GPs was anonymous, and therefore no ethical approval was necessary according to local institutional protocols. Because all data were collected anonymously, data protection agency registration was not necessary according to the General Data Protection Regulation.

Statistics

Analysis used descriptive statistics. Data are presented as number (percentages) for categorical variables and median [interquartile range (IQR)] for continuous variables. Countries were grouped by income and geographical region based on the World Bank classifications for the rheumatologist data [17]. This was not performed on GP data due to the lower number of countries with GP respondents. Data from countries with >15 respondents are shown separately, data from countries with <15 respondents were pooled into a single category ('other countries'). Data from countries with >15 respondents from both rheumatologist and GP were compared directly.

Results

In total, 394 GPs and 937 rheumatologists responded to the questionnaire. Eleven and 27 countries had >15 respondents for GPs and rheumatologists, respectively. Countries with <15 respondents are presented in Supplementary Tables S1 and S2, available at *Rheumatology* online. Nine countries (Austria, Canada, Colombia, Denmark, Italy, the Netherlands, Romania, Switzerland and the United Kingdom) had >15 respondents for both GPs (264 respondents) and rheumatologists (297 respondents).

Respondent characteristics

Respondent characteristics are summarized in Supplementary Tables S3 and S4, available at *Rheumatology* online. Median age (IQR) of respondents was 46 (39–55) years for GPs and 44 (36–53) years for rheumatologists. Most GPs were working in urban areas (70%) and rheumatologists in university hospitals (55%). GPs reported seeing a median of three people with new onset PMR yearly and rheumatologists a median of 10 people with new onset PMR yearly. A national or local PMR guideline was available for 56% of GPs and 52% of rheumatologists and almost all respondents stated that they adhered to the guideline.

Referrals

GPs referred a median of 25 (IQR 5–90)% of people with suspected PMR for diagnosis, and 50 (1–100)% of these patients were subsequently discharged to their GP for treatment (Table 1). Most frequently GPs referred people with suspected new PMR to departments of rheumatology at the hospital (72%), followed by rheumatologists working in private practice (35%) (Supplementary Table S5, available at *Rheumatology* online). The major reasons for referral were uncertainty of diagnosis (64%), risk of glucocorticoid related adverse events (25%), and patient requests (34%). During the disease course, 20 (10–50)% of patients with established PMR were referred by their GP (Table 1).

Overall, 64% of GPs could discuss patients with a rheumatologist before referring and all referred patients were seen by a rheumatologist (Table 2 and Supplementary Tables S6–S10, available at *Rheumatology* online). In general, 39% of rheumatologists evaluated people with suspected new onset PMR >2 weeks, and 19% >4 weeks, from referral by GP. However, 61% were evaluated within 2 weeks. The referral diagnosis was changed upon evaluation by rheumatologist in 15 (5–30)% of patients with an already established PMR diagnosis.

Treatment with prednisolone

Overall, a median of 50 (IQR 15–75)% of patients newly diagnosed with PMR had started treatment before rheumatologic evaluation (Table 2 and Supplementary Tables S6–S10, available at *Rheumatology* online). As reported by rheumatologists, patients seen within 14 days, compared with those seen >14 days from the initial referral, were less frequently started on prednisolone [median 40 (IQR 10–60)% *vs* median 50 (IQR 25–80)%], and in patients seen by a rheumatologist within 28 days compared with those seen >28 days from referral [50 (10–63)% *vs* 70 (30–90)%].

Direct comparison between GP and rheumatologist data in nine countries with >15 respondents showed a median prednisolone/equivalent starting dose of 20 (IQR 15–30) mg for

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Table 1. Characteristics of referral pattern and treatment strategy in general practice

	All participants	Austria	Canada	Colombia	Denmark	Italy	Netherlands	New Zealand	Romania	Russia	Switzerland	United Kingdom	Other countries
Referrals													
New PMR patients referred for diagnosis (%), median (IQR)	25 (5–90)	58 (10–100)	50 (2–100)	100 (13–100)	50 (20–100)	60 (28–100)	20 (10–50)	10 (10–20)	60 (10–88)	1 (1–2)	28 (10–50)	10 (1–25)	50 (10–100)
Patients returned to GP for treatment (%), median (IQR)	50 (1–100)	100 (50–100)	50 (2–100)	8 (0–50)	85 (40–100)	50 (0–100)	50 (10–90)	100 (90–100)	80 (50–98)	1 (1–1)	80 (10–100)	100 (100–100)	10 (0–60)
Patients referred during treatment (%), median (IQR)	20 (10–50)	50 (25–90)	50 (10–100)	100 (50–100)	20 (10–33)	50 (15–80)	15 (10–30)	20 (10–25)	30 (10–80)	1 (1–1)	20 (10–30)	10 (10–20)	50 (20–80)
Prednisolone													
Initial dose (mg), median (IQR)	20 (15–30)	38 (25–50)	20 (20–50)	20 (10–30)	25 (15–40)	25 (25–25)	15 (15–15)	20 (15–40)	15 (12–20)	15 (15–15)	50 (25–50)	15 (15–20)	20 (10–40)
Initial dose >25 mg, *n* (%)	120 (30)	13 (50)	5 (33)	6 (35)	16 (30)	8 (22)	3 (14)	7 (41)	7 (20)	5 (12)	19 (73)	3 (9)	28 (39)
Duration of treatment (months), Median (IQR)	6 (3–12)	9 (6–12)	6 (2–9)	6 (4–24)	12 (8–18)	5 (3–12)	11 (6–12)	12 (10–18)	2 (2–5)	6 (6–6)	12 (12–14)	15 (12–24)	6 (2–10)
Duration of treatment <6 month, *n* (%)	111 (28)	6 (23)	6 (40)	5 (29)	7 (13)	18 (50)	3 (14)	0 (0)	24 (69)	8 (20)	2 (8)	1 (3)	31 (43)

Other countries: data from countries with <15 respondents were pooled.
IQR: interquartile range; GP: general practitioner.

Table 2. Management of referrals and treatment strategy for rheumatologists

		Geographical region						Income	
	All participants	Europe and Central Asia	North America	Latin America	East Asia and Pacific	South Asia	Middle East and Africa	High- income countries	Low- and middle- income countries
Management of referrals									
GPs can discuss patients prior to referral, *n* (%)	579 (64)	260 (81)	61 (79)	67 (46)	45 (78)	32 (57)	114 (47)	359 (78)	220 (50)
Referred patients seen by rheumatologist (%), median (IQR)	100 (80–100)	100 (90–100)	100 (100–100)	100 (90–100)	100 (100–100)	100 (80–100)	90 (10–100)	100 (95–100)	100 (20–100)
Evaluation of suspected new PMR patients >2 weeks after referral, *n* (%)	348 (39)	127 (40)	57 (75)	86 (59)	30 (53)	3 (6)	43 (18)	234 (51)	117 (27)
Evaluation of suspected new PMR patients >4 weeks after referral, *n* (%)	166 (19)	63 (20)	18 (24)	48 (33)	14 (24)	1 (2)	24 (10)	106 (23)	61 (14)
Referred patients with established PMR diagnosis (%), median (IQR)	20 (3–50)	30 (10–50)	37 (10–55)	10 (1–50)	50 (15–70)	10 (0–25)	5 (0–25)	30 (10–50)	5 (0-33)
Diagnosis changed upon evaluation of patients with established PMR diagnosis (%), median (IQR)	15 (5–30)	15 (10–30)	20 (10–45)	10 (0–50)	20 (15–40)	20 (0–50)	10 (0–30)	20 (10–30)	10 (0–30)
Prednisolone									
Started prior to evaluation (%), median (IQR)	50 (15–75)	50 (30–80)	60 (50–80)	50 (10–60)	55 (30–90)	50 (10–60)	25 (5–50)	50 (30–80)	30 (5–50)
Initial dose (mg), median (IQR)	20 (15–20)	16 (15–20)	20 (15–20)	20 (15–30)	15 (15–15)	20 (15–30)	20 (15–30)	15 (15–20)	20 (15–30)
Initial dose > 25 mg, *n* (%)	216 (23)	34 (10)	5 (6)	47 (31)	0 (0)	20 (35)	110 (41)	4 (8)	178 (38)
Duration of treatment (months), median (IQR)	12 (6–18)	12 (12–18)	12 (10–18)	10 (6–12)	15 (12–18)	11 (6–12)	6 (3–18)	12 (12–18)	6 (3–12)
Duration of treatment <6 month, *n* (%)	133 (14)	13 (4)	2 (3)	35 (23)	4 (7)	6 (11)	72 (27)	14 (3)	118 (25)

IQR: interquartile range; GP: general practitioner.

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GPs and 15 (15–20) mg for rheumatologists. The percentage of patients receiving >25 mg daily was 30% for GPs and 12% for rheumatologists. Overall, duration of prednisolone treatment was shorter if patients were managed by a GP than by a rheumatologist [median 9 months (IQR 4–12) *vs* 12 months (11–18)]. The percentage of respondents prescribing treatment for <6 months was 27% for GPs and 5% for rheumatologists. Data from all countries are shown in Tables 1 and 2 and Supplementary Tables S6–S10, available at *Rheumatology* online.

Diagnostics

Diagnostic workup to confirm PMR is illustrated in Fig. 1 for comparison between GPs and rheumatologists in nine countries with >15 responders. In general, diagnostic workup to confirm PMR was more frequently performed by rheumatologists than GPs. Clinical examination was always performed by 97% of rheumatologists and 90% of GPs and C-reactive protein was always performed by 97% of rheumatologists and 88% of GPs to confirm PMR. Imaging to confirm the diagnosis was not routinely performed. All data for GPs and rheumatologists are shown in Supplementary Fig. S1, available at *Rheumatology* online.

Diagnostic procedures applied by rheumatologists to investigate for GCA in people with PMR without cranial symptoms are detailed in Fig. 2. Vascular ultrasound was the most utilized diagnostic imaging technique, and 16% of respondents stated to use vascular ultrasound in all new PMR patients.

In the nine compared countries, rheumatologists more often utilized laboratory tests than GPs to investigate differential diagnoses other than GCA (Supplementary Fig. S2, available at *Rheumatology* online). In general, imaging (e.g. X-ray of the chest) to investigate differential diagnoses other than GCA was rarely performed by either GPs or rheumatologists (Fig. 3). All data for GPs and rheumatologists are presented in Supplementary Fig. S2, available at *Rheumatology* online.

Assessment and management of comorbidities

Direct comparison between GPs and rheumatologists in nine countries demonstrated that screening for comorbidities at diagnosis and follow-up was not routinely performed by neither GPs nor rheumatologists (Fig. 4). Notably, dual energy X-ray absorptiometry was always performed by only 41% of rheumatologists and 23% of GPs at diagnosis, but 55% of GPs *vs* 45% of rheumatologists always performed diabetes screening at diagnosis. All data for GPs and rheumatologists are demonstrated in Supplementary Fig. S3, available at *Rheumatology* online.

Direct comparison between GPs and rheumatologists in nine countries showed that treatment with vitamin D and calcium, proton pump inhibitors, and bisphosphonates were always prescribed by 50% *vs* 87%, 30% *vs* 28%, and 9% *vs* 27%, respectively (Fig. 4). All data for GPs and rheumatologists are shown in Supplementary Fig. S3, available at *Rheumatology* online.

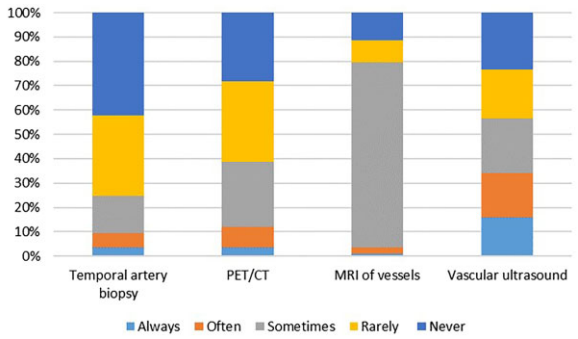


Figure 2. Diagnostic workup among rheumatologists worldwide to evaluate giant cell arteritis in people with new polymyalgia rheumatica without cranial symptoms

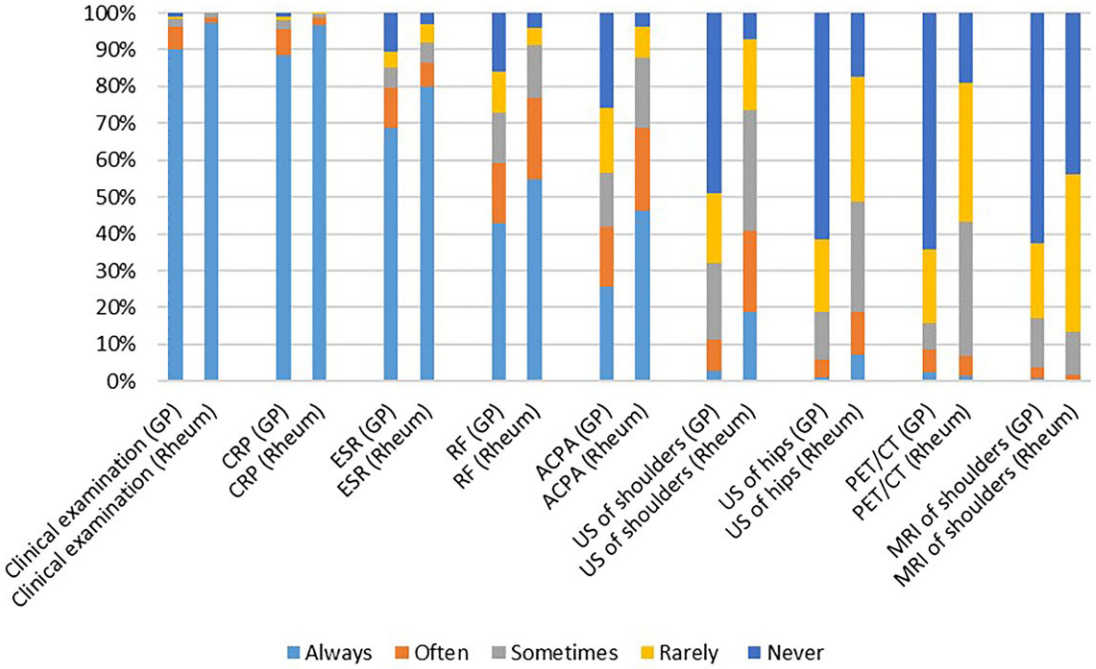


Figure 1. Diagnostic workup to confirm diagnosis of PMR. A comparison between GPs and rheumatologists in nine countries with more than 15 respondents. RF: IGM RF; GP: general practitioners; Rheum: rheumatologists

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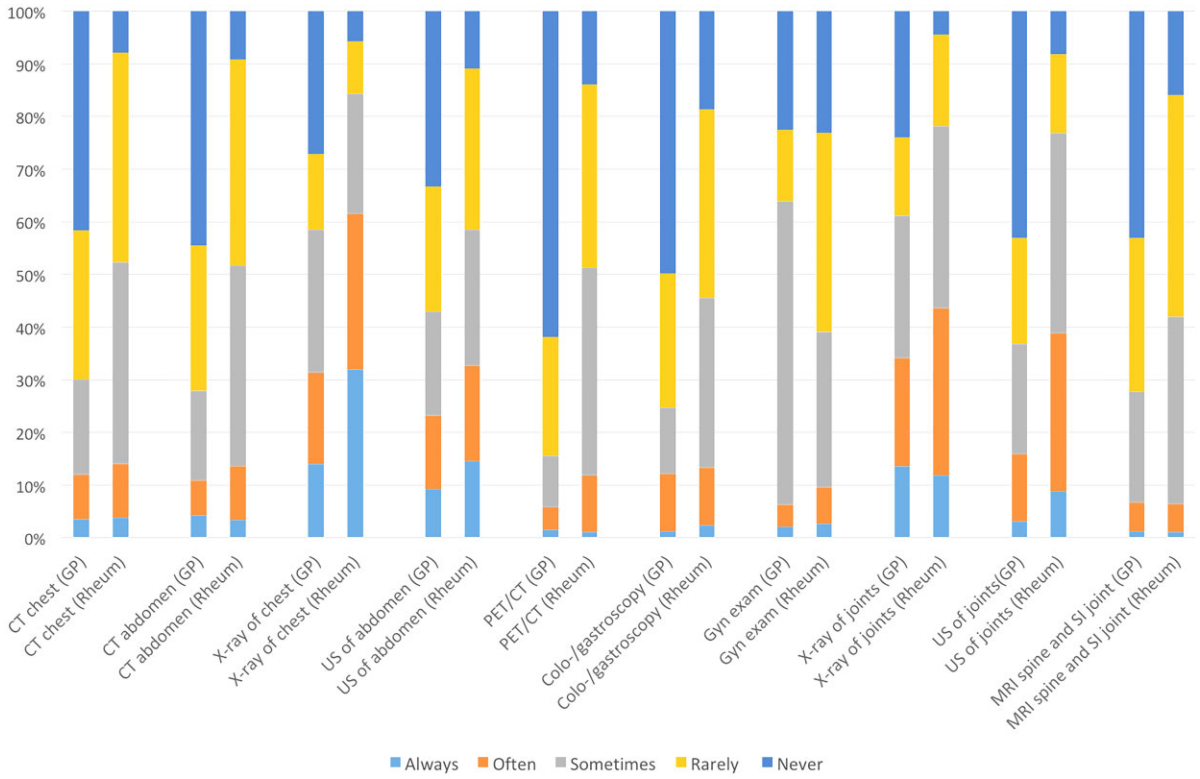


Figure 3. Imaging to investigate differential diagnosis in people with PMR. A comparison between GPs and rheumatologists regarding use of imaging in nine countries with more than 15 respondents. Gyn Ex: gynecological examination including ultrasound; SI: sacroiliac. GP: general practitioners; Rheum: rheumatologists

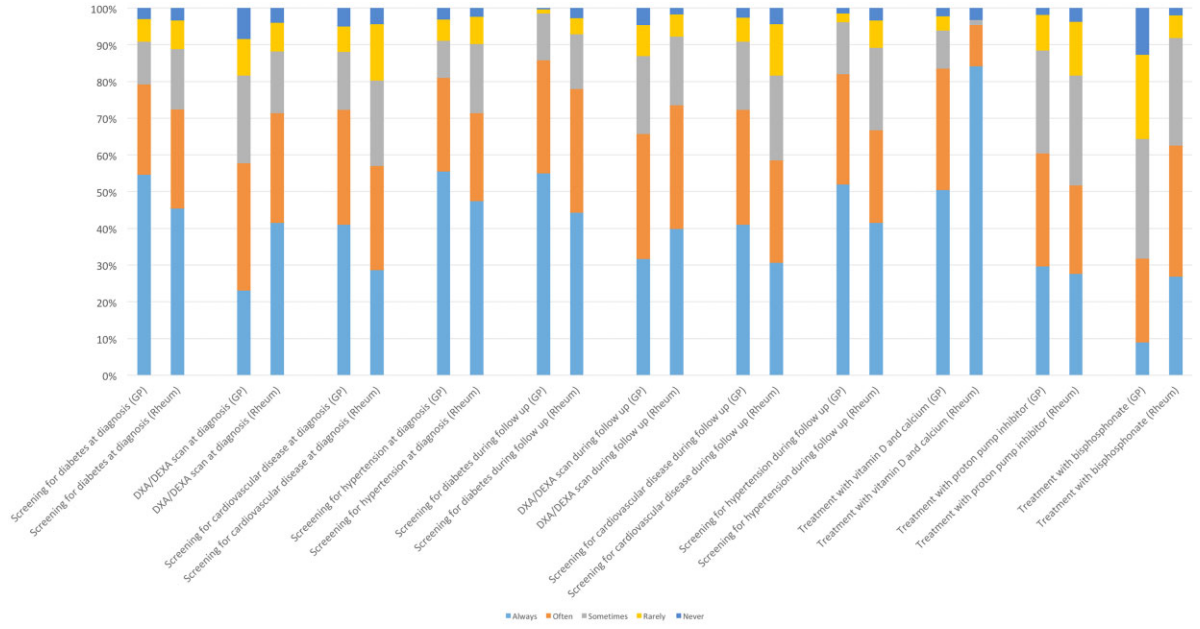


Figure 4. Assessment and management of common comorbidities in PMR patients. A comparison between GPs and rheumatologists in nine countries with more than 15 respondents. DXA/DEXA: dual energy X-ray absorptiometry; GP: general practitioners; Rheum: rheumatologists

Barriers to research

Fifteen percent of the responding rheumatologists ($n = 129$) performed research in PMR, of which 64/129 (52%) had participated in clinical trials. Of these, 36/64 (56%) had experienced difficulties with recruitment to trials. Finally, 19/36 (52%) answered that not enough patients were referred, 27/36 (75%) that patients had received prednisolone prior to rheumatologic evaluation, 17/36 (47%) that patients did not want to participate, and 14/36 (39%) that diagnosis were uncertain due to prednisolone treatment.

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Discussion

This is the first international study exploring current management practices for PMR by general practitioners and rheumatologists including implications for clinical trial recruitment. Our results show that only a minority of people with PMR were referred to rheumatologists. Time from referral to actual visit was long and many received prednisolone before rheumatologist evaluation. Finally, initial prednisolone dose was often above the guideline recommendation for PMR. Many of these factors were also major barriers to clinical trial recruitment.

Clinical management

PMR is a challenging clinical diagnosis with many differential diagnoses, and a high risk of misdiagnosis [8, 18]. In addition, people with PMR may be diagnosed with GCA or rheumatoid arthritis during the disease course [19]. Hence, it is interesting that only a minority of people with PMR were actually referred to rheumatologists for diagnosis or second opinion during follow-up. Earlier findings from the United Kingdom and United States of America also demonstrated that only 44% and 60% of people with PMR were referred for rheumatologist evaluation at some point during the disease course [4, 5]. Current EULAR/ACR guidelines on PMR do not specify which patients should be managed in general practice or by rheumatologists, and local variations in referral policy may influence referral practices [1]. In addition, the main reason for referral for diagnosis was diagnostic uncertainty in most countries, which indicates that referred patients represent a subgroup of people with PMR. Clinical recommendations that more clearly describe when GPs should refer patients with uncertainty related to PMR diagnosis to a rheumatologist could help standardize the referral process. In patients with diagnostic uncertainty, we used the term 'suspected PMR'. In future work, the term polymyalgic syndrome could be considered, referring to the symptomatology (even though ill-defined in literature) in opposite to the term 'suspected PMR', referring to the disease.

This study demonstrated that a large proportion of people with suspected new onset PMR were evaluated a long time after referral and had received prednisolone prior to evaluation by rheumatologist. Interestingly, we also found a relationship between the percentage of patients starting prednisolone prior to rheumatologic evaluation and the time from referral to evaluation. The often-disabling symptoms associated with PMR may compel GPs to start glucocorticoids if the waiting time for rheumatologist is too long. The time lag to rheumatologist evaluation may therefore be an obstacle for improvement of clinical practice and recruitment to trials in PMR. Recently introduced fast-track setups, typically offering GPs an opportunity to refer people with suspected new onset PMR for rheumatologist evaluation within one week, may be part of the solution and reduce waiting time for evaluation by rheumatologist [6]. Previously, fast-track strategies for GCA have improved the diagnostic process in this disease and reduced permanent visual impairment [20].

This study demonstrated that higher initial doses of prednisolone and shorter treatment durations than recommended by existing guidelines were more commonly employed by GPs than by rheumatologists [1]. A higher initial dose of prednisolone increases the risk of comorbidities [21]. Therefore, future initiatives should focus on how the prednisolone starting dose could be reduced among GPs. The short treatment duration seen in general practice and in some parts of the world raises questions regarding the level of diagnostic certainty in these settings as rapid prednisolone tapers in PMR increase the risk of relapse [22]. However, people with PMR solely seen in general practice may also represent a subgroup with milder or more typical disease and a smaller proportion of patients with concurrent GCA than the 22% usually reported [23]. Further studies are needed to determine the correct treatment duration in different subsets of PMR.

Diagnostic imaging was not widely used to confirm PMR. This may reflect that no diagnostic imaging has currently been validated for the diagnosis of PMR but may also indicate a lack of available expertise or resources for this investigation. Ultrasound may have a role in the diagnosis of PMR [7]. In addition, PET/CT and MRI may have a future role in the diagnosis of a PMR sub-population, but have not been validated yet. It is recognized that these are expensive and currently not widely available internationally outside of large specialist centres. More studies are needed to evaluate if PMR sub-populations should be evaluated with these modalities [24, 25].

While cancer and chronic infections are important differential diagnoses to consider, imaging was rarely used, and no guidelines support the routine use of imaging to investigate differential diagnoses in people with suspected new-onset PMR. Previous studies have shown that PMR symptoms may be related to cancer for up to 2 years after diagnosis [26, 27]. Although not presently supported by guidelines, there could be a rationale to screen people with PMR without cranial symptoms for GCA with vascular ultrasound in the future. GCA in patients with PMR is common, but future studies should focus on evaluating GCA in different subsets of PMR [23].

Considering the potential high prednisolone dose applied by many rheumatologists and GPs, screening frequency for osteoporosis and diabetes both at diagnosis and during the disease course was surprisingly low. In addition, both diseases commonly occur after the diagnosis and are often attributed to prednisolone treatment [10, 13]. Management guidelines recommend screening for comorbidities and initiation of treatment when needed [1, 14, 28]. In addition, this international study and previous studies from the UK demonstrated that not all patients received drugs for bone prophylaxis [4]. Further initiatives should focus on improving the adherence to existing guidelines and treatment schemes.

Barriers to research

In the last few years, research in PMR has expanded considerably. The first few randomized controlled trials with biologics have recently been published and several are ongoing [29, 30]. To perform larger trials, it is essential that researchers can recruit treatment-naive patients, but the extent of difficulties with recruitment has not previously been evaluated. In this study we demonstrate that more than half of researchers performing clinical trials in PMR experienced difficulties with recruitment. The biggest obstacle for recruitment was that patients had received prednisolone prior to rheumatologic evaluation, followed by not enough patients being referred. This may be attributed to the widespread handling of PMR in primary care and the long duration between referral and evaluation by a rheumatologist also demonstrated in this study as well as previous studies from the UK and Denmark [4, 6, 31].

The major strength of this study is the large number of respondents from many countries worldwide. Study

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limitations include, first, the decentralized recruitment process and unknown actual survey response rates. This may result in response bias, possibly overestimating the adherence to guidelines, as rheumatologists and GPs with an interest in the field may potentially be more likely to answer the questionnaire. Second, a high percentage of rheumatologists participating in the survey were from university hospitals and most GPs were based in urban areas, where clinical practice might differ from that of non-university hospitals and rural areas, for example due to better availability of imaging tests or research interest in PMR in the former places. Third, GP respondents primarily came from Europe, and the direct comparison of nine countries between GPs and rheumatologists therefore especially reflects clinical practice in Europe. Fourth, we cannot exclude misinterpretation of questions in some countries because of lacking language skills. Answers from GPs in Russia were notably uniform, raising this suspicion. However, we were unable to examine this observation because all responses were anonymous. Lastly, the structure of primary health care shows global variation which may be reflected in the differences in referral patterns between countries [32, 33].

In conclusion, this study shows that a large proportion of people with PMR are not referred for diagnosis, and that the proportion of treatment-naive patients declined with increasing time from referral to assessment. Strategies are needed to improve current referral processes and care of people with PMR. This would improve clinical practice and could facilitate more opportunity for trial recruitment.

Supplementary material

Supplementary material is available at *Rheumatology* online.

Data availability

The data underlying this study are available from the corresponding author upon reasonable request.

Funding

No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

Disclosure statement: E.M.H. Speakers bureau: AbbVie, Sanofi, Sobi, MSD, UCB, Consultant of: AbbVie, Sanofi, Sobi, MSD, UCB, Grant/research support from: Novo Nordic Foundation, Danish Rheumatism Association, Danish Regions Medicine Grants, Roche, Novartis, Celgene, MSD, Pfizer, Roche, Sobi. C.E.T.-G. Speakers bureau: AbbVie, BMS, Biopas, Boehringer Ingelheim, Novartis, Pfizer, Janssen, Roche. B.D.N. Paid instructor for: Roche. R.C. Speakers bureau: Janssen, Roche, Sanofi, Abbvie, Fresenius, Galapagos, Viatris, Clinical Trials: Abbvie, Argenx, Grant/Research Support: Janssen, Nordic Pharma. E.L.M. Consultant of: Boehringer-Ingelheim, Grant/research support from: Boehringer Ingelheim. S.E.S. Grant/research support from: AstraZeneca, Rheumatology Research Foundation RISE Pilot Award. V.O. Speakers bureau: Abbvie. S.A. Grant/research support from: GSK. R.G. Speakers bureau: AbbVie, Pfizer, Novartis, Cornerstones and Janssen. Support to attend meetings from Janssen. N.C. Speakers bureau: Laboratorios FAPASA (Farmacéutica Paraguay). H.I.K. Speakers bureau: Roche, Abbvie. G.H. Speakers bureau: Abvie, Johnson and johnson, Lilly, Novartis. N.Z. MK Consultant of: Boehringer-Ingelheim, Chugai, Mochida, Kissei; Grant/research support from: Boehringer Ingelheim, MBL, Ono Pharmaceutical; Speakers bureau: AbbVie, Asahi Kasei, Astellas, Boehringer-Ingelheim, Chugai, Eisai, Mitsubishi Tanabe, Ono Pharmaceutical. K.S.M.VdG. Speakers bureau: Roche. T.H. Grant/research support from: Valneva. E.B. Speakers bureau: Roche. C.D. Speakers bureau: Abbvie, Eli Lilly, Janssen, Novartis, Pfizer, Roche, Galapagos and Sanofi, Consultant of: Abbvie, Eli Lilly, Janssen, Roche, Galapagos and Sanofi. Research grant from AbbVie. S.L.M.: consultancy on behalf of her institution for Roche/Chugai, AbbVie, AstraZeneca, Sanofi; support to attend educational meetings from Roche/Chugai and Pfizer; Patron of PMRGAuk. KSMG speaker fee from Roche. A.K.H. Grant/research support from: the Swiss Foundation for Research on Muscle Diseases (FSRMM). All other authors had no disclosures.

Acknowledgements

This study was endorsed by the International PMR/GCA Study Group. K.K.K. was supported by Aarhus University Hospital and Central Denmark Region.

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