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Long-term use of glucocorticoids for polymyalgia rheumatica: follow-up of the PMR Cohort Study

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Abstract

Objectives. Polymyalgia rheumatica (PMR) is a common inflammatory condition in older adults, characterised by bilateral hip and shoulder pain and stiffness. Reducing oral glucocorticoids, classically used for up to two years are the mainstay of treatment. This study considers the factors early in the disease course that might be associated with prolonged treatment.

Methods. 652 people with incident PMR were recruited from English general practices (2012-2014). Participants completed seven questionnaires over two years (used to allocate people to pain/stiffness trajectories) and a further long-term follow-up questionnaire (LTFUQ) a median of 5.16 years after diagnosis. Characteristics of those still taking and having ceased glucocorticoids were described and compared using Kruskal-Wallis and chi-square and t-tests as appropriate.

Results. Of the 197 people completing the LTFUQ, 179 people reported ever having taken glucocorticoids. Of these, 40.1% were still on treatment with a mean daily dose of 5 (1.5,9) mg. People still taking glucocorticoids were more likely to be older (72.5 vs 70.2 years, $p=0.035$), live alone (31.8% v 15.0%, $p=0.01$), and have self-managed their glucocorticoid dose (39.1% versus 11.0%, $p<0.0001$). They were also more likely to belong to a pain-stiffness trajectory class with sustained symptoms.

Conclusions. PMR is not always a time limited condition. Few patient characteristics are associated with prolonged treatment early in the disease course, but those who are older and have sustained symptoms may be at greater risk. Whilst accurate prediction is not possible yet, clinicians should carefully monitor people with PMR to manage symptoms and reduce cumulative glucocorticoid dose.

Keywords: Polymyalgia Rheumatica; Cohort studies; Primary Health Care

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KEY MESSAGES

- Polymyalgia rheumatica (PMR) is usually treated with oral glucocorticoids tapering over two years.
- We show that 40% of PMR patients are still treated after a median of 5.16 years.
- No predictors of extended PMR treatment were identified; therefore, all patients should be carefully monitored.

INTRODUCTION

Polymyalgia rheumatica (PMR) is the commonest inflammatory rheumatic disease in older adults. It causes severe pain and stiffness in the hip and shoulder girdles and is usually accompanied by an acute phase inflammatory response. As such, PMR can cause significant disability[1] and severely impact on quality of life.[1,2]

A gradually reducing regimen of oral glucocorticoids is usually used to treat PMR and provides rapid relief from symptoms. Clinical guidelines recommend a starting dose of 12.5-25mg of prednisolone daily, tapered to a stop over 18 to 24 months.[3,4] There are concerns from professionals and patients regarding the potential side-effects of such long-term glucocorticoid treatment[1,5–7] and evidence is emerging that people with PMR experience a high burden of incident glucocorticoid-related morbidities, including vascular (23% increased risk), respiratory (25% increased risk), endocrine (41% increased risk), and gastroenterological (21% increased risk). Glucocorticoid treatment can also affect the eyes (37% increased risk) as well as bone health (111% increased fragility fracture risk), and can cause or exacerbate mood problems (29% increased risk) or in some cases lead to psychosis in psychiatric conditions.[8,9]

There is also growing evidence that for some people with PMR, treatment is more protracted than guidelines suggest. [10,11] A recent systematic review and meta-analysis,[12] has estimated that

51% (95% CI 41%, 61%) of people were still taking glucocorticoid treatment 2 years after diagnosis and 25% (95% CI 15, 36%) after 5 years and that symptoms do not necessarily remain well-controlled during glucocorticoid treatment. The reasons for the heterogeneity in treatment and symptom course remain poorly understood, although it is plausible that they could be related to the initial presentation of PMR, the comorbidity profile of an individual, which may change over time, or to the “symptom tail”[13] or “steroid legacy”. This latter concept has been described as the long-term impact of glucocorticoid treatment, after the resolution of the PMR itself, including for example weight gain, hair loss, fragility fracture, and diabetes. A “symptom tail” may relate to comorbidities present prior to PMR diagnosis (which may have been to some extent masked by the glucocorticoid treatment), or development of comorbidities with onset during PMR treatment (related or unrelated to PMR), having an impact of the individual’s functioning when glucocorticoid treatment is reduced. The most recent guidance from the European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR),[3] recommend consideration of specialist referral in patients experiencing, or at high risk of therapy-related side-effects, PMR refractory to glucocorticoid therapy and/or relapses/prolonged therapy. It remains to understand how these patients at higher risk can be identified to facilitate early specialist referral.

The PMR Cohort study is an inception cohort of UK primary care patients diagnosed with PMR between 2012 and 2014 and initially followed-up by mail over a two-year period.[14–16] In this paper, we report on a further follow-up, between 4.5 and 6.5 years after the initial PMR diagnosis, in which we describe the characteristics of those with prolonged treatment and try to understand the reasons for this. Factors considered include the heterogeneity of the disease group, comorbidity profile, the potential role of glucocorticoid treatment patterns, and the initial trajectory of pain and stiffness symptoms after diagnosis.[14]

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METHODS

PMR cohort study

Full details of the PMR Cohort study have been published previously.[14–16] Briefly, 652 individuals were recruited from general practices across England at the time of their PMR diagnosis (2012-14). They completed postal surveys at diagnosis and after 1, 4, 8, 12, 18, and 24 months. Of the 571 individuals who had not withdrawn from the study or died by the time of the 24-month follow-up, 306 (53.6%) were still alive and registered with practices that agreed to participate in a further follow-up in 2019 (Figure 1). These individuals were mailed the long-term follow-up (LTFU) questionnaire requesting information regarding their current PMR symptoms and treatment and their overall health. Those who did not respond were sent postal reminders after 2 and 4 weeks.

Data collected

At each wave of the survey, participants reported their current levels of PMR-related pain and stiffness on numerical rating scales (scored 0-10) and the locations of their pain and stiffness on body manikins. Physical functioning was assessed by the mHAQ questionnaire.[17,18] Current prednisolone dose was recorded at each data collection point and information on other medications was collected at baseline. Participants were also asked to report on their general health (EQ5D[19]), mental health (PHQ8,[20] GAD7[21]), sleep (Insomnia Severity Index[22]), and fatigue levels (FACIT-Fatigue[23]). The LTFU questionnaire requested additional information regarding glucocorticoid treatment over time, comorbidities and when they were diagnosed, other relevant health problems, symptom flares, and weight changes.

Sample size

The justification for the sample size recruited to this cohort has been described previously[15] and was based on the likely numbers of people diagnosed with PMR in UK primary care each year. The current study presents data from an additional follow-up where all those who had not withdrawn

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their consent and whose general practice agreed to continue participation, were invited to continue to complete a final questionnaire.

Statistical analyses

Responders to the LTFU survey were compared to the overall baseline sample and to the responders at 24-month follow-up using simple descriptive statistics to understand the extent of any attrition bias. Due to the number of comparisons made, hypothesis testing was not used.

Responders to the LTFU who reported themselves to be still taking or to have stopped treatment were compared in terms of their glucocorticoid exposure over time, their baseline characteristics and changes in PMR symptoms between baseline and 1-, 4-, and 24-months follow-up using Kruskal-Wallis, chi-square and t-tests as appropriate.

Changes in key PMR symptoms and other health characteristics between baseline and 1 month, and baseline and 4 months, were compared between those who had and had not stopped treatment.

Adjusted mean scores or probability of the outcomes were calculated as appropriate.

Adjustment to the association between participant characteristics and continued treatment for other variables was not made, as interest was in association and not potential causation.

Responders to the baseline survey have previously been allocated to one of five classes based on the dual trajectory of their pain and stiffness over the first two years after their PMR diagnosis (1 Sustained symptoms; 2 Partial recovery, sustained moderate symptoms; 3 Recovery before worsening; 4 Rapid and sustained recovery; 5 Slow and continuous recovery)[14]. Continued use of glucocorticoids was also compared across these classes.

Content analysis

Participants were asked if they had ever changed their prednisolone dose without going to see their doctor and if so, how? This free text question was analysed using content analysis[24], whereby each response was read repeatedly by one author (BSS) to achieve data immersion and then classified according to the overall meaning of the comments. Codes that were closely related were combined into broader categories. A second author (SM) then repeated the process, and any disagreements were resolved by discussion. This process was carried out in Microsoft Excel. Ethical approval for the study was received from the Staffordshire Research Ethics Committee (REC Reference number: 12/WM/0021) and all patients provided written informed consent.

Patient and Public Involvement

Patients were involved in the design of study materials for all stages of the mailing process. A discussion was held with members of the Health Unlocked PMRGCAuk forum to understand aspects of the PMR diagnosis and treatment experience that patients felt were important to how their condition progressed.

RESULTS

Cohort attrition

197 responses to the LTFU were received (68.6% of those eligible). Those eligible to receive the LTFU questionnaire were broadly similar to the overall baseline sample (Supplementary Table S1, available at *Rheumatology Advances in Practice* online). Similarly, groups eligible and ineligible to receive the LTFU questionnaire after the 2-year follow-up were broadly similar in terms of their characteristics at baseline. However, at 2 years, the group eligible for the LTFU reported slightly higher pain and stiffness scores and a higher proportion reported morning stiffness of >60 minutes and lived in less deprived areas. In those eligible for the LTFU, responders and non-responders were broadly similar in terms of their sociodemographic and PMR characteristics at baseline and 2 years, with the

exception that responders lived in less deprived areas. Participants completed the LTFU questionnaire a median (quartile1, quartile3) of 5.16 (4.87, 5.57) years after their PMR diagnosis, with the longest time since diagnosis being 6.89 years.

Prolonged treatment for PMR

Of the 179 people who reported ever taking glucocorticoid treatment for their PMR, 67 (40.1%) reported that they were still taking this treatment, with a median (quartile 1, quartile 3) daily dose of 5 (1.5, 9) mg (Table 1). Those who had stopped treatment reported having taken glucocorticoids for a total of 20.1 (13.8) months (mean, standard deviation).

Treatment characteristics over time

There was little difference in the highest ever reported dose of prednisolone between those who had stopped and who were still receiving glucocorticoid treatment, but those who were still receiving treatment were significantly more likely to report having changed their dose without consulting their doctor (39.1% versus 11.0%, $p < 0.0001$). From content analysis of the 40 responses to the open question, we found that of those describing the changes to their dose ($n=28$), six described having agreed to self-management with their doctor (three specifically to reduce the dose, three to manage more broadly), 11 described reducing their own dose (1 faster and 3 slower than advised, 3 reported a specific reduction regimen), two discontinued their treatment, while two people described increasing their dose and seven reported returning to a previously effective dose. Numbers were too small to consider whether how participants self-managed their glucocorticoid treatment was associated with continued long-term treatment. There were no significant differences in the age and gender of those responding to the open question and those not.

Differences in baseline characteristics between those continuing and ceasing treatment

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3 Those still taking glucocorticoids were older (72.5 vs 70.2 years at baseline, $p=0.035$) (Table 1) and
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5 more likely to live alone (31.8% v 15.0%, $p=0.01$). There were no other significant differences in
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7 reported care for PMR, comorbidities, function, or other health constructs between those still
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9 receiving and those who had ceased treatment.
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14 **Changes in PMR symptoms and general health over time in those continuing and ceasing**
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16 **treatment**
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19 There was a significant association between class membership (defined by pain and stiffness
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21 trajectory over the first 2 years of the study[14]) and glucocorticoid treatment at LTFU (Table 2).
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23 Those still on treatment were more likely to belong to pain-stiffness trajectories classes 2 (Partial
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25 recovery, sustained moderate symptoms) and 3 (Recovery before worsening) and less likely to
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27 belong to classes 4 (Rapid and sustained recovery) or 5 (Slow and continuous recovery).
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29 There were no significant differences in baseline-adjusted PMR symptoms or general health
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31 measures at 1-month follow-up, between those who had and had not ceased treatment at the LTFU.
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33 At the 4-month follow-up, there were no baseline-adjusted differences in pain or stiffness severity or
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35 in physical function. The baseline-adjusted probability of reporting stiffness at lunchtime and in the
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37 afternoon was lower in those still on treatment at the LTFU than in those who had stopped
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39 treatment.
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45 **Comorbidities and medication use**
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48 There was no significant difference in any specific self-reported comorbidity, or the number of
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50 comorbidities reported on the LTFU questionnaire, either ever or with onset during the study period
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52 (Supplementary Table S2 available at *Rheumatology Advances in Practice* online). Those still
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54 receiving glucocorticoid treatment at the LTFU were more likely to be treated with proton pump
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56 inhibitors (65.7% v 41.0%, $p=0.002$), calcium and vitamin D (67.2% v 27.0%, $p<0.001$) and bone
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58 prophylaxis (e.g. bisphosphonates) (31.3% v 8.0%, $p<0.001$) at the LTFU than those who had ceased
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3 glucocorticoids. There were no other differences between those still receiving and having stopped
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5 treatment at either at baseline or at the LTFU (Table 3).
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10 **DISCUSSION**

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12 In keeping with some recent studies,[10,11] 40% of people in this study reported using
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14 glucocorticoid treatment at a median follow-up time of over five years after their initial PMR
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16 diagnosis. Despite having collected detailed data on this cohort, we were unable to find associations
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18 either at baseline, or early follow-ups to provide insight into those more likely to require prolonged
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20 treatment. People continuing treatment were older at diagnosis and more likely to live alone. They
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22 were also more likely to have changed their glucocorticoid dose without consulting their doctor, but
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24 it is unclear whether this is a cause of prolonged treatment or a result of difficulties in dose
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33 The only clear indicator of long-term treatment was the trajectory of pain and stiffness over the first
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35 two years of the condition. This is unlikely to aid in understanding prognosis at an early enough
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37 stage to suggest who needs specialist referral for glucocorticoid sparing treatment. It may however
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39 be possible for GPs to identify people within this two-year period who report sustained high levels of
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41 symptoms and to enhance the monitoring of these patients.
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47 The finding of prolonged treatment for 40% of people is congruent with the findings from an
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49 American cohort[10] where the median time to treatment discontinuation was 5.95 years. Although
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51 it is higher than the estimated 25% still using glucocorticoids 5 years after diagnosis in a recent
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53 meta-analysis.[12] In the UK Clinical Practice Research Datalink, the median time with continuous
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55 treatment after diagnosis (defined as less than 90 days between prescriptions) was reported to be
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57 15.8 months with 25% receiving treatment for longer than 4 years in total.[11] In the current study,
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59 we do not know whether treatment was stopped and restarted between follow ups. Regardless of
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cause and effect of this prolonged treatment, it has been shown to be of concern to patients[6,7] and there is evidence for the development of iatrogenic morbidities, even at relative low doses of glucocorticoid.[25]

This study has numerous strengths, including recruitment and follow-up in real time from primary care. This will reduce recall bias (although some may remain in terms of length of glucocorticoid treatment reported in the LTFU questionnaire, especially in those patients no longer taking glucocorticoids) and provides a more representative sample than might be the case in samples recruited from a specialist care settings given that the majority of patients in the UK are diagnosed and managed exclusively in general practice.[26,27] Although it could be argued that the GP diagnosis of PMR may be less accurate than a diagnosis made by a rheumatologist, we did not exclude those with a diagnosis made by a specialist and GPs were provided with diagnostic guidelines from the British Society for Rheumatology[4] to support accurate participant recruitment. The age and gender profile of the current cohort is similar to those reported in studies in specialist settings and we have previously conducted sensitivity analyses, producing similar findings in a subgroup of the cohort meeting a stricter definition of PMR at baseline.[14]

The level of loss to follow-up at the LTFU stage is to be expected from a longitudinal cohort of older people. A large contributor to study attrition was the withdrawal of GP practices from the study, often due to competing clinical pressures and changes in GP administrative arrangements. Whilst the smaller numbers will result in less stable statistical estimates, we think this is unlikely to result in substantial differences between responders and non-responders, as practice withdrawal was not related to the PMR status of patients. The number of early disease characteristics (at baseline, 1- and 4-month follow-ups) considered in the analysis, combined with the relatively small sample size, increases the chances of a type I error (i.e. a falsely significant finding). To counteract this possibility,

we have avoided over-interpreting the findings. We have also chosen not to attempt to fit formal prognosis models, which would risk being under-powered and of less use to clinicians.

Previous work in this cohort has suggested that there are potentially subtypes of PMR.[14] Whilst the current study has not been able to identify these subtypes at an earlier point in the disease course, the association of these classes of individuals based on pain and stiffness scores over two years, with the continued use of glucocorticoids a median of 5 years after diagnosis provides further evidence of these subtypes. Cessation of treatment after 5 years was more likely in those considered to have “rapid and sustained” or “slow and continuous” recovery than those classified as “partial recovery, sustained moderate symptoms” or “recovery before worsening”. This strengthens the need for on-going and close monitoring of PMR patients over the long term and, as advised by guidance, referral for specialist review in circumstances where either symptoms persist (reflecting the “sustained moderate symptoms” group) or if people are still taking glucocorticoids by 2 years.[4] However, referral may also be considered if patients fall into the classes described above, which are associated with prolonged glucocorticoid treatment.

Whilst there are some limitations to this study, including the self-reported nature of the data and lack of information on inflammatory markers, there is evidence that many chronic conditions are well-reported by research participants.[28,29] The notable exception to this is participants ability to self-report subtypes of arthritis, which might explain the high prevalence of reported rheumatoid arthritis.[30] Also, we did not have records on the concomitant presence of giant cell arteritis, which often co-occurs with PMR and requires a higher starting dose of glucocorticoids, but has previously been shown to have a shorter treatment duration.[31] Nor were we able to investigate the effect of the participants’ general practice on continued glucocorticoid use, due to the small numbers of participants recruited from each practice. However, we are not aware of any other cohorts as detailed, representative or large as the current study in which to take forward a prognosis model for

treatment cessation in PMR. If it were possible to set up a new study in which to attempt to fit such a model, it would expensive and time-consuming. It is therefore unlikely that the PMR research community will be able to predict who requires early specialist referral for glucocorticoid sparing treatment in the foreseeable future. With this in mind, and with clear evidence that glucocorticoid medication and its withdrawal are major concerns for patients,[6,7] clinicians should give careful consideration to how treatment and its potential side-effects are managed in PMR. This may be possible through structured regular reviews, perhaps with other members of the multidisciplinary team such as nurses or pharmacists, to identify when moderate symptoms persist or glucocorticoid reduction is not proceeding as expected.[32] Research should also work towards safe and cost-effective alternative and adjunct treatments.

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DATA AVAILABILITY: Keele University is a member of the UK Reproducibility Network and committed to the principles of the UK Concordat on Open Research Data. The School of Medicine and Keele Clinical Trials Unit have a longstanding commitment to sharing data from our studies to improve research reproducibility and to maximise benefits for patients, the wider public, and the health and care system. We encourage collaboration with those who collected the data, to recognise and credit their contributions.

The School of Medicine and Keele Clinical Trials Unit make data available to bona-fide researchers upon reasonable request via open or restricted access through a strict controlled access procedure. The release of data may be subject to a data use agreement (DUA) between the Sponsor and the third party requesting the data. In the first instance, data requests and enquiries should be directed to medicine.datasharing@keele.ac.uk.

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Figure 1. Participant flow chart - long-term follow-up study.

Table 1: Association of glucocorticoid treatment experience and baseline characteristics of continued glucocorticoid treatment at LFTU.

	PMR still treated, n/N (%)	PMR treatment stopped, n/N (%)	Missing, n/N (%)
	(67/167 (40.1%))	(100/167 (59.9%))	(27/197 (13.7%))
Glucocorticoid treatment experience			
Total time on glucocorticoid treatment, Mean (SD) months ¹	N/A	20.1 (13.8)	22/100 (24.0)
Current glucocorticoid dose, Median (Q1, Q3) mg	5 (1.5, 9)	N/A	7/67 (10.5)
Highest ever glucocorticoid dose, Mean (SD) mg	20 (10, 20)	20 (15, 30)	65/179 (36.3)
Ever changed dose of own accord, n (%)	25/64 (39.1)	11/100 (11.0)	6/179 (3.4)
Baseline characteristic			
<i>Sociodemographics and lifestyle</i>			
Age, mean (SD)	72.5 (6.8)	70.2 (8.5)	0
Gender, n (%)			
Female	44/67 (65.7)	62/100 (62.0)	0
Male	23/67 (34.3)	38/100 (38.0)	
IMD rank tertile, n (%)			5/179 (2.8)
Most deprived	16/66 (24.2)	23/97 (23.7)	
Middle	28/66 (42.4)	37/97 (38.1)	

Least deprived	22/66 (33.3)	37/97 (38.1)	
Occupational class, n (%)			50/179 (27.9)
Higher managerial, admin & professional	21/53 (39.6)	18/70 (25.7)	
Intermediate	13/53 (24.5)	27/70 (38.6)	
Routine & manual	19/53 (36.9)	25/70 (35.7)	
Living alone, n (%)			1/179 (0.6)
Yes	2/66 (31.8)	15/100 (15.0)	
No	45/66 (68.2)	85/100 (85.0)	
BMI category, n (%)			5/179 (2.8)
≤24.9 kg/m ²	21/63 (33.3)	36/99 (36.4)	
25 to 29.9 kg/m ²	24/63 (38.1)	40/99 (47.5)	
≥30 kg/m ²	18/99 (28.6)	16/99 (16.2)	
Never smoked, n (%)	40/66 (60.6)	59/99 (59.6)	3/179 (1.7)
Alcohol drinking frequency, n (%)			1 /179 (0.6)
Daily/almost daily	7/66 (10.6)	21/100 (21.0)	
3 or 4 times a week	10/66 (15.2)	11/100 (11.0)	
Once or twice a week - 1 to 3 times a month	22/66 (33.3)	30/100 (30.0)	
Special occasions only / Never	27/66 (40.9)	38/100 (38.0)	
PMR symptoms			
Pain severity (0-10 NRS) (higher score=more intense pain) (Median (Q1, Q3))	8 (7, 10)	8 (7, 9)	1/179 (0.6)

Stiffness severity (0-10 NRS) (higher score=worse stiffness) (Median (Q1, Q3))	8 (7, 9)	8 (6, 9)	0
Time of day stiffness is experienced, n (%)			0
None	*(6.0)	0	
Morning	65/67 (97.0)	98/100 (98.0)	
Lunchtime	44/67 (65.7)	54/100 (54.0)	
Afternoon	43/67 (64.2)	50/100 (50.0)	
Early evening	47/67 (70.2)	60/100 (60.0)	
Late evening	54/67 (80.6)	71/100 (71.0)	
During the night	51/67 (76.1)	77/100 (77.0)	
Duration of early morning stiffness, n (%)			1 (0.6)
Less than one hour	14/67 (20.9)	34/99 (34.3)	
Greater than one hour	53/67 (79.1)	65/99 (65.7)	
Able to raise arms above head when first diagnosed, n (%)			1 (0.6)
Yes	22/67 (32.8)	25/99 (25.3)	
No	43/67 (64.2)	67/99 (67.7)	
Don't know	*(3.0)	7/99 (7.1)	
Duration of symptoms prior to initial consultation			1 (0.6)
<1 week	*(6.0)	5 (5.0)	
1-2 weeks	14 (20.9)	14 (14.4)	
2-4 weeks	15 (22.4)	24 (24.2)	
≥4 weeks	34 (57.8)	56 (56.6)	

<i>Treatment and care</i>				
Visits to doctor before PMR diagnosis, n (%)				4/179 (2.2)
1	25/65 (38.5)	33/99 (33.3)		
2	22/65 (33.9)	31/99 (31.3)		
3	9/65 (13.4)	17/99 (17.2)		
≥4	9/65 (13.4)	18/99 (18.2)		
Medicines taken for PMR (other than glucocorticoids), n (%)				
Paracetamol	30/67 (44.8)	37/100 (37.0)	0	
Paracetamol and codeine	18/67 (26.9)	24/100 (24.0)	0	
Non-steroidal anti-inflammatories	9/67 (13.4)	12/100 (12.0)	0	
Strong prescription painkillers	6/67 (9.0)	9/100 (9.0)	0	
Proton pump inhibitors	40/67 (59.7)	46/100 (46.0)	0	
Calcium and Vitamin D	31/67 (46.3)	46/100 (46.0)	0	
Bone protection	18/67 (26.9)	28/100 (28.0)	0	
Anti-depressants	*(4.5)	7/100 (7.0)	0	
General health				
EQ5D score (higher score=better quality of life), Mean (SD)		0.76 (0.62, 0.93)	0.80 (0.69, 1.00)	13/179 (7.3)
Fallen in the last 12 months, n (%)		16/64 (25.0)	21/99 (21.2)	4/179 (2.2)
Experience of other symptoms, n (%)				
GCA ²	33/67 (49.3)	38/100 (38.0)	0	
Swollen joints	19/67 (28.4)	32/100 (32.0)	0	
Systemic ³	25/67 (37.3)	31/100 (31.0)	0	

mHAQ score (higher score=poorer function), Mean (SD)	0.43 (0.06, 1.19)	0.38 (0.00, 0.75)	7/179 (3.9)
FACIT-Fatigue score (higher score=less fatigue), Mean (SD)	36.5 (26.0 ,44.1)	40.0 (27.1, 44.1)	5/179 (2.8)
ISI category, n (%)			6/179 (3.4)
No clinically significant/subthreshold insomnia	52/66 (78.8)	79/98 (80.6)	
Moderate/severe insomnia	14 /66(21.2)	19/98 (19.4)	
PHQ8 category, n(%)			10/179 (5.6)
None/mild depression	49/64 (76.6)	76/94 (80.9)	
Moderate/severe depression	15/64 (23.4)	18/4 (19.2)	
GAD7 category, n(%)			11/179 (6.2)
None/mild anxiety	56/62 (90.3)	87/95 (91.6)	
Moderate/severe anxiety	6/62 (9.7)	8/95 (8.4)	

N/A – not applicable

¹Excluding those who reported ≥80months treatment duration in line with study mailing timeline; ²sudden headache, tender scalp, vision problems, jaw pain; ³ fever, loss of appetite, weight loss

Q1 – quartile 1; Q3 – quartile 3; SD – standard deviation

*value suppressed due to cell count<5

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Table 2: Changes in PMR symptoms and general health between baseline and 1 and 4 months with and without continued glucocorticoid treatment at LFTU.

	PMR still treated, n/N (%)	PMR treatment stopped, n/N (%)	Missing, n/N (%)
	(67/167 (40.1%))	(100/167 (59.9%))	(27/197 (13.7))
Pain and stiffness class membership over 2 years, n/N (%)			0
1 – Sustained symptoms	*(1.5)	*(1.0)	
2 – Partial recovery, sustained moderate symptoms	23/67 (34.3)	19/100 (19.0)	
3 – Recovery before worsening	17/67 (25.4)	11/100 (11.0)	
4 – Rapid and sustained recovery	15/67 (22.4)	46/100 (46.0)	
5 – Slow and continuous recovery	11/67 (16.4)	23/100 (23.0)	
1 month			
<i>PMR symptoms</i>			
Pain severity (0-10 NRS) (higher score=more intense pain), Adjusted mean (95% CI)	1.59 (1.55, 1.63)	1.60 (1.57, 1.63)	4 /179 (2.2)
Stiffness severity (0-10 NRS) (higher score=worse stiffness), Adjusted mean (95% CI)	1.66 (1.63. 1.70)	1.65 (1.63. 1.67)	4 /179 (2.2)
Time of day stiffness is experienced, Adjusted percentage (95% CI) ^a			
None	23.2 (22.6, 23.8)	31.6	3/179 (1.7)
Morning	64.1	62.5	3/179 (1.7)

Lunchtime	13.9 (12.7, 15.0)	14.9 (13.6, 16.2)	3/179 (1.7)
Afternoon	20.9	13.9 (13.1, 14.6)	3/179 (1.7)
Early evening	27.7	18.7 (18.0, 19.3)	3/179 (1.7)
Late evening	34.0 (33.0, 34.9)	22.9 (21.9, 24.0)	3/179 (1.7)
During the night	16.9 (16.0, 17.7)	20.3 (19.0, 21.6)	3/179 (1.7)
<i>General health</i>			
mHAQ score (higher score=poorer function), adjusted mean (95% CI)	0.28 (0.26, 0.30)	0.29 (0.28, 0.31)	4 /179 (2.2)
FACIT-Fatigue score (higher score=less fatigue), adjusted mean (95% CI)	41.53 (41.07, 42.00)	41.28 (40.90, 41.66)	4 /179 (2.2)
ISI moderate/severe insomnia, adjusted probability (95% CI)	36.7 (34.7, 38.8)	39.0 (35.7, 42.3)	6/179 (3.4)
PHQ8 moderate/severe depression, adjusted probability (95% CI)	12.1 (9.80 14.4)	11.0 (8.9, 13.0)	14/179 (7.8)
GAD7 moderate/severe anxiety, adjusted probability (95% CI)	9.4 (6.6, 12.1)	12.7 (10.6, 14.8)	11/179 (6.1)
4 months			
<i>PMR symptoms</i>			
Pain severity (0-10 NRS) (higher score=more intense pain), adjusted mean (95% CI)	2.00 (1.97, 2.03)	2.01 (1.99, 2.04)	5/179 (2.8)
Stiffness severity (0-10 NRS) (higher score=worse stiffness), adjusted mean (95% CI)	2.26 (2.07, 2.45)	2.35 (2.22, 2.48)	6/179 (3.4)
Time of day stiffness is experienced, n (%)			

None	0.26	0.23	4/179 (2.2)
Morning	72.4 (71.8, 72.9)	0.67	6/179 (3.4)
Lunchtime	11.1 (10.8, 11.4)	21.4 (20.5, 22.4)	6 /179 (3.4)
Afternoon	16.4 (16.0, 16.8)	25.3 (23.6, 27.0)	6/179 (3.4)
Early evening	25.6 (25.1, 26.2)	23.6 (22.4, 24.9)	6/179 (3.4)
Late evening	34.5 (33.5, 35.5)	34.8 (32.7, 36.9)	6/179 (3.4)
During the night	17.2 (16.3, 18.0)	28.0 (27.3, 28.7)	6/179 (3.4)
<i>General health</i>			
mHAQ score (higher score=poorer function), adjusted mean (95% CI)	0.39 (0.36, 0.43)	0.37 (0.34, 0.39)	4/179 (2.2)

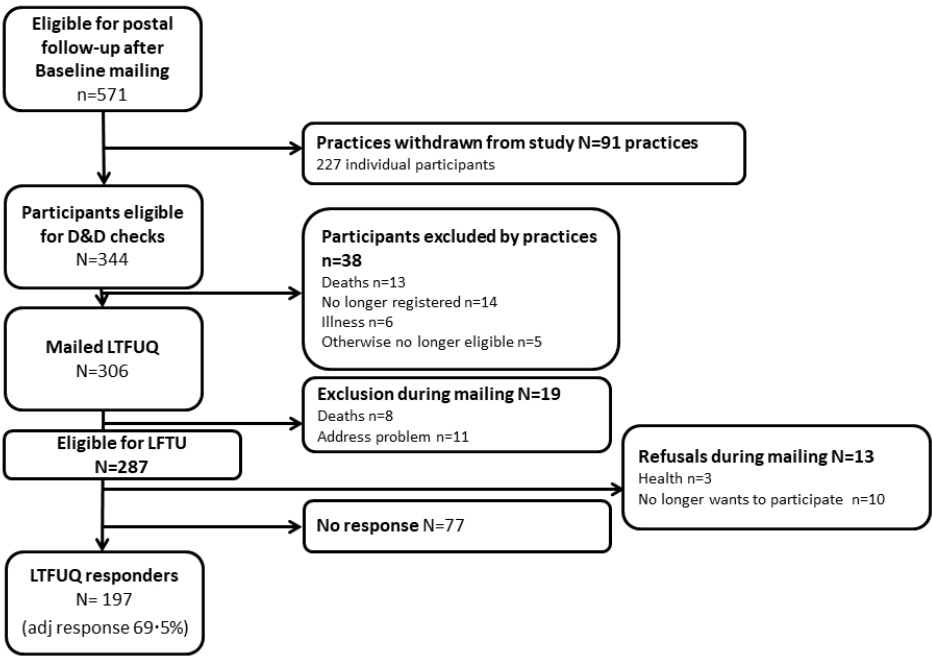
*value suppressed due to cell count<5; ^a where no CI is given, the given value is the raw percentage because the model was not adjusted for the baseline value due to perfect prediction.

Table 3: Self-reported medications at baseline.

Medication	Current at LTFU years, n (%)		Before PMR diagnosis, n (%)	
	PMR still treated (67 (40.1))	PMR treatment stopped (100 (59.9))	PMR still treated (67 (40.1))	PMR treatment stopped (100 (59.9))
Paracetamol	25/67 (37.3)	45/100 (45.0)	19/67 (28.4)	36/100 (36.0)
Paracetamol and codeine	11/67 (16.4)	17/100 (17.0)	6/67 (9.0)	11/100 (11.0)
Non-steroidal anti-inflammatories	*(6.0)	12/100 (12.0)	7/67 (10.5)	17/100 (17.0)
Strong prescription painkillers	6/67 (9.0)	12/100 (12.0)	*(6.0)	8/100 (8.0)
Proton pump inhibitors	44/67 (65.7)	41/100 (41.0)	12/67 (17.9)	17/100 (17.0)
Calcium and Vitamin D	45/67 (67.2)	27/100 (27.0)	*(6.0)	11/100 (11.0)
Bone protection	21/67 (31.3)	8/100 (8.0)	*(1.5)	7/100 (7.0)
Azathioprine	0	0	0	0
Methotrexate	*(3.0)	*(2.0)	*(1.5)	0
Anti-anxiety/depressants	5/67 (7.5)	10/100 (10.0)	*(4.5)	10/100 (10.0)

Participants could report using a medication in both time periods. Participants were not asked to specify that this was for their PMR

*value suppressed due to cell count<5.



Participant flow chart - Long-term Follow-up Study

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