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A Targeted Literature Review of the Clinical and Humanistic Burden of Polymyalgia Rheumatica and the Associated Unmet Medical Needs

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KEY FINDINGS & CONCLUSIONS

- PMR is associated with an increased risk of comorbidities (cardiovascular, cerebrovascular, and malignancies) and can affect mobility and daily activities, increase fatigue and impact psychological well-being.
- Key unmet needs include diagnostic uncertainty and delays, HCP awareness, and the need for alternative treatments.
- PMR, the second most prevalent rheumatic disease after RA in certain populations, can be expected to lead to increased disease burden as populations continue to age.[35] This highlights the need for effective GC-sparing alternatives providing sustained remission and reducing adverse effects of long-term GC use.

INTRODUCTION

- Polymyalgia Rheumatica (PMR) is an inflammatory disorder, characterized by pain and stiffness in the neck, shoulders and hips, affecting people ≥50 years.[1,2] PMR can cause a significant burden, impacting patients' daily lives and overall health.[2]
- Despite almost half of patients relapsing within a year and an unfavorable safety profile, glucocorticoids (GC) remain the standard of care.[1] There is a need for effective alternatives to minimize side effects and maintain remission.[3]
- Reported prevalence and incidence of PMR is quite variable. In the UK, the estimated percentage prevalence among people aged ≥55 years is 2.27% (95% CI: 1.86-2.67)[4] and incidence is reported at 62.5 cases per 100,000 person years.[5]
- **OBJECTIVE:** To identify and summarize existing literature on the clinical and humanistic burden of PMR and/or GCA* and the associated unmet medical needs.

* Refer to poster SA108 for further details on studies relating to GCA

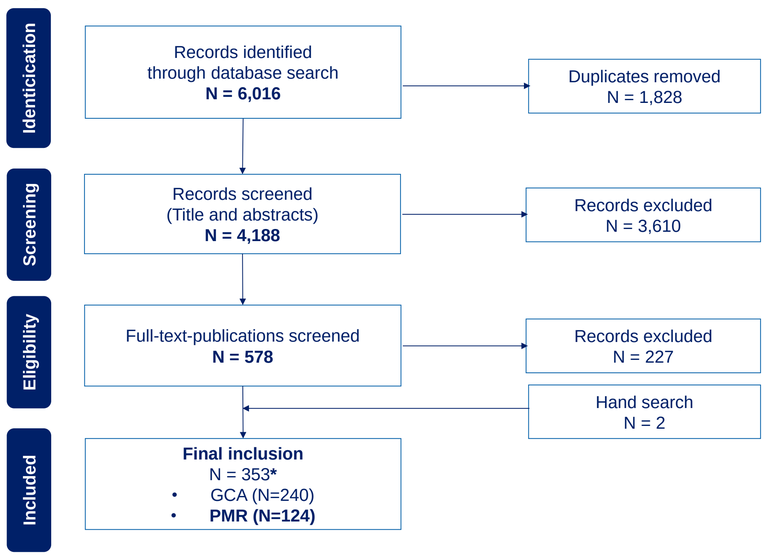
METHODS

- A targeted literature review was conducted in March 2024. Search strategies were applied in MEDLINE, EMBASE, CENTRAL and CDSR. Hand searches were performed on key congress websites and bibliographic sources.
- Pre-defined PICOS criteria were employed to screen identified records (**Table 1**) during the title/abstract (first pass) and full text (second pass) screening.
- English language studies were included, with the exception of editorials, case reports, case series, comments, notes, narrative reviews and animal studies.
- A first reviewer completed initial screening and data extractions. Quality checks of extracted data were undertaken by an independent reviewer, who also discussed any uncertainties.
- The selection of studies, data extraction and results summarization followed established and current best practices.

RESULTS

- A total of 6,016 records were identified, of which 353 were included and 124 specifically related to PMR (**Figure 1**).

Figure 1. PRISMA Flow*



Reasons of exclusion:
- Outcome not of interest/not reported
- Patient population not of interest
- Disease not of interest
- Study design not of interest
- Publication type
- Animal/In vitro studies
- Duplicate

*Note: The final included publications (n=353) encompass publications for both GCA and PMR indications, with 11 publications overlapping for both indications
Abbreviations: GCA, Giant Cell Arteritis; PMR, Polymyalgia Rheumatica; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SLRs, Systematic Literature Reviews. *Page et al. BMJ 2021;372:n71 – Applied to a targeted literature review process

Table 1. PICOS Criteria*

Category	Inclusion Criteria		
Population	• Adult patients aged ≥50 years with Polymyalgia Rheumatica (PMR)		
Interventions/ Comparator	• Not applicable		
Outcomes	**Clinical Burden** – Clinical presentation – Complications – Disease severity – Comorbidities – Morbidity – Mortality – Therapy burden	**Humanistic Burden** – Symptomatic burden – Quality of life – Impact on daily activities – Physical, mental and emotional health/disabilities – Other Patient reported outcomes	**Unmet Needs** – Identified from Patient's, Payer's and Physician's perspective
Study type	• All studies except case reports, case series, comments, editorials and notes		

*Methley et al. BMC Health Services Research (2014) 14:579

Therapy related burden

- There is still a high rate of relapse and risk associated with long-term GC use. It was reported that 43% of patients may experience ≥1 GC-related adverse event after 31 months' mean treatment duration.[22]
- GC related events include osteoporosis, fractures, arterial hypertension and diabetes mellitus.[22]

Clinical Burden

- PMR patients experience physical symptoms (pain and stiffness in shoulders, pelvic girdles, neck and lower back muscles) and systemic symptoms (fatigue, fever, weight loss). Some patients with PMR may also exhibit symptoms of GCA, such severe headache, tenderness of the scalp, jaw claudication and visual disturbances (**Figure 2**).

Figure 2. Symptoms in PMR Patients

Physical Symptoms (% of pts)
- Bilateral shoulder stiffness or pain (~91%)[6,7]
- Pelvic girdle pain (82%)[6]
- Hip pain or range of motion restricted (90%)[8]
- Neck and lower back pain[9]

Constitutional Symptoms[1,2]
- **40%-50% of patients** experience these symptoms, mostly concomitantly with pain and stiffness, including; **Fever, Fatigue, Weight loss**[1]
- Symptoms reported to be driven by IL-6 signalling[2]

Distal Features[9,10]
- Tenosynovitis, hand arthritis, carpal tunnel syndrome[10]
- Can cause swelling and pitting oedema in hands and feet[9]

Giant Cell Arteritis (GCA)[6,10]
- **GCA can develop in 9%-20% of PMR patients**[6]
- **~50%** of GCA patients have **PMR symptoms**[6,10]
- **GCA Symptoms:** Headache, scalp tenderness, jaw claudication and visual disturbances[2,10]

Abbreviations: IL-6: Interleukin-6; PMR: Polymyalgia Rheumatica; Pts: Patients

- There are challenges with PMR diagnosis due to symptom overlap with other conditions (GCA, infection, myositis, rheumatoid arthritis, osteoarthritis), non-specific laboratory findings and a lack of definitive diagnostic testing.[2,10,11]
- PMR patients have an increased risk of cardiovascular and cerebrovascular comorbidities. There is also an association between PMR and increased early-stage malignancies (**Figure 3**).[12]
- While there is limited evidence to suggest that PMR significantly impacts mortality, CVDs appear to be the leading cause of death in PMR patients.[13,14]

Figure 3. Comorbidities in PMR

Cerebrovascular Events
- PMR patients had 1.87 times higher risk of cerebrovascular accidents vs. non-PMR patients[15]
- 14.47% of PMR patients had a stroke within three years of diagnosis vs. 6.98% non-PMR patients[16]

Cardiovascular Disease
- Common comorbidities (%) include hypertension (81%), congestive heart failure (52%), hyperlipidemia (41%), ischemic heart disease (36%)[17]
- Increased risk of atherosclerosis and subsequent cardiovascular diseases such as coronary artery disease and peripheral artery disease due to a large inflammatory burden[18-20]

Malignancies
- Increased cancer diagnoses post PMR diagnosis, particularly during the first 6 months after diagnosis (Adjusted HR: 1.69)[21]
  - 23.2% of cohort with PMR developed cancer vs. 19.5% non-PMR patients
- Risk factors: Older age, male sex, higher levels of joint involvement[18]
- PMR patients reported to have an increased risk of lymphoma and subtypes of hematological malignancy[18]

Abbreviations: HR: Hazard Ratio; PMR: Polymyalgia Rheumatica

Humanistic Burden

- Limited evidence on health-related quality of life (HRQoL) of PMR patients exists, however poor physical and mental QoL has been reported, compared to general population (**Table 2**).
- Patients express frustration with long diagnostic delays and PMR anonymity among healthcare professionals.[23] Managing stiffness, pain, and steroid use were key priorities for living with PMR.[24]
- Morning stiffness, which is typically quite severe, can significantly impact patients' physical activities, such as getting dressed or other daily activities of the morning.[2]
- PMR patients experience higher levels of fatigue compared to the general population, which can be linked to the severity of pain and stiffness experienced, and quality of sleep can also be affected.[25,26]
- PMR can have a significant impact on patients' psychological well-being, leading to depression, and anxiety.[26,27]

Table 2. Humanistic Burden in PMR patients

Humanistic Burden	Burden data
High symptomatic burden[25]	Global pain, High (NRS 8-10): 66.1% High level of stiffness (NRS 8-10): 60.3% High level of fatigue: Mean (SD) FACIT-F score of 33.9 (12.4)
Sleep Disturbances	ISI score ≥15 (clinically significant insomnia): 23.6%[25] PSQI, Mean (SD) PMR vs Control: 8.8 (4.5) vs 5.3 (2.9); p<0.001[26]
Functional Impairment[27]	~12% of patients report a MHAQ score of ≥1.3 indicating moderate to severe functional impairment
Moderate to severe depression[27]	PHQ-8 depression score 10-24 (moderate to severe): 22%
Moderate to severe anxiety[27]	GAD-7 anxiety score 10-21 (moderate to severe): 13%
Impact on intimate sexual relationships[28]	41% patients
Poor HRQoL	
SF-36 Score Mean (95% CI) vs. general population[29]	PCS: 31.5 (30, 32.9) vs. 44.7; MCS: 38.9 (36.8, 40.9) vs. 53.2
EQ-5D utility, Median(IQR)[30]	0.73 (0.59-0.85)

Abbreviations: EQ-5D: EuroQoL-5 Dimensions; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; GAD-7: Generalised Anxiety Disorder; IQR: Inter-Quartile Range; ISI: Insomnia Severity Index; MHAQ: Modified Health Assessment Questionnaire; MCS: Mental Component Summary; NRS: Numeric Rating Scale; PCS: Physical Component Summary; PHQ-8: Patient Health Questionnaire; PMR: Polymyalgia Rheumatica; PSQI: Pittsburgh Sleep Quality Index; SF-36: 36-Item Short Form Health Survey questionnaire

Unmet Need

Lack of healthcare awareness & faster time to diagnosis:
- Diagnostic uncertainty, a lack of HCP awareness, and the need for alternative treatments represent major unmet needs for PMR patients. PMR diagnosis relies on clinical presentation, laboratory test findings and exclusion of diseases with common symptoms.[11]
- The lack of specific diagnostic testing and criteria, coupled with lack of disease awareness among healthcare providers leads to misdiagnosis and subsequent diagnostic delay (~3 months from symptom onset).[11,31]

Need for Alternative Treatments:
- There is a need for more efficacious GC-sparing therapies, resulting in less treatment associated adverse events and longer relapse-free periods.[1,23,32] Approximately 50% of patients do not reach complete remission after 4 weeks with GCs,[32] and relapses are experienced in up to half of patients within the first year.[1]
- Methotrexate is recommended in some cases to limit GC-related AEs, however the effect on relapse rates is conflicting.[33,34]

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