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Giant cell arteritis: Challenges of diagnosis and management in general practice.

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|---------------------------------|--|
| Journal: | <i>BMJ Open</i> |
| Manuscript ID | bmjopen-2017-019320 |
| Article Type: | Research |
| Date Submitted by the Author: | 25-Aug-2017 |
| Complete List of Authors: | Helliwell, Toby; Keele University, Research Institute for Primary Care and Health Sciences Muller, Sara; Keele University, Research Institute for Primary Care & Health Sciences Hider, Samantha; Keele University, Arthritis Research UK Primary Care Centre; Prior, James A.; Keele Univ, Research Institute for Primary Care and Health Sciences Richardson, Jane; Keele University, Primary Care and Health Sciences Mallen, Christian; Keele University, Arthritis Research UK Primary Care Centre |
| Primary Subject Heading: | General practice / Family practice |
| Secondary Subject Heading: | Rheumatology, Medical management |
| Keywords: | PRIMARY CARE, RHEUMATOLOGY, GERIATRIC MEDICINE |
| | |

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5 **Giant cell arteritis: Challenges of diagnosis and management in general practice.**
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28 **Funding:** This work was funded by an Arthritis Research UK Clinician Scientist Award awarded to
29 Christian Mallen (19634). CDM is funded by the National Institute for Health Research (NIHR),
30 Collaborations for Leadership in Applied Health Research and Care West Midlands, the NIHR School
31 for Primary Care Research and a NIHR Research Professorship in General Practice (NIHR-RP-2014-04-
32 026). TH is funded by a NIHR Clinical Lectureship in General Practice. SM is funded by the NIHR
33 School for Primary Care Research. JAP is funded by a Launching Fellowship from the NIHR School for
34 Primary Care Research. The views expressed are those of the author(s) and not necessarily those of
35 the NHS, the NIHR or the Department of Health.
36

37
38 **Data sharing statement:** The datasets analysed during the current study may be available from the
39 corresponding author on reasonable request.
40

41 **Keywords:** Giant cell arteritis, general practice, diagnosis, management
42

43 **Conflicts of interest:** There are no conflicts of interest to declare.
44

45 **Prior presentation:** Presented as a poster at BSR Conference 2015
46

47 Word count: 3823
48

49 Number of tables: 4
50
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52
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7 Background: In the UK, general practitioners (GPs) are usually the first medical contact for
8 patients with suspected giant cell arteritis (GCA). Whilst rare, it is critical not to miss, as
9 delayed treatment can lead to significant complications including permanent visual loss. To
10 date little is known about the approach and challenges to diagnosis and management of GCA
11 by GPs.
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20 Objective: To investigate the diagnosis and management of patients with suspected GCA in
21 UK general practice.
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25 Design and participants: A multi-methods approach was taken, comprising a postal survey of
26 5000 randomly selected UK GPs and semi-structured telephone interviews of 24 GPs from
27 across the UK.
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31
32

33 Setting: UK general practice
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35

36 Results: 1249 questionnaires were returned. 879 responders (70%) indicated that they had
37 diagnosed and managed a patient with GCA. A variety of clinical features were used to
38 identify GCA. 21.9% suggested that they would exclude GCA as a diagnosis if headache was
39 absent and less than half of GPs routinely initiate glucocorticoid treatment prior to referral.
40 Significant regional variations in referral pathways were reported. Thematic analysis of
41 interview transcripts highlighted fears relating to a missed diagnosis of GCA and the non-
42 specific nature of early GCA presentation. Accessing specialist care was highlighted as
43 challenging by many GPs and that a national standard fast track pathway is lacking to
44 support this patient group. Additionally there were significant concerns regarding potential
45 adverse effects relating to long term treatment with glucocorticoids.
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3 Conclusion: GPs over-rely on headache to identify GCA and marked geographical differences
4
5 in management, with conflicting referral pathways and difficulties in accessing appropriate
6
7 services exist in the UK. A national standard for fast-tracking suspected GCA patients to
8
9 relevant specialists would be beneficial to improve care and outcomes for patients with GCA.
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20 **Strengths**

- 21 1. Multi-methods approach, allowing the identification of significant challenges relating to GCA
22 management in primary care and subsequent in depth exploration of those issues.
- 23 2. First large study to investigate diagnosis and management of GCA in general practice
24
25
26
27

28 **Limitations**

- 29 1. Sub-optimal response rate and therefore potential lack of generalisability to findings
30 although responder demographics of the questionnaire study relating to age, gender and GP
31 role were comparable to national GP demographics.
- 32 2. Telephone interviews often viewed as inferior to face to face interviews for qualitative
33 studies
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- 35 3. There is the potential for discrepancies between reported behaviour and actual behaviour,
36 this is inherent in both survey and interview studies
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Background

Giant cell arteritis (GCA) is the most common large/medium vessel vasculitis¹. It is strongly associated with polymyalgia rheumatica (PMR) with an estimated incidence of 1.0 per 10000 patient years². Barraclough (2012) estimated that a full-time general practitioner (GP) will see one new case of GCA every 1-2 years, although this will greatly depend on practice population demographics³.

Classical presenting features of GCA include new onset headache or head pain (which may be unilateral and often temporal), scalp tenderness, jaw and tongue claudication, constitutional and visual symptoms¹. Usually there is a significant inflammatory response with raised inflammatory markers. However, it can present atypically which may lead to delays in diagnosis and potentially irreversible complications such as sight loss⁴. Once GCA is suspected, treatment with high dose glucocorticoids (often prednisolone in the UK) should be initiated along with early specialist referral to confirm diagnosis and prevent potential disease complications¹.

Suspected GCA patients are usually identified clinically, followed by specialist referral for temporal artery biopsy (TAB) to confirm diagnosis. Ultrasound scanning however has been shown to be a useful and non-invasive tool to help diagnose GCA⁵. However, the sensitivity of TAB can vary with 13% to 19% of patients with typical features of GCA having a negative temporal artery biopsy⁶.

In the UK, GPs are the first point of medical contact for most patients. The role of the GP involves maintaining a high index of suspicion for the disorder, to initiate early therapy and

1
2
3 urgently refer to an appropriate specialist for diagnostic confirmation ¹. Following diagnosis,
4
5 GPs are often key in tapering glucocorticoid treatment as well as monitoring and
6
7 management of glucocorticoid related adverse effects and impact on co-morbidity for
8
9 example osteoporosis, cardiovascular disease, diabetes and development of serious
10
11 infections ^{2,7}.

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16 The aim of this study was to investigate the diagnostic challenges and initial and on-going
17
18 management of GCA patients by GPs in the UK.
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24 **Materials and Methods**

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27 Given the potential variation in management practices due to multiple influences, such as
28
29 patient presentation, multi-morbidity, availability of services and variations in practice and
30
31 local policy, a multi-methods approach was chosen to produce a more complete description
32
33 of current GP practice ⁸. First, a national cross-sectional postal survey of 5000 randomly
34
35 selected UK GPs was undertaken, followed by a semi-structured telephone interview study
36
37 with a purposive sample of survey responders to investigate in depth the challenges of
38
39 diagnosis and management associated with GCA. The cross-sectional postal survey was
40
41 undertaken first, with the findings used to help develop the topic guide for the interview
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43 study.
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53 PMR national cross sectional postal questionnaire survey. A cross sectional survey was
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55 mailed to a random sample of 5000 GPs from across the UK identified from the Binley's
56
57 database. The Binley's database contains the names and addresses of the majority of GPs
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3 working in the UK. It also contains other forms of information including the type of practice,
4
5 the practice population size, practitioner seniority, and some of the clinical services
6
7 provided⁹. An online option for survey completion was also available through Survey
8
9 Monkey¹⁰. Non-responders were sent a reminder card after 2 weeks and a further survey
10
11 pack after 4 weeks. The survey was closed 6 weeks after the second survey pack was sent.
12
13

14
15 No standard survey instrument exists for assessing diagnosis and management of GCA by
16
17 GPs and so questions were specifically developed using current literature and guidelines for
18
19 GCA¹. Questions related to how diagnosis was made (signs and symptoms) and how the GP
20
21 managed patients with suspected GCA. A mixture of open and closed response questions
22
23 were used. The questionnaire was piloted amongst GPs, rheumatologists and patients.
24
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26

27
28 Descriptive statistics were generated (mean, standard deviation (SD) and interquartile range
29
30 (IQR)) using the statistical analysis package SPSS 22 for closed response questions¹¹. For
31
32 open response questions a thematic content analysis was used¹².
33
34
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39 The interview study. Participants in the interview study were purposively sampled from
40
41 responders to the GP survey who had agreed to further contact. To reflect as broad a range
42
43 of practitioner experience as possible, sampling was based on clinical experience, gender
44
45 and clinical seniority. The qualitative interview study topic guide which was used as a guide
46
47 for topics to discuss, was informed by findings from the cross-sectional survey and relevant
48
49 GCA literature. The topic guide was reviewed and refined with feedback from GPs,
50
51 rheumatologists and qualitative researchers. As transcripts were reviewed, the topic guide
52
53 was modified to focus on themes identified from early interviews. The topic guide was
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1
2
3 piloted with two GPs and refined within the research team. These interviews were not
4
5 included in the data analysis.
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7

8
9 Interviews were audio recorded and transcribed verbatim using an approved transcription
10
11 company¹³. The resulting transcripts were screened to remove any identifying information.
12
13 Thematic analysis, as described by Braun and Clarke, was used to analyse resulting transcript
14
15 data¹⁴. Analysis of the transcripts was managed using NVivo (NVivo10)¹⁵. TH performed the
16
17 analysis and an inter-rater exercise was undertaken in which three other researchers (SM,
18
19 SH, JR) were asked to independently analyse and identify general themes relating to a
20
21 randomly selected interview to compare with findings by TH. No changes resulted from this
22
23 exercise. Ethical approval for both studies was granted by the Keele University ethics review
24
25 panel (qualitative study ERP178, survey ERP2206).
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33 **Results**

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36 1249 (25%) completed questionnaires were received and analysed. 879 (70%) GPs had
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38 indicated that they had managed a patient with GCA. Responders to the survey had a mean
39
40 age of 44 years (SD 9.25) and a mean of 13.5 years since qualifying as a GP. 52% were female
41
42 and the majority were partners (74%), with salaried (21%) and locum GPs (3%) comprising
43
44 the remainder. For the qualitative study, 24 GP participants were telephone interviewed
45
46
47 from various regions across the UK. 16 participants were female and 15 participants were GP
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49 partners
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Questionnaire survey: Initial diagnosis and management

Free text open response questions in the questionnaire were used to ask all participants to describe how they made a diagnosis of GCA. The results summarised in Table 1.

Table 1

The predominant reported clinical feature used to diagnose GCA was headache, along with visual disturbance and scalp tenderness. Survey responders indicated that they often used a combination of features when making a new diagnosis. Of particular note however, was that 21.9% of responders indicated that they only use headache to identify GCA.

Management of GCA can be divided into i) initial treatment and referral and ii) long term glucocorticoid reduction and monitoring. For GPs, initial management is intimately associated with diagnosis as suspected GCA patients require urgent specialist referral for definitive diagnosis and treatment. Table 2 summarises the immediate subsequent actions of GPs who have identified patients with suspected GCA.

Table 2

Guidance advises that treatment should not be delayed and that appropriate urgent referral for specialist diagnostic confirmation should be made¹. 445 responders to the survey (35.6%) indicated that they would not routinely initiate treatment prior to referral. However, 78.7% (n=983) reported that if they were to initiate treatment, appropriate doses of between 40 and 60mg of prednisolone would be prescribed. GP responders indicated that they were referring suspected GCA patients to a variety of different specialities using an

1
2
3 assortment of referral pathways, depending on the geographical location in the UK. Table 3
4
5 summarises to which speciality survey responders refer suspected GCA patients.
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8 **Table 3**

9 Themes identified from the qualitative study

10 **Diagnosis**

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18 The two main themes identified from the interview study related firstly to the presenting
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features of GCA and secondly to fears of missing a diagnosis of GCA.

Presenting features of GCA

When asked about GCA symptoms in the interviews, participants often gave textbook descriptions of classical features of GCA.

“Headache in someone over 55 you think giant cell arteritis really, that’s my mantra, new different headache, classically unilateral but not always, focused around the temple, potentially some tenderness there, possibly protruding temporal artery, classically tender when they’re combing their hair, but also looking for things like jaw claudication or tongue symptoms, [.....] and obviously the dread of visual disturbance as well really which can be anything really”

GP6 (20, F, P)

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3 Key: GP identifier [time qualified as a GP (years), gender (male/female), seniority/role
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5 (S:salaried, L:locum, P:partner, SP: senior partner)]
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12 While textbook descriptions of classical GCA were given, there was recognition that some of
13
14 these features may be difficult to recognise or link to GCA.
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21 *“jaw claudication is interesting, because I know at the time, my colleague and myself,*
22
23 *kind of, looked a bit more up about GCA and he said, ‘I’ve never heard of jaw*
24
25 *claudication.’ ”*
26
27

28 **GP15 (25, F, P)**
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34 Fear of missing case of GCA

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38 GPs expressed considerable fear about missing a diagnosis of GCA given the potential for
39
40 irreversible visual loss.
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44 *“I find it, sort of, trickier, I think, to diagnose. I worry about it more. I worry about*
45
46 *missing it. And I feel far less confident about treating it. I think when I was first*
47
48 *qualified as a GP I think I thought somebody had got it every week. Anybody who’d*
49
50 *got a headache, you know”*
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54 **GP 24 (12, F, S)**
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3 Fears surrounding missing a diagnosis of GCA also related to the potential for a wide range
4
5 of symptoms and atypical presentations.
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8
9 *“Just with a vague headache, and hadn’t had any visual disturbance at that point in*
10
11 *time. And he didn’t really have a lot of temporal artery tenderness. [.....] We did some*
12
13 *bloods at that point, and the ESR and CRP were normal [.....]... I wrote in the notes at*
14
15 *the time, ‘Excludes GCA’.....which, having read a bit more about it since, after this*
16
17 *happened, doesn’t totally exclude it.”*
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21 **GP 15 (25, F, P)**
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24 25 26 27 28 **Management**

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30 Two main themes were identified from the interview transcripts. First, initial and on-going
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32 treatment and monitoring and second, referral for definitive diagnostic confirmation by a
33
34 specialist.
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42 Initial and on-going treatment

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45 Most participants indicated that they would initiate suspected GCA patients on appropriate
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47 doses of prednisolone.
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51 *“I think the rheumatologists would say start the 60[mg] and I will see them in clinic.”*
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55 **GP4 (6, M, P)**
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3 However, there was recognition that treatment could impact on the sensitivity of the
4
5 temporal artery biopsy, especially if it was going to be delayed.
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9 *“what then happens in secondary care, it's less than ideal, they seem to rotate who*
10
11 *might do a temporal artery biopsy between vascular, ophthalmology and general*
12
13 *surgery [.....] but the patient generally is having that temporal biopsy before ever*
14
15 *seeing a rheumatologist and the timeliness of that temporal artery biopsy is not*
16
17 *ideal.”*
18
19

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21 **GP6 (20, F, P)**
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27 Local policy also had a significant impact on how suspected GCA patients were initially
28
29 treated. This, as well as concerns surrounding the impact that treatment could have on
30
31 biopsy effectiveness, may account for some of the significant number of participants who
32
33 indicated that they would not initiate treatment prior to referral.
34
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36

37
38 *“Locally this gets referred to ophthalmology[.....] and our practice is actually within*
39
40 *the grounds of the hospital so we've got no issues really in terms of administering*
41
42 *steroids you know before they were seen, they would be seen within an hour by an*
43
44 *ophthalmologist.”*
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46

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48 **GP 7 (10, M, P)**
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54 The principal and over-arching concern relating to long-term management was the potential
55
56 adverse effects of glucocorticoid treatment.
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1
2
3 *“Well, it’s a good two years of treatment with steroids and all the complications and*
4 *side effects that they carry with them. So, yes, and high doses of it, which have been*
5 *poorly tolerated with the patients. [.....] One patient, she had diabetes, and she was*
6 *started on the steroids, and she was struggling with awful side effects from the*
7 *steroids. She developed, well, lots of depressive symptoms. Her blood sugars went all*
8 *over the place. She got a lot of pitting oedema of the legs, which was hampering her*
9 *mobility. She got unsteadiness due to the steroids.”*

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20 **GP21 (7, F, S)**

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26 Referral for definitive diagnostic confirmation by a specialist

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30 Specialist referral for definitive diagnostic confirmation was a significant issue for GPs, with
31 referral pathways being highly variable across the UK. The speciality to which suspected GCA
32 patients were referred can depend on presenting clinical features; however, some of this
33 variation reflects local policy and also the regional availability of services and specialities.

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39
40 *“If their history was suspicious and their inflammatory markers were raised, I would*
41 *then contact...well we’ve had this issue between rheumatology and ophthalmology*
42 *and who to contact, and the line seems to be that if they’ve got any visual symptoms*
43 *then they go to ophthalmology and if they haven’t then they go to rheumatology.”*

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50 **GP13 (5, F, S)**

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53 However, in some regions of the UK GPs reported that referral pathways were not clear and
54 that specialist referral can be challenging.
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1
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3 *“But, generally, you speak to the on-call medical team, and they will advise me to*
4 *speak to someone else. And then they advise me to speak to someone else. So you*
5 *end up making loads of phone calls to try and find out which route you go in.”*
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11 **GP21 (7, F, S)**
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13
14 Some participants reported that their local policy involved the GP requesting the temporal
15 artery biopsy prior to review by a specialist. This often created challenges in itself.
16
17

18
19 *“we would try and get a temporal artery biopsy fairly promptly. It has been a bit*
20 *difficult in the past, and you know, you’re supposed to get it done within a day or two.*
21 *We traipse round the ophthalmologists, who say, ‘No, speak to the vascular people.’*
22 *Who say, ‘No, speak to the general surgeons.’ Well, we tried, initially, referring to the*
23 *ophthalmologist, and they just aren’t keen at all [.....] at the moment we’ve had, a*
24 *general surgery team who have done a temporal artery biopsy for us, and the*
25 *vascular surgeons have.” GP15 (25, F, P)*
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40 Further quotations illustrating the two main themes can be seen in Table 4 below.
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43 **Table 4**
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Discussion

This is the first study of its kind to explore diagnosis and a critical aspect of the care pathway for patients with suspected GCA. GCA remains a diagnosis that GPs worry about missing.

Whilst GPs were comfortable with classical presentation patterns, an overreliance on headache to trigger consideration of a diagnosis of GCA was evident, with some GPs having limited awareness of the full range of symptoms associated with GCA.

The predominant findings from the cross sectional study, suggest initiation of treatment for suspected GCA patients is not always routine. However a significant finding from both the cross sectional survey and qualitative interview study demonstrated that referral pathways across the UK vary greatly. Additionally GPs have significant concerns relating to treatment with long term glucocorticoids in this patient group, especially in conjunction with co-existing multi-morbidity.

Recommendations

Early identification, referral and initiation of appropriate treatment for suspected GCA patients in general practice is critical to prevent complications such as irreversible visual loss¹.

GPs responding to the survey seem to be over-relying on headache when diagnosing GCA. Given that almost half of patients do not present with a classical temporal headache and that 24% of patients with proven GCA have no headache symptoms at all¹⁶, excluding GCA on the basis of no headache has the potential to miss a significant proportion of patients with GCA. However symptoms like headache, are common¹⁷ with over half of over 65 year

1
2
3 olds having had a headache in the previous 12 months,¹⁸ yet serious pathology is rare in
4
5 general practice. Therefore the collective clinical picture needs to be considered and has to
6
7 include the full range of features of GCA.
8
9

10
11 The group of patients with no headache are recognised to be at higher risk of permanent
12
13 visual loss as a result of delayed diagnosis^{4,19}. Therefore, if alternative presentations are not
14
15 recognised by GPs they will continue to remain a high risk group. Educating clinicians about
16
17 other presenting symptoms and atypical presentations is essential to optimise diagnosis and
18
19 reduce delays in instigating appropriate treatment and referral, which could reduce the
20
21 potential for visual loss and serious long term complications for this patient group.
22
23

24
25 A considerable proportion of GPs indicated that they would not initiate treatment prior to
26
27 referral for specialist review. From the questionnaire responses, current primary care
28
29 practice would seem to be in line with UK recommendations¹, indicating that appropriate
30
31 doses of glucocorticoids, when given, are being prescribed at initiation. Additionally there
32
33 seems to be wide variation in practice across the UK relating to routes of referral and who
34
35 arranges and performs temporal artery biopsy. Rheumatology remains the predominant
36
37 speciality to whom GPs refer suspected GCA patients, but a range of different specialities
38
39 were identified by participants. These findings may in part reflect variations in local policy
40
41 and the availability of specialities regionally. However, it may also identify a lack of GP
42
43 awareness of current national GCA guidelines.
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50 Research into conditions such as rheumatoid arthritis highlights that delays in diagnosis can
51
52 occur at several points in the patient journey. These include the patient recognising that
53
54 there is a problem requiring consultation (patient level), the patient then getting an
55
56 appointment with the GP, the GP recognising that referral is needed and making the referral
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1
2
3 (GP delay) and the patient getting an appointment with the specialist (specialist delay)²⁰.

4
5 These points of delay are also likely to be relevant to patients with GCA. Health promotion
6
7 could be used to improve patients' awareness of GCA, but may be of limited value given the
8
9 rarity of the condition and the wide and non-specific symptoms that patients experience
10
11 early in the disease course. However, educational strategies for front line clinicians in the
12
13 early recognition and management of GCA is critical; although some responders indicated
14
15 that there do not appear to be robust fast track clinical pathways in their local region for
16
17 patients with suspected GCA . Given the relative rarity of GCA and variation in its early
18
19 presentation¹⁶, the potential for it not being recognised or for initial misdiagnosis is high. In
20
21 regions where temporal artery biopsy is arranged by the GP or undertaken before seeing the
22
23 relevant specialist, there is the possibility that a significant amount of unnecessary biopsies
24
25 are being performed especially given that there is a great burden of temporal artery biopsies
26
27 on surgical departments with sometimes low yield rates of positive biopsy²¹. This potentially
28
29 could be avoided if patients with suspected GCA were carefully selected by a clinician with
30
31 significant experience in diagnosing and identifying suspected GCA. No participants
32
33 discussed temporal artery ultrasound which can be used to help identify patients with GCA⁵.
34
35 Ultrasound techniques may be a preferred option for those with significant co-morbidities or
36
37 too frail to undergo biopsy. Additionally, it is less invasive and would be more appropriate to
38
39 being embedded in a care pathway for the rapid assessment of GCA in primary care to
40
41 streamline patient pathways to help reduce diagnostic confusion, or to better identify
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43 patients for temporal artery biopsy²² thereby improving outcomes for patients with GCA²³,
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24. Further studies are being conducted to determine whether availability and accuracy of
temporal artery ultrasound will alter requirements for biopsy²⁵.

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3 Delays in assessment for definitive diagnosis creates several conundrums surrounding initial
4
5 treatment. Current guidance is clear that treatment should not be delayed and should be
6
7 initiated in patients with suspected GCA, although the sensitivity of temporal artery biopsy
8
9 declines the longer treatment has been given before biopsy ²⁶. Additionally the American
10
11 College of Rheumatology criteria for GCA suggests that a positive temporal artery biopsy is
12
13 not essential to diagnose GCA ²⁷. High dose glucocorticoid treatment may have a significant
14
15 impact on symptoms by the time they present to the reviewing specialist and therefore
16
17 definitive diagnosis for patients who have had a negative biopsy can become extremely
18
19 challenging. However, an accurate diagnosis is critical and a decision to delay treatment in
20
21 patients with true GCA could result in visual loss. Equally, a decision to continue treatment in
22
23 someone who does not truly have GCA will expose that patient to an inappropriate
24
25 treatment course (and therefore associated potential adverse effects) of glucocorticoids, as
26
27 treatment often continues for many patients, despite a negative temporal artery biopsy ²⁶.

28
29 Our quantitative data suggested that over a third of participants would not initiate
30
31 treatment prior to referral despite UK national guidance which advises the immediate
32
33 initiation of high dose glucocorticoids ¹. This represents an area where further education to
34
35 encourage the immediate initiation of treatment could improve outcomes for patients with
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37 GCA. However, not initiating treatment may be in part due to variations in local or practice
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39 policy.
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Strengths and limitations of this study

The predominant strength of this study is the use of a multi-methods approach, which has allowed the identification of significant challenges relating to GCA management in primary care and subsequent in depth exploration of those issues.

The main weakness in this study was the sub-optimal response rate and therefore the potential lack of generalisability of our findings. However a response rate of 25% is comparable to similar musculoskeletal GP surveys conducted in the same setting²⁸. Additionally, while low response rates may increase the possibility of bias, responder demographics of the questionnaire study relating to age, gender and GP role were comparable to national GP demographics²⁹. The standard limitations of telephone interviews also apply in this study. While such interviews enabled participants to be interviewed from a wide geographical area and therefore generate rich data on differing local management policies, they may reduce rapport and non-verbal communication. However, the questions used in the topic guide were highly clinical and therefore the lack of rapport building or visual cues is unlikely to have significantly impacted on data quality, as participants were not revealing personal details. TH undertook all of the qualitative data analysis which potentially could impact on theme development due to personal preconceptions and misinterpretations. However, an inter-rater analysis was undertaken to ensure concordance of themes identified. This did not show any difference between raters. Finally, there is the potential for discrepancies between reported behaviour and actual behaviour, this is inherent in both survey and interview studies.

Conclusion

An increased focus on education and awareness of GCA (given its rarity and the range of presenting features) may aid better identification of potential GCA patients. However, significant challenges around GCA remain in primary care, some of which need to be addressed in conjunction with specialist settings. National guidelines suggest that GCA is a medical emergency and so treatment should not be delayed. However, as yet there are no UK national standardised fast track referral/care pathways enabling rapid referral of patients suspected of having GCA yet fast track pathways have been shown to potentially reduce the complication of sight loss in GCA²³. This study identifies wide variations in the way that patients are initially managed across the UK and therefore adopting standardised fast track services for patients with suspected GCA could enable effective and accurate diagnosis and management and therefore improve outcomes for patients with GCA.

Acknowledgements

TH is currently funded by an NIHR Clinical Lectureship in General Practice and was funded by an NIHR in practice fellowship and an NIHR School for Primary Care Research GP career progression award during the time that this research was undertaken. CDM is funded by the National Institute for Health Research (NIHR) Collaborations for Leadership in Applied Health Research and Care West Midlands, the NIHR School for Primary Care Research and an NIHR Research Professorship in General Practice (NIHR-RP-2014-04-026). The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NIHR (UK). The views expressed are those of the author(s) and not necessarily those of the NHS,

1
2
3 the NIHR or the Department of Health. We are grateful for the participation of all of the
4
5 General Practitioners who responded to the questionnaire and gave up their precious time
6
7 to participate in the telephone interviews. Special thanks go to Dr Antonia Middleditch and
8
9 Dr Edward Jutsum for their help in interview and topic guide development.
10

11
12 Acknowledgements are also given to the Research Institute for Primary Care and Health
13
14 Sciences, Keele University and the professional services staff who supported the study.
15
16

17 18 19 20 21 **Contributorship Statement**

22
23 Authors had access to all the study data, take responsibility for the accuracy of the analysis,
24
25 and had authority over the manuscript and the decision to submit for publication. Guarantor
26
27 of overall study integrity: TH & CDM. Study concept & design: TH, SM, SLH, JR & CDM. Data
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29 collection and interpretation: TH, SM, SLH, JR & CDM. Analyses: TH, SM, SLH, JR & CDM.
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31 Manuscript preparation: TH, SM, SLH, JAP JR & CDM. Final approval of manuscript: TH, SM,
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33 SLH JAP, JR & CDM
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41 **Conflicts of interest.**

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44 We have no conflicts of interest to report.
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Table 1 Table demonstrating the features used by responders to identify GCA

| GCA Feature | Theme Frequency |
|------------------------|-----------------|
| Headache/Head Symptoms | 1071 |
| Visual disturbances | 671 |
| Scalp Tenderness | 468 |
| Jaw Symptoms | 420 |
| PMR symptoms | 69 |
| Systemic Symptoms | 65 |
| Fatigue | 29 |
| Joint/Muscle symptoms | 20 |
| Tongue symptoms | 12 |

Table 2. Actions undertaken by GPs with patients with suspected GCA

| Action | n | (%) |
|---|-----|------|
| Urgent blood tests, initiate treatment and refer for out-patient review urgently, if blood tests positive | 554 | 44.4 |
| Refer to hospital immediately without investigation | 244 | 19.5 |
| Urgent blood tests and refer to hospital immediately if positive | 201 | 16.1 |
| Urgent blood tests, initiate treatment and refer for out-patients review routinely | 66 | 5.3 |

Table 3 Specialties to which GCA patients are referred

| Speciality | Frequency | (%) |
|------------------------|-----------|------|
| Rheumatology | 478 | 38.3 |
| Ophthalmology | 366 | 29.3 |
| General Medicine | 144 | 11.5 |
| Accident and Emergency | 35 | 2.8 |
| Neurology | 12 | 1.0 |
| Elderly Care | 9 | 0.7 |
| Other | 41 | 3.3 |
| Missing | 164 | 13.1 |

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Table 4. Verbatim quotations from the qualitative study and open responses from the cross-sectional survey

| Theme | Sub-theme | Verbatim quotation |
|-------------------------|---|---|
| Challenges of diagnosis | Fear of Missing GCA and non-specific presentation | <p>“an elderly lady who was having headaches and kind of pain around her eyes and I’m trying to think what other symptoms she had, general misery really. And it sort of came and went and came and went and she didn’t really have any visual problems which is good and when you said to her, “Does it hurt to chew?” she’d say, “Oh yes I think it does”. And so yes all of that so in the end I started, I did discuss it with our local physicians because just in that situation where you don’t want to miss it but on the other hand it doesn’t seem like it’s probably the most likely diagnosis. And we got as far as them saying, “Well if it’s maybe a possibility then go ahead and treat with steroids”, at which point she said, “No I’m feeling much better thank you”. And that was that until she started complaining about it again another few months later”</p> <p>GP17 (11, F, P)</p> |
| Initial and on-going | Starting treatment | <p>“And, certainly, in the past couple of years, we’ve started them on steroids first, because, kind of, getting anybody</p> |

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3 treatment to see them quickly, you know, within a day or two, not
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5 and been possible, which doesn't seem very ideal to me. And
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8 monitoring we've taken the view if it turns out to be wrong, we can
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10 stop it, but if we don't start it, there might be a problem
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12 before they get the biopsy. So that's, kind of, what we've
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14 done here.”

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18 GP15 (25, F, P)

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22 “Yes again just I think in terms of the ongoing
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24 management really because my experience with another
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26 patient, the one that ended up with visual disturbance,
27
28 she sort of then fell between ophthalmology and
29
30 rheumatology without either necessarily taking full
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32 responsibility for her and actually she was a patient of a
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34 partner of mine so he was kind of following her up but his
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36 experience was that he was piggy in the middle really”

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41 GP 6 (20, F, P)

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45 Expediency “you refer them under a two-week wait, and it's not that
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47 of review much of an emergency, whereas we all thought you
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49 referred them acutely, because it was that much of an
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51 emergency. So there was a big discrepancy of views
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53 between what we felt we'd been taught about it, and
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what other people were now doing.”

GP23 (12, F, S)

“I know we, kind of, all get it drummed into us, you know, we should all get these things sent in on the day. But I think, well, one of them was hanging round for a year, and he didn’t really come to any harm, except undue pain and distress that he had. And the other one was hanging round for a couple of months, you know. And they were both proved – as I say, I’m turning the clock back 15 years - but I think they were both proven to be temporal arteritis. It maybe isn’t that, kind of, you know, you must get them in on the day, as I thought as a medical student, you know”

GP22 (15, M, P)

| | | |
|--|---|---|
| <p>Challenges with referral for definitive diagnostic confirmation by specialist</p> | <p>Delays in temporal artery biopsy</p> | <p>“The patient that I referred on the NHS, she ended up having a biopsy before she saw a consultant rheumatologist. So, yes, it was done that way round. The biopsy, of course, came back negative because the two week delay before getting it done meant the steroids had treated it.” GP21 (7, F, S)</p> |
|--|---|---|

“Local issue regarding whether ophthalmology or vascular

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surgery will perform temporal artery biopsy, reliability of
this procedure and steroid response whilst waiting for the
biopsy”

Participant 2506 (4, 2, P)

Key to participant demographic: GP (n) (qualitative study identifier), Participant (n) (survey identifier) [time qualified as a GP (years), gender (Male/Female), seniority/role (S:salaried, L:locum, P:partner)]

For peer review only

BMJ Open

The challenges of diagnosis and management of giant cell arteritis in general practice: a multi-methods study

| | |
|---------------------------------|--|
| Journal: | <i>BMJ Open</i> |
| Manuscript ID | bmjopen-2017-019320.R1 |
| Article Type: | Research |
| Date Submitted by the Author: | 02-Nov-2017 |
| Complete List of Authors: | Helliwell, Toby; Keele University, Research Institute for Primary Care and Health Sciences Muller, Sara; Keele University, Research Institute for Primary Care & Health Sciences Hider, Samantha; Keele University, Arthritis Research UK Primary Care Centre; Prior, James A.; Keele Univ, Research Institute for Primary Care and Health Sciences Richardson, Jane; Keele University, Primary Care and Health Sciences Mallen, Christian; Keele University, Arthritis Research UK Primary Care Centre |
| Primary Subject Heading: | General practice / Family practice |
| Secondary Subject Heading: | Rheumatology, Medical management |
| Keywords: | PRIMARY CARE, RHEUMATOLOGY, GERIATRIC MEDICINE |
| | |

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Manuscripts

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5 **The challenges of diagnosis and management of giant cell arteritis in general practice: a multi-**
6 **methods study**
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28 **Funding:** This work was funded by an Arthritis Research UK Clinician Scientist Award awarded to
29 Christian Mallen (19634). CDM is funded by the National Institute for Health Research (NIHR),
30 Collaborations for Leadership in Applied Health Research and Care West Midlands, the NIHR School
31 for Primary Care Research and a NIHR Research Professorship in General Practice (NIHR-RP-2014-04-
32 026). TH is funded by a NIHR Clinical Lectureship in General Practice. JAP is funded by a Launching
33 Fellowship from the NIHR School for Primary Care Research. The views expressed are those of the
34 author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.
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37 **Data sharing statement:** The datasets analysed during the current study may be available from the
38 corresponding author on reasonable request.
39

40 **Keywords:** Giant cell arteritis, general practice, diagnosis, management
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42 **Conflicts of interest:** There are no conflicts of interest to declare.
43

44 **Prior presentation:** Presented as a poster at BSR Conference 2015
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46 Word count: 3940
47

48 Number of tables: 4
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7 Background: In the UK, general practitioners (GPs) are usually the first medical contact for
8 patients with suspected giant cell arteritis (GCA). Whilst rare, it is critical not to miss, as
9 delayed treatment can lead to significant complications including permanent visual loss. To
10 date little is known about the approach and challenges to diagnosis and management of GCA
11 by GPs.
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19 Objective: To investigate the diagnosis and management of patients with suspected GCA in
20 UK general practice.
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24 Design and participants: A multi-methods approach was taken, comprising a postal survey of
25 5000 randomly selected UK GPs and semi-structured telephone interviews of 24 GPs from
26 across the UK.
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32 Setting: UK general practice
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35 Results: 1249 questionnaires were returned. 879 responders (70%) indicated that they had
36 diagnosed and managed a patient with GCA. A variety of clinical features were used to
37 identify GCA. 21.9% suggested that they would exclude GCA as a diagnosis if headache was
38 absent and around one third do not routinely initiate glucocorticoid treatment prior to
39 referral. Significant regional variations in referral pathways were reported. Thematic analysis
40 of interview transcripts highlighted fears relating to a missed diagnosis of GCA and the non-
41 specific nature of early GCA presentation. Accessing specialist care was highlighted as
42 challenging by many GPs and that a national standard fast track pathway is lacking to
43 support this patient group. Additionally there were significant concerns regarding potential
44 adverse effects relating to long term treatment with glucocorticoids.
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3 Conclusion: GPs appear to over-rely on headache to identify GCA and marked geographical
4 differences in management, with conflicting referral pathways and difficulties in accessing
5 appropriate services exist in the UK. A national standard for fast-tracking suspected GCA
6 patients to relevant specialists would be beneficial to improve care and outcomes for
7 patients with GCA.
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20 **Strengths**

- 21 1. Multi-methods approach, allowing the identification of significant challenges relating to GCA
- 22 management in primary care and subsequent in depth exploration of those issues.
- 23 2. First large study to investigate diagnosis and management of GCA in general practice
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29 **Limitations**

- 30 1. Sub-optimal response rate and therefore potential lack of generalisability of findings
- 31 although responder demographics of the questionnaire study relating to age, gender and GP
- 32 role were comparable to national GP demographics.
- 33 2. Telephone interviews often viewed as inferior to face to face interviews for qualitative
- 34 studies
- 35 3. There is the potential for discrepancies between reported behaviour and actual behaviour,
- 36 this is inherent in both survey and interview studies
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Background

Giant cell arteritis (GCA) is the most common large/medium vessel vasculitis¹. It is strongly associated with polymyalgia rheumatica (PMR) with an estimated incidence of 1.0 per 10000 patient years². Barraclough (2012) estimated that a full-time general practitioner (GP) will see one new case of GCA every 1-2 years, although this will greatly depend on practice population demographics³.

Classical presenting features of GCA include new onset headache or head pain (which may be unilateral and often temporal), scalp tenderness, jaw and tongue claudication, constitutional and visual symptoms¹. Usually there is a significant inflammatory response with raised inflammatory markers. However, it can present atypically which may lead to delays in diagnosis and potentially irreversible complications such as sight loss⁴. Once GCA is suspected, treatment with high dose glucocorticoids (often prednisolone in the UK) should be initiated along with early specialist referral to confirm diagnosis and prevent potential disease complications¹.

Suspected GCA patients are usually identified clinically, followed by specialist referral for temporal artery biopsy (TAB) to confirm diagnosis. Ultrasound scanning however has been shown to be a useful and non-invasive tool to help diagnose GCA⁵ although typical ultrasound features of GCA may diminish after just a few days of glucocorticoid treatment, whereas histological features of GCA may still be evident on TAB several months after initiation of treatment⁶. However, the sensitivity of TAB can vary with 13% to 19% of patients with typical features of GCA having a negative temporal artery biopsy⁷.

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3 In the UK, GPs are the first point of medical contact for most patients. The role of the GP
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5 involves maintaining a high index of suspicion for the disorder, to initiate early therapy and
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7 urgently refer to an appropriate specialist for diagnostic confirmation¹. Following diagnosis,
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9 GPs are often key in tapering glucocorticoid treatment as well as monitoring and
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11 management of glucocorticoid related adverse effects and impact on co-morbidity for
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13 example osteoporosis, cardiovascular disease, diabetes and development of serious
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15 infections^{2,8}.

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19 The aim of this study was to investigate the diagnostic challenges and initial and on-going
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21 management of GCA patients by GPs in the UK.
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28 **Materials and Methods**

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31 Given the potential variation in management practices due to multiple influences, such as
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33 patient presentation, multi-morbidity, availability of services and variations in practice and
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35 local policy, a multi-methods approach combining two study methodologies was chosen to
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37 produce a more complete overall description of current GP diagnostic and management
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39 practices for GCA⁹. First, a national cross-sectional postal survey of 5000 randomly selected
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41 UK GPs was undertaken to investigate PMR and its closely associated illness of GCA, followed
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43 by a semi-structured telephone interview study with a purposive sample of survey
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45 responders to investigate in depth the challenges of diagnosis and management associated
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47 with GCA and PMR. The cross-sectional postal survey was undertaken first, with the findings
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49 used to help develop the topic guide for the interview study. This paper presents the
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51 combined findings from the two studies relating to GCA.
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3 PMR national cross sectional postal questionnaire survey. A cross sectional survey was
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5 mailed to a random sample of 5000 GPs from across the UK identified from the Binley's
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7 database. The Binley's database contains the names and addresses of the majority of GPs
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9 working in the UK. It also contains other forms of information including the type of practice,
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11 the practice population size, practitioner seniority, and some of the clinical services
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13 provided¹⁰. An online option for survey completion was also available through Survey
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15 Monkey¹¹. Non-responders were sent a reminder card after 2 weeks and a further survey
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17 pack after 4 weeks. The survey was closed 6 weeks after the second survey pack was sent.
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22 No standard survey instrument exists for assessing diagnosis and management of GCA by
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24 GPs and so questions were specifically developed using current literature and guidelines for
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26 GCA¹. Questions related to how diagnosis was made (signs and symptoms) and how the GP
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28 managed patients with suspected GCA. A mixture of open and closed response questions
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30 were used. The questionnaire was piloted amongst GPs, rheumatologists and patients.
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34 Descriptive statistics were generated (mean, standard deviation (SD) and interquartile range
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36 (IQR)) using the statistical analysis package SPSS 22 for closed response questions¹². For
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38 open response questions a thematic content analysis was used¹³.

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45 The interview study. Participants in the interview study were purposively sampled from
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47 responders to the GP survey who had agreed to further contact. To reflect as broad a range
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49 of practitioner experience as possible, sampling was based on clinical experience, gender
50
51 and clinical seniority. The qualitative interview study topic guide which was used as a guide
52
53 for topics to discuss, was informed by findings from the cross-sectional survey and relevant
54
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1
2
3 GCA literature. The topic guide was reviewed and refined with feedback from GPs,
4
5 rheumatologists and qualitative researchers. As transcripts were reviewed, the topic guide
6
7 was modified to focus on themes identified from early interviews. The topic guide was
8
9 piloted with two GPs and refined within the research team. These interviews were not
10
11 included in the data analysis.
12
13

14
15 Interviews were audio recorded and transcribed verbatim using an approved transcription
16
17 company¹⁴. The resulting transcripts were screened to remove any identifying information.
18
19 Thematic analysis, as described by Braun and Clarke, was used to analyse resulting transcript
20
21 data¹⁵. Analysis of the transcripts was managed using NVivo (NVivo10)¹⁶. TH performed the
22
23 analysis and an inter-rater exercise was undertaken in which three other researchers (SM,
24
25 SH, JR) were asked to independently analyse and identify general themes relating to a
26
27 randomly selected interview to compare with findings by TH. No changes resulted from this
28
29 exercise. Ethical approval for both studies was granted by the Keele University ethics review
30
31 panel (qualitative study ERP178, survey ERP2206).
32
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40 **Results**

41
42 1249 (25%) completed questionnaires were received and analysed. 879 (70%) GPs had
43
44 indicated that they had managed a patient with GCA. Responders to the survey had a mean
45
46 age of 44 years (SD 9.25) and a mean of 13.5 years since qualifying as a GP. 52% were female
47
48 and the majority were partners (74%), with salaried (21%) and locum GPs (3%) comprising
49
50 the remainder. For the qualitative study, 24 GP participants were telephone interviewed
51
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3 from various regions across the UK. 16 participants were female and 15 participants were GP
4
5 partners.
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11 Questionnaire survey: Initial diagnosis and management

12
13
14 Free text open response questions in the questionnaire were used to ask all participants to
15
16 describe how they made a diagnosis of GCA. The results summarised in Table 1.
17
18

19 **Table 1**

20
21
22 The predominant reported clinical feature used to diagnose GCA was headache, along with
23
24 visual disturbance and scalp tenderness. Survey responders indicated that they often used a
25
26 combination of features when making a new diagnosis. Of particular note however, was that
27
28 21.9% of responders indicated that they only use headache to identify GCA.
29
30

31
32 Management of GCA can be divided into i) initial treatment and referral and ii) long term
33
34 glucocorticoid reduction and monitoring. For GPs, initial management is intimately
35
36 associated with diagnosis as suspected GCA patients require urgent specialist referral for
37
38 definitive diagnosis and treatment. Table 2 summarises the immediate subsequent actions
39
40 of GPs who have identified patients with suspected GCA.
41
42
43
44

45 **Table 2**

46
47
48 Guidance advises that treatment should not be delayed and that appropriate urgent referral
49
50 for specialist diagnostic confirmation should be made¹. 445 responders to the survey
51
52 (35.6%) indicated that they would not routinely initiate glucocorticoid treatment prior to
53
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1
2
3 referral. However, 78.7% (n=983) reported that if they were to initiate treatment,
4
5 appropriate doses of between 40 and 60mg of prednisolone would be prescribed. GP
6
7 responders indicated that they were referring suspected GCA patients to a variety of
8
9 different specialities using an assortment of referral pathways, depending on the
10
11 geographical location in the UK. Table 3 summarises to which speciality survey responders
12
13 refer suspected GCA patients.
14
15

16 17 **Table 3**

18 19 20 21 22 23 Themes identified from the qualitative study

24 25 26 **Diagnosis**

27
28 The two main themes identified from the interview study related firstly to the presenting
29
30 features of GCA and secondly to fears of missing a diagnosis of GCA.
31
32
33
34
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36
37

38 39 Presenting features of GCA

40
41 When asked about GCA symptoms in the interviews, participants often gave textbook
42
43 descriptions of classical features of GCA.
44
45

46
47 *“Headache in someone over 55 you think giant cell arteritis really, that's my mantra,*
48
49 *new different headache, classically unilateral but not always, focused around the*
50
51 *temple, potentially some tenderness there, possibly protruding temporal artery,*
52
53 *classically tender when they're combing their hair, but also looking for things like*
54
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1
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3 *jaw claudication or tongue symptoms, [.....] and obviously the dread of visual*
4
5 *disturbance as well really which can be anything really”*
6
7

8 **GP6 (20, F, P)**
9

10
11 Key: GP identifier [time qualified as a GP (years), gender (male/female), seniority/role

12
13 (S:salaried, L:locum, P:partner, SP: senior partner)]
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21
22
23 While textbook descriptions of classical GCA were given, there was recognition that some of
24
25 these features may be difficult to recognise or link to GCA.
26
27

28
29 *“jaw claudication is interesting, because I know at the time, my colleague and myself,*
30
31 *kind of, looked a bit more up about GCA and he said, ‘I’ve never heard of jaw*
32
33 *claudication.’ ”*
34
35

36 **GP15 (25, F, P)**
37
38

39 40 41 42 Fear of missing case of GCA 43

44
45 GPs expressed considerable fear about missing a diagnosis of GCA given the potential for
46
47 irreversible visual loss.
48
49

50
51 *“I find it, sort of, trickier, I think, to diagnose. I worry about it more. I worry about*
52
53 *missing it. And I feel far less confident about treating it. I think when I was first*
54
55

1
2
3 *qualified as a GP I think I thought somebody had got it every week. Anybody who'd*
4
5 *got a headache, you know"*
6
7

8 **GP 24 (12, F, S)**
9

10
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14
15 Fears surrounding missing a diagnosis of GCA also related to the potential for a wide range
16
17 of symptoms and atypical presentations.
18

19
20 *"Just with a vague headache, and hadn't had any visual disturbance at that point in*
21 *time. And he didn't really have a lot of temporal artery tenderness. [.....] We did some*
22 *bloods at that point, and the ESR and CRP were normal [.....]... I wrote in the notes at*
23 *the time, 'Excludes GCA'.....which, having read a bit more about it since, after this*
24 *happened, doesn't totally exclude it."*
25
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33 **GP 15 (25, F, P)**
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39 **Management**
40

41
42 Two main themes were identified from the interview transcripts. First, initial and on-going
43
44 treatment and monitoring and second, referral for definitive diagnostic confirmation by a
45
46 specialist.
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Initial and on-going treatment

Most participants indicated that they would initiate suspected GCA patients on appropriate doses of prednisolone.

“I think the rheumatologists would say start the 60[mg] and I will see them in clinic.”

GP4 (6, M, P)

However, there was recognition that treatment could impact on the sensitivity of the temporal artery biopsy, especially if it was going to be delayed.

“what then happens in secondary care, it's less than ideal, they seem to rotate who might do a temporal artery biopsy between vascular, ophthalmology and general surgery [.....] but the patient generally is having that temporal biopsy before ever seeing a rheumatologist and the timeliness of that temporal artery biopsy is not ideal.”

GP6 (20, F, P)

Local policy also had a significant impact on how suspected GCA patients were initially treated. This, as well as concerns surrounding the impact that treatment could have on biopsy effectiveness, may account for some of the significant number of participants who indicated that they would not initiate treatment prior to referral.

1
2
3 *“Locally this gets referred to ophthalmology[.....] and our practice is actually within*
4 *the grounds of the hospital so we’ve got no issues really in terms of administering*
5 *steroids you know before they were seen, they would be seen within an hour by an*
6 *ophthalmologist.”*

7
8
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11
12
13 **GP 7 (10, M, P)**

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18
19 The principal and over-arching concern relating to long-term management was the potential
20 adverse effects of glucocorticoid treatment.

21
22
23
24 *“Well, it’s a good two years of treatment with steroids and all the complications and*
25 *side effects that they carry with them. So, yes, and high doses of it, which have been*
26 *poorly tolerated with the patients. [.....] One patient, she had diabetes, and she was*
27 *started on the steroids, and she was struggling with awful side effects from the*
28 *steroids. She developed, well, lots of depressive symptoms. Her blood sugars went all*
29 *over the place. She got a lot of pitting oedema of the legs, which was hampering her*
30 *mobility. She got unsteadiness due to the steroids.”*

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41 **GP21 (7, F, S)**

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47 Referral for definitive diagnostic confirmation by a specialist

48
49
50 Specialist referral for definitive diagnostic confirmation was a significant issue for GPs, with
51 referral pathways being highly variable across the UK. The speciality to which suspected GCA
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1
2
3 patients were referred can depend on presenting clinical features; however, some of this
4
5 variation reflects local policy and also the regional availability of services and specialities.
6
7

8 *“If their history was suspicious and their inflammatory markers were raised, I would*
9 *then contact...well we’ve had this issue between rheumatology and ophthalmology*
10 *and who to contact, and the line seems to be that if they’ve got any visual symptoms*
11 *then they go to ophthalmology and if they haven’t then they go to rheumatology.”*
12
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18 **GP13 (5, F, S)**
19

20
21 However, in some regions of the UK GPs reported that referral pathways were not clear and
22
23 that specialist referral can be challenging.
24
25

26 *“But, generally, you speak to the on-call medical team, and they will advise me to*
27 *speak to someone else. And then they advise me to speak to someone else. So you*
28 *end up making loads of phone calls to try and find out which route you go in.”*
29
30
31
32
33

34 **GP21 (7, F, S)**
35

36
37 Some participants reported that their local policy involved the GP requesting the temporal
38
39 artery biopsy prior to review by a specialist. This often created challenges in itself.
40
41

42 *“we would try and get a temporal artery biopsy fairly promptly. It has been a bit*
43 *difficult in the past, and you know, you’re supposed to get it done within a day or two.*
44 *We traipse round the ophthalmologists, who say, ‘No, speak to the vascular people.’*
45 *Who say, ‘No, speak to the general surgeons.’ Well, we tried, initially, referring to the*
46 *ophthalmologist, and they just aren’t keen at all [.....] at the moment we’ve had, a*
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3 *general surgery team who have done a temporal artery biopsy for us, and the*
4
5 *vascular surgeons have.” GP15 (25, F, P)*
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11 Further quotations illustrating the two main themes can be seen in Table 4 below.
12
13

14 **Table 4**

15 16 17 18 19 20 **Discussion**

21
22
23 This is the first study of its kind to explore diagnosis and a critical aspect of the care pathway
24 for patients with suspected GCA. GCA remains a diagnosis that GPs worry about missing.
25

26
27
28 Whilst GPs were comfortable with classical presentation patterns, an overreliance on
29 headache to trigger consideration of a diagnosis of GCA was evident, with some GPs having
30 limited awareness of the full range of symptoms associated with GCA.
31
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36 The predominant findings from the cross sectional study, suggest initiation of treatment for
37 suspected GCA patients is not always routine. However a significant finding from both the
38 cross sectional survey and qualitative interview study demonstrated that referral pathways
39 across the UK vary greatly. Additionally GPs have significant concerns relating to treatment
40 with long term glucocorticoids in this patient group, especially in conjunction with co-
41 existing multi-morbidity.
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Recommendations

Early identification, referral and initiation of appropriate treatment for suspected GCA patients in general practice is critical to prevent complications such as irreversible visual loss¹.

GPs responding to the survey seem to be over-relying on headache when diagnosing GCA. Given that almost half of patients do not present with a classical temporal headache and that 24% of patients with proven GCA have no headache symptoms at all¹⁷, excluding GCA on the basis of no headache has the potential to miss a significant proportion of patients with GCA. However symptoms like headache, are common¹⁸ with over half of over 65 year olds having had a headache in the previous 12 months,¹⁹ yet serious pathology is rare in general practice. Therefore the collective clinical picture needs to be considered and has to include the full range of features of GCA.

The group of patients with no headache are recognised to be at higher risk of permanent visual loss as a result of delayed diagnosis^{4,20}. Therefore, if alternative presentations are not recognised by GPs they will continue to remain a high risk group. Educating clinicians about other presenting symptoms and atypical presentations is essential to optimise diagnosis and reduce delays in instigating appropriate treatment and referral, which could reduce the potential for visual loss and serious long term complications for this patient group.

A considerable proportion of GPs indicated that they would not initiate treatment prior to referral for specialist review. From the questionnaire responses, current primary care practice would seem to be in line with UK recommendations¹, indicating that appropriate doses of glucocorticoids, when given, are being prescribed at initiation. Additionally there

1
2
3 seems to be wide variation in practice across the UK relating to routes of referral and who
4
5 arranges and performs temporal artery biopsy. Rheumatology remains the predominant
6
7 speciality to whom GPs refer suspected GCA patients, but a range of different specialities
8
9 were identified by participants. These findings may in part reflect variations in local policy
10
11 and the availability of specialities regionally. However, it may also identify a lack of GP
12
13 awareness of current national GCA guidelines.
14
15

16
17 Research into conditions such as rheumatoid arthritis highlights that delays in diagnosis can
18
19 occur at several points in the patient journey. These include the patient recognising that
20
21 there is a problem requiring consultation (patient level), the patient then getting an
22
23 appointment with the GP, the GP recognising that referral is needed and making the referral
24
25 (GP delay) and the patient getting an appointment with the specialist (specialist delay)²¹.
26
27

28
29 These points of delay are also likely to be relevant to patients with GCA. Health promotion
30
31 could be used to improve patients' awareness of GCA, but may be of limited value given the
32
33 rarity of the condition and the wide and non-specific symptoms that patients experience
34
35 early in the disease course. However, educational strategies for front line clinicians in the
36
37 early recognition and management of GCA is critical; although some responders indicated
38
39 that there do not appear to be robust fast track clinical pathways in their local region for
40
41 patients with suspected GCA . Given the relative rarity of GCA and variation in its early
42
43 presentation¹⁷, the potential for it not being recognised or for initial misdiagnosis is high. In
44
45 regions where temporal artery biopsy is arranged by the GP or undertaken before seeing the
46
47 relevant specialist, there is the possibility that a significant amount of unnecessary biopsies
48
49 are being performed especially given that there is a great burden of temporal artery biopsies
50
51 on surgical departments with sometimes low yield rates of positive biopsy²². This potentially
52
53 could be avoided if patients with suspected GCA were carefully selected by a clinician with
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1
2
3 significant experience in diagnosing and identifying suspected GCA. No participants
4
5 discussed temporal artery ultrasound which can be used to help identify patients with GCA⁵
6
7 and this may be because this imaging modality where available, is requested by the treating
8
9 specialist and not the GP. Ultrasound techniques may be a preferred option for those with
10
11 significant co-morbidities or too frail to undergo biopsy but will have to be rapidly available
12
13 to clinicians given the importance of starting glucocorticoid treatment in GCA and the rapid
14
15 effects treatment has on typical ultrasound features⁶. It is however, less invasive and could
16
17 be appropriate to being embedded in a care pathway for the rapid assessment of GCA in
18
19 primary care to streamline patient pathways to help reduce diagnostic confusion, or to
20
21 better identify patients for temporal artery biopsy²³ thereby improving outcomes for
22
23 patients with GCA^{24,25}. Further studies are being conducted to determine whether
24
25 availability and accuracy of temporal artery ultrasound will alter requirements for biopsy²⁶.
26
27
28 Delays in assessment for definitive diagnosis creates several conundrums surrounding initial
29
30 treatment. Current guidance is clear that treatment should not be delayed and should be
31
32 initiated in patients with suspected GCA, although the sensitivity of temporal artery biopsy
33
34 declines the longer treatment has been given before biopsy²⁷. High dose glucocorticoid
35
36 treatment may have a significant impact on symptoms by the time they present to the
37
38 reviewing specialist and therefore definitive diagnosis for patients who have had a negative
39
40 biopsy can become extremely challenging. However, an accurate diagnosis is critical and a
41
42 decision to delay treatment in patients with true GCA could result in visual loss. Equally, a
43
44 decision to continue treatment in someone who does not truly have GCA will expose that
45
46 patient to an inappropriate treatment course (and therefore associated potential adverse
47
48 effects) of glucocorticoids, as treatment often continues for many patients, despite a
49
50 negative temporal artery biopsy²⁷.
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3 Our quantitative data suggested that over a third of participants would not initiate
4
5 treatment prior to referral despite UK national guidance which advises the immediate
6
7 initiation of high dose glucocorticoids ¹. This represents an area where further education to
8
9 encourage the immediate initiation of treatment could improve outcomes for patients with
10
11 GCA. However, not initiating treatment may be in part due to variations in local or practice
12
13 policy.
14
15

16 17 18 19 20 Strengths and limitations of this study

21
22
23 The predominant strength of this study is the use of a multi-methods approach, which has
24
25 allowed the identification of significant challenges relating to GCA management in primary
26
27 care and subsequent in depth exploration of those issues.
28
29

30
31 The main weakness in this study was the sub-optimal response rate and therefore the
32
33 potential lack of generalisability of our findings. However a response rate of 25% is
34
35 comparable to similar musculoskeletal GP surveys conducted in the same setting ²⁸.
36
37

38 Additionally, while low response rates may increase the possibility of bias, responder
39
40 demographics of the questionnaire study relating to age, gender and GP role were
41
42 comparable to national GP demographics ²⁹. The standard limitations of telephone
43
44 interviews also apply in this study. While such interviews enabled participants to be
45
46 interviewed from a wide geographical area and therefore generate rich data on differing
47
48 local management policies, they may reduce rapport and non-verbal communication.
49
50

51 However, the questions used in the topic guide were highly clinical and therefore the lack of
52
53 rapport building or visual cues is unlikely to have significantly impacted on data quality, as
54
55 participants were not revealing personal details. TH undertook all of the qualitative data
56
57
58
59

1
2
3 analysis which potentially could impact on theme development due to personal
4
5 preconceptions and misinterpretations. However, an inter-rater analysis was undertaken to
6
7 ensure concordance of themes identified. This did not show any difference between raters.
8
9 Finally, there is the potential for discrepancies between reported behaviour and actual
10
11 behaviour, this is inherent in both survey and interview studies.
12
13
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18 Conclusion

19
20
21 An increased focus on education and awareness of GCA (given its rarity and the range of
22
23 presenting features including more subtle features such as limb claudication, constitutional
24
25 symptoms, vascular bruits, asymmetry of pulses and or blood pressure, anaemia¹) may aid
26
27 better identification of potential GCA patients. However, significant challenges around GCA
28
29 remain in primary care, some of which need to be addressed in conjunction with specialist
30
31 settings. National guidelines suggest that GCA is a medical emergency and so treatment
32
33 should not be delayed. However, as yet there are no UK national standardised fast track
34
35 referral/care pathways enabling rapid referral of patients suspected of having GCA yet fast
36
37 track pathways have been shown to potentially reduce the complication of sight loss in GCA
38
39 ²⁴. This study identifies wide variations in the way that patients are initially managed across
40
41 the UK and therefore adopting standardised fast track services for patients with suspected
42
43 GCA could enable effective and accurate diagnosis and management and therefore improve
44
45 outcomes for patients with GCA.
46
47
48
49

50 **Acknowledgements**

1
2
3 TH is currently funded by an NIHR Clinical Lectureship in General Practice and was funded by
4
5 an NIHR in practice fellowship and an NIHR School for Primary Care Research GP career
6
7 progression award during the time that this research was undertaken. CDM is funded by the
8
9 National Institute for Health Research (NIHR) Collaborations for Leadership in Applied Health
10
11 Research and Care West Midlands, the NIHR School for Primary Care Research and an NIHR
12
13 Research Professorship in General Practice (NIHR-RP-2014-04-026). The views and opinions
14
15 expressed therein are those of the authors and do not necessarily reflect those of the NIHR
16
17 (UK). The views expressed are those of the author(s) and not necessarily those of the NHS,
18
19 the NIHR or the Department of Health. We are grateful for the participation of all of the
20
21 General Practitioners who responded to the questionnaire and gave up their precious time
22
23 to participate in the telephone interviews. Special thanks go to Dr Antonia Middleditch and
24
25 Dr Edward Jutsum for their help in interview and topic guide development.
26
27

28
29 Acknowledgements are also given to the Research Institute for Primary Care and Health
30
31 Sciences, Keele University and the professional services staff who supported the study.
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38 **Contributorship Statement**

39
40
41 Authors had access to all the study data, take responsibility for the accuracy of the analysis,
42
43 and had authority over the manuscript and the decision to submit for publication. Guarantor
44
45 of overall study integrity: TH & CDM. Study concept & design: TH, SM, SLH, JR & CDM. Data
46
47 collection and interpretation: TH, SM, SLH, JR & CDM. Analyses: TH, SM, SLH, JR & CDM.
48
49 Manuscript preparation: TH, SM, SLH, JAP JR & CDM. Final approval of manuscript: TH, SM,
50
51 SLH JAP, JR & CDM
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Conflicts of interest.

We have no conflicts of interest to report.

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Table 1 Table demonstrating the features used by responders to identify GCA

| GCA Feature | Theme Frequency |
|--|------------------------|
| Headache/Head Symptoms | 1071 |
| Visual disturbances | 671 |
| Scalp (including temporal artery tenderness) | 468 |
| Jaw Symptoms | 420 |
| PMR symptoms | 69 |
| Systemic Symptoms | 65 |
| Fatigue | 29 |
| Joint/Muscle symptoms | 20 |
| Tongue symptoms | 12 |

Table 2. Actions undertaken by GPs with patients with suspected GCA

| Action | n | (%) |
|---|-----|------|
| Urgent blood tests, initiate treatment and refer for out-patient review urgently, if blood tests positive | 554 | 44.4 |
| Refer to hospital immediately without investigation | 244 | 19.5 |
| Urgent blood tests and refer to hospital immediately if positive | 201 | 16.1 |
| Urgent blood tests, initiate treatment and refer for out-patients review routinely | 66 | 5.3 |

Table 3 Specialties to which GCA patients are referred

| Speciality | Frequency | (%) |
|------------------------|-----------|------|
| Rheumatology | 478 | 38.3 |
| Ophthalmology | 366 | 29.3 |
| General Medicine | 144 | 11.5 |
| Accident and Emergency | 35 | 2.8 |
| Neurology | 12 | 1.0 |
| Elderly Care | 9 | 0.7 |
| Other | 41 | 3.3 |
| Missing | 164 | 13.1 |

Table 4. Verbatim quotations from the qualitative study and open responses from the cross-sectional survey

| Theme | Sub-theme | Verbatim quotation |
|------------------------------------|---|---|
| Challenges of diagnosis | Fear of Missing GCA and non-specific presentation | <p>“an elderly lady who was having headaches and kind of pain around her eyes and I’m trying to think what other symptoms she had, general misery really. And it sort of came and went and came and went and she didn’t really have any visual problems which is good and when you said to her, “Does it hurt to chew?” she’d say, “Oh yes I think it does”. And so yes all of that so in the end I started, I did discuss it with our local physicians because just in that situation where you don’t want to miss it but on the other hand it doesn’t seem like it’s probably the most likely diagnosis. And we got as far as them saying, “Well if it’s maybe a possibility then go ahead and treat with steroids”, at which point she said, “No I’m feeling much better thank you”. And that was that until she started complaining about it again another few months later”</p> <p>GP17 (11, F, P)</p> |
| Initial and on-going treatment and | Starting treatment | <p>“And, certainly, in the past couple of years, we’ve started them on steroids first, because, kind of, getting anybody to see them quickly, you know, within a day or two, not been possible, which doesn’t seem very ideal to me. And</p> |

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3 monitoring we've taken the view if it turns out to be wrong, we can
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5 stop it, but if we don't start it, there might be a problem
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7 before they get the biopsy. So that's, kind of, what we've
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9 done here."

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12 GP15 (25, F, P)

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17 "Yes again just I think in terms of the ongoing
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19 management really because my experience with another
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21 patient, the one that ended up with visual disturbance,
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23 she sort of then fell between ophthalmology and
24
25 rheumatology without either necessarily taking full
26
27 responsibility for her and actually she was a patient of a
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29 partner of mine so he was kind of following her up but his
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31 experience was that he was piggy in the middle really"

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35 GP 6 (20, F, P)

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39 Expediency "you refer them under a two-week wait, and it's not that
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41 of review much of an emergency, whereas we all thought you
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43 referred them acutely, because it was that much of an
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45 emergency. So there was a big discrepancy of views
46
47 between what we felt we'd been taught about it, and
48
49 what other people were now doing."

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53 GP23 (12, F, S)

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5 “I know we, kind of, all get it drummed into us, you know,
6 we should all get these things sent in on the day. But I
7 think, well, one of them was hanging round for a year, and
8 he didn’t really come to any harm, except undue pain and
9 distress that he had. And the other one was hanging round
10 for a couple of months, you know. And they were both
11 proved – as I say, I’m turning the clock back 15 years - but
12 I think they were both proven to be temporal arteritis. It
13 maybe isn’t that, kind of, you know, you must get them in
14 on the day, as I thought as a medical student, you know”

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28 GP22 (15, M, P)

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33 Challenges Delays in “The patient that I referred on the NHS, she ended up
34 with referral temporal having a biopsy before she saw a consultant
35 for definitive artery rheumatologist. So, yes, it was done that way round. The
36 diagnostic biopsy biopsy, of course, came back negative because the two
37 confirmation week delay before getting it done meant the steroids had
38 by specialist treated it.” **GP21 (7, F, S)**

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49 “Local issue regarding whether ophthalmology or vascular
50 surgery will perform temporal artery biopsy, reliability of
51 this procedure and steroid response whilst waiting for the
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54

biopsy”

Participant 2506 (4, 2, P)

Key to participant demographic: GP (n) (qualitative study identifier), Participant (n) (survey identifier) [time qualified as a GP (years), gender (Male/Female), seniority/role (S:salaried, L:locum, P:partner)]

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