

Systemic vasculitis and patient-reported outcomes: how the assessment of patient preferences and perspectives could improve outcomes

Joanna C Robson^{1,2}

David Jayne³

Peter A Merkel^{4,5}

Jill Dawson⁶

¹Faculty of Health and Applied Sciences, University of the West of England, Bristol, UK; ²Faculty of Health and Applied Sciences, University Hospitals Bristol NHS Trust, Bristol, UK; ³Department of Medicine, University of Cambridge, Cambridge, UK; ⁴Division of Rheumatology, Department of Medicine, ⁵Department of Biostatistics, Epidemiology, and Informatic, University of Pennsylvania, Philadelphia, PA, USA; ⁶Nuffield Department of Population Health (HSRU), University of Oxford, Oxford, UK

Abstract: The systemic vasculitides are a group of multisystem diseases, which can be life and organ threatening. High-dose immunosuppressants are required to control inflammation in vital organs, such as the kidneys, lungs, skin, joints, and eyes. Patients report a range of impacts on their health-related quality of life due to symptoms, irreversible damage, and the adverse effects of medications. The measurement of patient perspectives within clinical studies in vasculitis is essential to capture outcomes of greatest importance to patients. Validated generic, disease-specific and symptom-specific patient-reported outcomes available for use in patients with systemic vasculitis are reviewed here.

Keywords: patient-related outcomes, vasculitis, ANCA-associated vasculitis, large-vessel vasculitis, Behçet's syndrome, clinical trials

Introduction

The systemic vasculitides present clinically with inflammation in multiple regions of the body and can be life and organ threatening.¹⁻³ Randomized controlled trials with standardized, physician-derived outcome measurement of disease activity and damage have revolutionized the treatment of these diseases.⁴⁻⁶ Systemic vasculitis is no longer invariably fatal, but patients can still suffer ongoing activity, organ damage that cannot be repaired, and adverse effects of immunosuppression.⁷⁻⁹

The impact of symptoms and side effects of treatment in systemic vasculitis can affect all aspects of health-related quality of life (HRQoL).^{8,10,11} Systemic vasculitis affects people of working age¹² and those planning a family^{13,14} or active retirement.¹⁵ Patients also face the situation of having a rare autoimmune rheumatic disease,¹⁶ which can be isolating, resulting in delays to get a diagnosis and treatment, and difficulties in navigating health care systems between different specialists.¹⁶ Patients with vasculitis rank items of importance (in terms of symptoms and impact), differently to how their clinicians would rank those items.^{17,18}

The Outcome Measurement in Rheumatology (OMERACT) initiative is an international collaboration of patients, researchers, clinicians, and methodologist to define core sets of outcome measurements for use in randomized controlled trials.¹⁹ Stakeholder groups including the Food and Drug Administration and pharmaceutical companies also participate.¹⁹ OMERACT has endorsed a core set of domains and outcome measures for use in clinical trials in ANCA-associated vasculitis (AAV)²⁰, large-vessel vasculitis²¹, and Behçet's syndrome,²² each set developed by the OMERACT Vasculitis Working Group. Measurement of disease activity levels and irreversible damage within clini-

Correspondence: Joanna C Robson
Faculty of Health and Applied Sciences,
University of the West of England,
Room 5-054, Rheumatology Research
B502, Bristol Royal Infirmary, Bristol
BS28HW, UK
Tel +44 0117 342 7418
Email jo.robson@uwe.ac.uk

cal trials has been facilitated by physician-derived outcome measures, for example, the Vasculitis Damage Index.²³ In recent years, the patient perspective in systemic vasculitis has been a major focus for the vasculitis research community. A new disease-specific patient-reported outcome (PRO), the AAV-PRO,²⁴ has been validated; underpinning qualitative work in Takayasu's arteritis (TAK) and Behçet's syndrome has been performed;^{25,26} and evaluation of alternative generic PROs including the Patient-Reported Outcome Measurement Information System (PROMIS) is underway.²⁷

Measurement of HRQoL in vasculitis has mostly relied on the use of "generic" PROs, mainly the Short Form 36 (SF-36),²⁸ which is a well-recognized and validated outcome measure that allows comparison between patients with systemic vasculitis and other conditions.²⁸ As generic PROs were not designed for use in a specific disease, these measures can have reduced face and content validity in some settings.²⁹ This lack of specificity may reduce the ability to detect differences in disease states between patients and in the same patient over time.²⁹ Trials in AAV, for example comparing cyclophosphamide to rituximab, have not demonstrated a difference in SF-36 scores between arms, despite differences in the toxicities of the medications.³⁰ This may be due to a lack of sensitivity of the SF-36 or the high levels of glucocorticoids used in both trial arms. In a randomized trial of Avacopan (C5a receptor inhibitor) in AAV, patients not on glucocorticoids scored better on the physical domain of the SF-36.³¹

Disease-specific PROs should be developed with patient involvement throughout, in line with guidance from the US Food and Drug Administration on the development of PROs.³² Good face and content validity is ensured by incorporating qualitative research with patients with the disease in question, to identify the full range of impacts of the disease and its treatment.³³ Questionnaire items are then based on the themes identified and are refined through piloting and cognitive interviews.³⁴ A survey including exploratory factor analysis³⁵ and Rasch analysis³⁶ can be used to identify the final structure of the PRO and to validate its measurement properties.^{24,37}

This article describes the impact on HRQoL of living with AAV, TAK, giant cell arteritis (GCA), and Behçet's syndrome. Measurements of the patient perspective in the systemic vasculitides, through the complimentary use of generic and disease-specific and symptom-specific PROs, are also described.

AAV

AAV encompasses three multisystem diseases: granulomatosis with polyangiitis, microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis.³⁸ The AAVs

are multisystem disorders resulting in inflammation and damage occurring in the kidneys, lungs, skin, ear nose and throat, eyes, and neurological system, and these manifestations can impact on HRQoL.^{2,10}

Newly diagnosed patients with AAV have demonstrated impairments in HRQoL at entry into European Vasculitis Study Group trials³⁹, the Wegener's Granulomatosis Etanercept Trial,⁴¹ and the French MAINRITSAN trial.⁴² Physical functioning scores are the most affected, particularly in those with neurological involvement and older ages. Patients with AAV also report high levels of fatigue and rank this aspect as being of greatest importance to their overall HRQoL.^{17,43} Survey data suggest that AAV-related fatigue is likely to be multifactorial and associated with pain, sleep disturbance, and higher levels of inflammation.⁴⁴ More than 40% of patients with vasculitis report symptoms of anxiety, and one-quarter report symptoms of depression, as measured by the Hospital Anxiety and Depression Scale.⁹ Fifty in-depth qualitative interviews with patients with AAV-identified themes related to fear, anxiety, and stress in 70% of participants, while 50% of interviewees reported depression and 50% reported anger due to their disease or its treatment.¹⁰

Within the 2010 OMERACT core set for AAV, the OMERACT Vasculitis Group included the generic –SF-36 as the outcome measure to capture HRQoL.²⁰ They also identified the need for further work around capturing patient perspectives in AAV including exploration of alternative generic item banks and a disease-specific PRO.⁴⁵

An international collaboration of patients and researchers from the United Kingdom, United States, and Canada formed a steering committee to oversee the development of a disease-specific PRO.⁴⁵

Qualitative interviews with 50 patients with AAV from the three countries identified the following themes: symptom severity, and the impact of problems and limitations imposed by patients' AAV and treatment, on their work; domestic roles; family and social interactions (including activities and interests outside the home) and psychological state.¹⁰ Underpinning themes were then recast as candidate questions for the new disease-specific PRO, and these questions were reduced and refined via piloting and cognitive interviewing.²⁴ A large-scale survey was then used to determine the ideal structure of the PRO, including domains and items, and to validate its measurement properties.²⁴ AAV-PRO domain scores distinguish between patients who self-report active disease vs disease in remission, has good construct validity, and is reliable and feasible to use.²⁴ It has good face validity due to having four patient partners on the steering committee and involvement of patients at each stage.²⁴

The AAV-PRO questionnaire 29-item includes six subscales/domains: “Organ-Specific Symptoms”, “Systemic Symptoms”, “Treatment Side Effects”, “Social and Emotional Impact”, “Concerns about the Future”, and “Physical Function”. The domains provide a profile of the impact of AAV and its treatment on patients’ everyday life.²⁴

Each domain is scored separately to provide a profile of the overall impact of the disease and its treatment on HRQoL. Certain domains may be of interest in specific contexts; for example, the treatment and adverse effects domain may be important within therapeutic drug trials, but it would be important to collect the range of domain scores to identify the full impact on patients HRQoL and symptoms. In future, summary component scores may be derived, but this approach needs further investigation.

The AAV-PRO survey identified that women scored higher (ie, worse) on all six subscales.²⁴ Trends toward worse scores have been previously seen in female patients with AAV,⁴⁰ and HRQoL is reduced in other chronic conditions.^{46,47} Younger people with AAV (<65) scored higher (worse) on the Social and Emotional Impact subscale of the AAV-PRO; this is also seen in other chronic diseases.^{46,48} Younger age is a risk factor for fatigue and negative illness perceptions in AAV.⁴⁹

The OMERACT Vasculitis Working Group gained endorsement by OMERACT for use of certain PROMIS domains and the AAV-PRO in clinical trials of vasculitis.⁵⁰ These instruments are complementary to each other. Both require further work to assess their validity in longitudinal settings, including their ability to discriminate between treatments of varying efficacy in the setting of a randomized controlled trial. Comparison of AAV-PRO domain scores with SF-36 domain scores in clinical studies of patients with AAV, to examine different aspects of construct validity, will also be an important validation step for the AAV-PRO.

GCA

GCA is caused by inflammation of the blood vessels around the head and neck, and elsewhere.⁵¹ GCA frequently presents with severe headache, jaw claudication, systemic features including flu-like symptoms, fevers, and weight-loss, and polymyalgia rheumatica (inflammatory pain and stiffness in the hips and shoulders).⁵² There is a risk of visual loss in 20% of untreated cases^{52,53} and high-dose glucocorticoids are required to protect sight.^{54,55} Glucocorticoids alone have been the only treatment available, but patients can suffer adverse frequent adverse effects including hypertension, diabetes, osteoporosis, psychiatric disturbance, and change in appearance.^{56–59} A novel biologic medication, the interleukin-6-receptor inhibitor tocilizumab, appears to

improve HRQoL at 1 year in patients with GCA;⁶⁰ this finding should be examined further but may be associated with the drug’s glucocorticoid-sparing effect. The impact of GCA on patients’ lives is due to a combination of symptoms (eg, visual disturbance, musculoskeletal symptoms and pain), adverse effects of glucocorticoids, and the disruption to normal life.¹⁵ Patients fear blindness, have concerns about delay in diagnosis,¹⁵ and rank losing sight in both eyes permanently’, “having intense or severe pain” and “feeling weak, tired or exhausted” as key domains of HRQoL.¹¹ In patients with GCA, SF-36 scores do not correlate with visual loss or systemic complications, so generic PROs may be unable to differentiate between clinically important groups.^{61,62} The OMERACT Vasculitis Working Group has, therefore, identified the development of a disease-specific PRO for GCA within their research agenda.^{21,63}

At OMERACT 2018, qualitative work from patients with GCA in the United Kingdom and Australia was presented and included the following salient themes: “Anxieties around getting a diagnosis of GCA”, “Description of symptoms related to GCA and its treatment”, “Lack of bodily strength, stability and stamina; difficulties with completing daily tasks”, “Difficulties with participating in social activities, work and caring roles”, “Not feeling normal and impact on general perception of health”, and “Anxiety and fear of the future”.⁶⁴ These themes could be developed further into candidate questionnaire items for a disease-specific PRO for GCA.

The PROMIS is a bank of items, which have been generated from disease-specific PRO measures in a range of different diseases (examples include osteoarthritis, cancer, or asthma), to create generic item banks for particular domains eg, physical or mental health. Items within the PROMIS domains of Fatigue and Physical Function have been tested in patients with GCA and were found to be feasible to use, scores correlating with relevant SF-36 domain scores; but further validation work is needed.²⁷

TAK

TAK is a systemic inflammatory condition that affects the large arteries, specifically the aorta and its major branches and the pulmonary arteries.⁶⁵ Symptoms can be systemic including weight loss, fever and fatigue, or due to vascular inflammation and occlusion, leading to pain, claudication and tissue loss.⁶⁵ Patients with TAK are diagnosed early in life. Patients with TAK have physical limitations and high levels of anxiety and depression compared with healthy controls;⁶⁶ scores are comparable to those from patients with ankylosing spondylitis and rheumatoid arthritis.⁶⁷ Younger patients and

those in remission have better HRQoL, while those requiring immunosuppression have worse HRQoL.⁷

The OMERACT Large Vessel Vasculitis Working Group identified the lack of a disease-specific PRO for TAK.⁶⁸ Qualitative research was performed through individual interviews and focus groups with patients with TAK from the United States and Turkey.²⁵ Salient themes identified included “Pain and Discomfort”, “Fatigue and Low Energy Levels”, and “Emotional Effects”, and these themes could underpin the development of a disease-specific PRO for TAK.²⁵

Behçet’s syndrome

Behçet’s syndrome affects a spectrum of various veins and arteries of different sizes³⁸; patients can therefore present with a range of symptoms.⁶⁹ Oral and genital ulcers, nodular and papulopustular skin lesions, pan-uveitis, inflammatory arthritis and bowel disease, and a range of neurological disorders can occur.^{69,70}

Oral and genital ulcers, neurological and ophthalmological involvement, joint pain, female sex, and high disease activity are specifically associated with worse HRQoL in patients with Behçet’s syndrome; all patients have worse SF-36 scores compared with healthy controls.^{8,71} Sexual function can be impaired in men and women.⁷²

A systematic review of outcome measures used in Behçet’s syndrome by the OMERACT Vasculitis Working Group revealed large variability in terms of outcomes, including PROs used across trials.⁷³ Generic measures to evaluate HRQoL in Behçet’s syndrome include the EQ-5D,⁷³ but mainly the SF-36,⁷⁴. Symptom-specific PROs have also been used in Behçet’s syndrome, including the Oral Health and Related Quality of Life Scale⁷⁵ and the Arizona Sexual Experience Scale.⁷² Psychological impact has most commonly been measured using Beck Anxiety Scale^{76,77} and the Beck Depression Index.⁷⁸

The review identified a validated disease-specific PRO, the Behçet’s Disease Quality of Life Scale (BD-QoL),^{37,77,79,80} which was developed in the United Kingdom and has undergone cross-cultural adaptation and validation in Korean and Arabic.^{79,81} Item development was based on the qualitative work with patients with BD and included the following salient themes: “Relationships”, “Emotions”, “Limitations in Day to Day Activities”, and “Self-Image”.³⁷

Conclusion

Patients with systemic vasculitides have different perspectives on their disease and its impact to their clinicians. It is important to capture the patient perspective accurately and reliably within clinical studies using validated outcome measures, which assess areas of greatest importance to patients.

A limitation of PROs is that some aspects of a condition, which are objectively important to measure and very relevant to outcome (eg, blood pressure), may not be experienced by patients and therefore not represented. PROs are, therefore, complementary to physician-derived outcomes in terms of determining what matters most to patients with vasculitis, in relation to their disease and its treatment. Greater precision when measuring the impact on patients, for example, in terms of adverse effects and fatigue, will facilitate targeted assessment of novel pharmacological and non-pharmacological interventions. There are advantages of using generic PROs, such as the SF-36, which facilitates direct comparison across diseases and, in some contexts, allows for unforeseen side effects to be detected; and the disease-specific PROs, such as the BD-QoL, which has fine-tuned, specific elements, with high face validity to patients with the disease in question. There is, therefore, a role for both.

The growing recognition of the importance of PROs in the assessment of vasculitis, and the availability of validated instruments to capture PROs in vasculitis may also mean that patients’ perspectives will be incorporated into composite outcome measures in future trials.

Disclosure

JCR, PAM, and JD developed the AAV-PRO. The authors report no other conflicts of interests in this work.

References

1. Luqmani R, Suppiah R, Edwards CJ, et al. Mortality in Wegener’s granulomatosis: a bimodal pattern. *Rheumatology (Oxford)*. 2011;50(4):697–702.
2. Robson J, Doll H, Suppiah R, et al. Damage in the ANCA-associated vasculitides: long-term data from the European vasculitis study group (EUVAS) therapeutic trials. *Ann Rheum Dis*. 2015;74(1):177–184.
3. Nazareth R, Mason JC. Takayasu arteritis: severe consequences of delayed diagnosis. *QJM*. 2011;104(9):797–800.
4. Jones RB, Tervaert JW, Hauser T, et al; European Vasculitis Study Group. Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis. *N Engl J Med*. 2010;363(3):211–220.
5. Stone JH, Tuckwell K, Dimonaco S, et al. Trial of Tocilizumab in giant-cell arteritis. *N Engl J Med*. 2017;377(4):317–328.
6. Guillevin L, Pagnoux C, Karras A, et al. Rituximab versus azathioprine for maintenance in ANCA-associated vasculitis. *N Engl J Med*. 2014;371(19):1771–1780.
7. Abularrage CJ, Slidell MB, Sidawy AN, Kreishman P, Amdur RL, Arora S. Quality of life of patients with Takayasu’s arteritis. *J Vasc Surg*. 2008;47(1):131–137.
8. Bodur H, Borman P, Ozdemir Y, Atan C, Kural G. Quality of life and life satisfaction in patients with Behçet’s disease: relationship with disease activity. *Clin Rheumatol*. 2006;25(3):329–333.
9. Koutantji M, Harrold E, Lane SE, Pearce S, Watts RA, Scott DG. Investigation of quality of life, mood, pain, disability, and disease status in primary systemic vasculitis. *Arthritis Rheum*. 2003;49(6):826–837.
10. Robson JC, Dawson J, Cronholm PF, et al. Health-related quality of life in ANCA-associated vasculitis and item generation for a disease-specific patient-reported outcome measure. *Patient Relat Outcome Meas*. 2018;9:17–34.

11. Hellmann DB, Uhlfelder ML, Stone JH, et al. Domains of health-related quality of life important to patients with giant cell arteritis. *Arthritis Rheum.* 2003;49(6):819–825.
12. Benarous L, Terrier B, Laborde-Casterot H, et al. Employment, work disability and quality of life in patients with ANCA-associated vasculitides. The EXPOVAS study. *Clin Exp Rheumatol.* 2017;35 (Suppl) 103(1):40–46.
13. Fredi M, Lazzaroni MG, Tani C, et al. Systemic vasculitis and pregnancy: a multicenter study on maternal and neonatal outcome of 65 prospectively followed pregnancies. *Autoimmun Rev.* 2015;14(8):686–691.
14. Clowse ME, Richeson RL, Pieper C, Merkel PA; Vasculitis Clinical Research Consortium. Pregnancy outcomes among patients with vasculitis. *Arthritis Care Res (Hoboken).* 2013;65(8):1370–1374.
15. Liddle J, Bartlam R, Mallen CD, et al. What is the impact of giant cell arteritis on patients' lives? A UK qualitative study. *BMJ Open.* 2017;7(8):e017073.
16. RARDA. Reduce, improve, empower. *Addressing the shared needs of rare autoimmune rheumatic diseases*; 2018.
17. Herlyn K, Hellmich B, Seo P, Merkel PA. Patient-reported outcome assessment in vasculitis may provide important data and a unique perspective. *Arthritis Care Res (Hoboken).* 2010;62(11):1639–1645.
18. Seo P, Jayne D, Luqmani R, Merkel PA. Assessment of damage in vasculitis: expert ratings of damage. *Rheumatology (Oxford).* 2009;48(7):823–827.
19. Tugwell P, Boers M, Brooks P, Simon L, Strand V, Idzerda L. OMERACT: an international initiative to improve outcome measurement in rheumatology. *Trials.* 2007;8:38.
20. Merkel PA, Aydin SZ, Boers M, et al. The OMERACT core set of outcome measures for use in clinical trials of ANCA-associated vasculitis. *J Rheumatol.* 2011;38(7):1480–1486.
21. Sreih AG, Alibaz-Oner F, Kermani TA, et al. Development of a core set of outcome measures for large-vessel vasculitis: report from OMERACT 2016. *J Rheumatol.* 2017;44(12):1933–1937.
22. Hatemi G, Meara A, Ozguler Y. The omeract core domain set for clinical trials in behcet's syndrome. *Arthritis Rheum.* 2018;70.
23. Exley AR, Bacon PA, Luqmani RA, et al. Development and initial validation of the vasculitis damage index for the standardized clinical assessment of damage in the systemic vasculitides. *Arthritis Rheum.* 1997;40(2):371–380.
24. Robson JC, Dawson J, Doll H, et al. Validation of the ANCA-associated vasculitis patient-reported outcomes (AAV-PRO) questionnaire. *Ann Rheum Dis.* 2018;77(8):1157–1164.
25. Sreih AG, Alibaz-Oner F, Easley E, et al. Health-related outcomes of importance to patients with Takayasu's arteritis. *Clin Exp Rheumatol.* 2018;36(Suppl 111):51–57.
26. Hatemi G, Meara A, Ozguler Y, et al. Developing a core set of outcome measures for Behçet disease: report from OMERACT 2016. *J Rheumatol.* 2017;44(11):1750–1753.
27. Tomasson G, Farrar JT, Cuthbertson D. Fatigue and physical functioning in patients with giant cell arteritis. *Arthritis Rheum.* 2016;68(suppl 10).
28. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* 1992;30(6):473–483.
29. Fitzpatrick R, Davey C, Buxton MJ, Jones DR. Evaluating patient-based outcome measures for use in clinical trials. *Health Technol Assess.* 1998;2(14):i–iv, 1–74.
30. Stone JH, Merkel PA, Spiera R, et al; RAVE-ITN Research Group. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. *N Engl J Med.* 2010;363(3):221–232.
31. Jayne DRW, Bruchfeld AN, Harper L, et al; CLEAR Study Group. Randomized trial of c5a receptor inhibitor avacopan in ANCA-associated vasculitis. *J Am Soc Nephrol.* 2017;28(9):2756–2767.
32. Patrick DL, Burke LB, Powers JH, et al. Patient-reported outcomes to support medical product labeling claims: FDA perspective. *Value Health.* 2007;10 (Suppl) 2:S125–S137.
33. Fereday J, Muir-Cochrane E. Demonstrating rigor using thematic analysis: a hybrid approach of inductive and deductive coding and theme development. *Int J Qual Methods.* 2006;5(1):80–92.
34. Drennan J. Cognitive interviewing: verbal data in the design and pretesting of questionnaires. *J Adv Nurs.* 2003;42(1):57–63.
35. Costello A, Osborne J. Best practices in exploratory factor analysis: four recommendations for getting the most from your analysis. *Practical Assessment Res Eval.* 2005;10(7):1–9.
36. Tennant A, Conaghan PG. The Rasch measurement model in rheumatology: what is it and why use it? When should it be applied, and what should one look for in a Rasch paper? *Arthritis Rheum.* 2007;57(8):1358–1362.
37. Gilworth G, Chamberlain MA, Bhakta B, Haskard D, Silman A, Tennant A. Development of the BD-QoL: a quality of life measure specific to Behçet's disease. *J Rheumatol.* 2004;31(5):931–937.
38. Jennette JC, Falk RJ, Bacon PA. 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum.* 2013;65(1):1–11.
39. Walsh M, Flossmann O, Berden A, et al; European Vasculitis Study Group. Risk factors for relapse of antineutrophil cytoplasmic antibody-associated vasculitis. *Arthritis Rheum.* 2012;64(2):542–548.
40. Walsh M, Mukhtyar C, Mahr A, et al. Health-related quality of life in patients with newly diagnosed antineutrophil cytoplasmic antibody-associated vasculitis. *Arthritis Care Res (Hoboken).* 2011;63(7):1055–1061.
41. Tomasson G, Boers M, Walsh M, et al. Assessment of health-related quality of life as an outcome measure in granulomatosis with polyangiitis (Wegener's). *Arthritis Care Res (Hoboken).* 2012;64(2):273–279.
42. Pugno G, Pagnoux C, Terrier B, et al; French Vasculitis Study Group. Rituximab versus azathioprine for ANCA-associated vasculitis maintenance therapy: impact on global disability and health-related quality of life. *Clin Exp Rheumatol.* 2016;34(3 Suppl 97):S54–S59.
43. Basu N, Jones GT, Fluck N, et al. Fatigue: a principal contributor to impaired quality of life in ANCA-associated vasculitis. *Rheumatology (Oxford).* 2010;49(7):1383–1390.
44. Basu N, McClean A, Harper L, et al. Explaining fatigue in ANCA-associated vasculitis. *Rheumatology (Oxford).* 2013;52(9):1680–1685.
45. Robson JC, Milman N, Tomasson G, et al. Exploration, development, and validation of patient-reported outcomes in antineutrophil cytoplasmic antibody-associated vasculitis using the OMERACT process. *J Rheumatol.* 2015;42(11):2204–2209.
46. Matcham F, Scott IC, Rayner L, et al. The impact of rheumatoid arthritis on quality-of-life assessed using the SF-36: a systematic review and meta-analysis. *Semin Arthritis Rheum.* 2014;44(2):123–130.
47. Singh K, Kondal D, Shivashankar R, et al. Health-related quality of life variations by sociodemographic factors and chronic conditions in three metropolitan cities of South Asia: the CARRS study. *BMJ Open.* 2017;7(10):e018424.
48. Bailey PK, Hamilton AJ, Clissold RL, et al. Young adults' perspectives on living with kidney failure: a systematic review and thematic synthesis of qualitative studies. *BMJ Open.* 2018;8(1):e019926.
49. Grayson PC, Amudala NA, Mclear CA, et al. Illness perceptions and fatigue in systemic vasculitis. *Arthritis Care Res (Hoboken).* 2013;65(11):1835–1843.
50. Robson JC, Tomasson G, Milman N, et al. OMERACT Endorsement of Patient-reported Outcome Instruments in Antineutrophil Cytoplasmic Antibody-associated Vasculitis. *J Rheumatol.* 2017;44(10):1529–1535.
51. Petri H, Nevitt A, Sarsour K, Napalkov P, Collinson N. Incidence of giant cell arteritis and characteristics of patients: data-driven analysis of comorbidities. *Arthritis Care Res (Hoboken).* 2015;67(3):390–395.
52. Salvarani C, Pipitone N, Versari A, Hunder GG. Clinical features of polymyalgia rheumatica and giant cell arteritis. *Nat Rev Rheumatol.* 2012;8(9):509–521.
53. Salvarani C, Cimino L, Macchioni P, et al. Risk factors for visual loss in an Italian population-based cohort of patients with giant cell arteritis. *Arthritis Rheum.* 2005;53(2):293–297.

54. Mukhtyar C, Guillevin L, Cid MC, et al; European Vasculitis Study Group. EULAR recommendations for the management of large vessel vasculitis. *Ann Rheum Dis*. 2009;68(3):318–323.
55. Dasgupta B, Borg FA, Hassan N, et al; BSR and BHPR Standards, Guidelines and Audit Working Group. BSR and BHPR guidelines for the management of giant cell arteritis. *Rheumatology (Oxford)*. 2010;49(8):1594–1597.
56. Robson JC, Dawson J, Cronholm PF, et al. Patient perceptions of glucocorticoids in anti-neutrophil cytoplasmic antibody-associated vasculitis. *Rheumatol Int*. 2018;38(4):675–682–682.
57. Black RJ, Goodman SM, Ruediger C, Lester S, Mackie SL, Hill CL. A survey of glucocorticoid adverse effects and benefits in rheumatic diseases: the patient perspective. *J Clin Rheumatol*. 2017;23(8):416–420.
58. McDonough AK, Curtis JR, Saag KG. The epidemiology of glucocorticoid-associated adverse events. *Curr Opin Rheumatol*. 2008;20(2):131–137.
59. Fardet L, Flahault A, Kettaneh A, et al. Corticosteroid-induced clinical adverse events: frequency, risk factors and patient's opinion. *Br J Dermatol*. 2007;157(1):142–148.
60. Strand V, Dimonaco S, Tuckwell K, Klearman M, Collinson N, Stone J. Health-related quality of life in patients with giant cell arteritis treated with Tocilizumab in a Randomized Controlled Phase 3 Trial. *Arthritis Rheum*. 2017;69(suppl 10).
61. Kupersmith MJ, Speira R, Langer R, et al. Visual function and quality of life among patients with giant cell (temporal) arteritis. *J Neuroophthalmol*. 2001;21(4):266–273.
62. Jobard S, Magnant J, Blasco H, et al. Quality of life of patients treated for giant cell arteritis: a case-control study. *Clin Rheumatol*. 2017;36(9):2055–2062.
63. Aydin SZ, Direskeneli H, Sreih A, et al. Update on outcome measure development for large vessel vasculitis: report from OMERACT 12. *J Rheumatol*. 2015;42(12):2465–2469.
64. Robson J, Almeida C, Dawson J, et al. A multinational qualitative study in giant cell arteritis: patient perceptions of diagnosis, treatment, impact on health-related quality of life and contextual factors. *Ann Rheum Dis*. 2018;17:777.
65. Mason JC. Takayasu arteritis – advances in diagnosis and management. *Nat Rev Rheumatol*. 2010;6(7):406–415.
66. Yilmaz N, Can M, Oner FA, et al. Impaired quality of life, disability and mental health in Takayasu's arteritis. *Rheumatology (Oxford)*. 2013;52(10):1898–1904.
67. Akar S, Can G, Binicier O, et al. Quality of life in patients with Takayasu's arteritis is impaired and comparable with rheumatoid arthritis and ankylosing spondylitis patients. *Clin Rheumatol*. 2008;27(7):859–865.
68. Direskeneli H, Aydin SZ, Kermani TA, et al. Development of outcome measures for large-vessel vasculitis for use in clinical trials: opportunities, challenges, and research agenda. *J Rheumatol*. 2011;38(7):1471–1479.
69. Hatemi G, Christensen R, Bang D. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. *Ann Rheum Dis*. 2018;2018;77(6):808–818.
70. Kalra S, Silman A, Akman-Demir G, et al. Diagnosis and management of neuro-Behçet's disease: international consensus recommendations. *J Neurol*. 2014;261(9):1662–1676.
71. Fabiani C, Vitale A, Orlando I, et al. Quality of life impairment in Behçet's disease and relationship with disease activity: a prospective study. *Intern Emerg Med*. 2017;12(7):947–955.
72. Gül IG, Kartalci Ş, Cumurcu BE, Karıncaoğlu Y, Yoloğlu S, Karlıdağ R. Evaluation of sexual function in patients presenting with Behçet's disease with or without depression. *J Eur Acad Dermatol Venereol*. 2013;27(10):1244–1251.
73. Hatemi G, Merkel PA, Hamuryudan V, et al. Outcome measures used in clinical trials for Behçet syndrome: a systematic review. *J Rheumatol*. 2014;41(3):599–612.
74. Ertam I, Kitapcioglu G, Aksu K, et al. Quality of life and its relation with disease severity in Behçet's disease. *Clin Exp Rheumatol*. 2009;27(2 Suppl 53):S18–S22.
75. Mumcu G, Niazi S, Stewart J, et al. Oral health and related quality of life status in patients from UK and Turkey: a comparative study in Behçet's disease. *J Oral Pathol Med*. 2009;38(5):406–409.
76. Calikoglu E, Onder M, Cosar B, Candansayar S. Depression, anxiety levels and general psychological profile in Behçet's disease. *Dermatol-ogy*. 2001;203(3):238–240.
77. Hatemi G, Melikoglu M, Tunc R, et al. Apremilast for Behçet's syndrome—a phase 2, placebo-controlled study. *N Engl J Med*. 2015;372(16):1510–1518.
78. Melikoglu MA, Melikoglu M. The relationship between disease activity and depression in patients with Behçet disease and rheumatoid arthritis. *Rheumatol Int*. 2010;30(7):941–946.
79. Touma Z, Ghandour L, Sibai A, et al. Cross-cultural adaptation and validation of Behçet's disease quality of life questionnaire. *BMC Med Res Methodol*. 2011;11:52.
80. Lee J, Kim SS, Jeong HJ, et al. Association of sleep quality in Behçet disease with disease activity, depression, and quality of life in Korean population. *Korean J Intern Med*. 2017;32(2):352–359.
81. Choi HJ, Seo MR, Ryu HJ, Baek HJ. Cross-cultural adaptation and validation of the Behçet's disease current activity form in Korea. *Korean J Intern Med*. 2015;30(5):714–718.

Patient Related Outcome Measures

Publish your work in this journal

Patient Related Outcome Measures is an international, peer-reviewed, open access journal focusing on treatment outcomes specifically relevant to patients. All aspects of patient care are addressed within the journal and practitioners from all disciplines are invited to submit their work as well as healthcare researchers and patient support groups.

Submit your manuscript here: <http://www.dovepress.com/patient-related-outcome-measures-journal>

Dovepress

The journal is included in PubMed. The manuscript management system is completely online and includes a very quick and fair peer-review system. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.