Updating OMERACT Core Set of Domains for ANCA-associated Vasculitis: Patient Perspective Using the International Classification of Function, Disability, and Health

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ABSTRACT. Objective. Aspects of antineutrophil cytoplasmic antibodies–associated vasculitis (AAV) prioritized by patients with AAV were described using the International Classification of Function, Disability, and Health (ICF).

Methods. Items identified during 14 individual interviews were incorporated into an ICF-based questionnaire administered to participants of 2 vasculitis patient symposia: 36 in the United Kingdom and 63 in the United States.

Results. Categories identified as at least "moderately relevant" by ≥ 5% of subjects included 44 body functions, 14 body structures, 35 activities and participation, 31 environmental factors, and 38 personal factors.

Conclusion. Identified categories differ from those identified by the current Outcome Measures in Rheumatology (OMERACT) core set and those prioritized by vasculitis experts. (First Release May 1 2019; J Rheumatol 2019;46:1415-20; doi:10.3899/jrheum.181073)

Key Indexing Terms:
OMERACT   VASCULITIS   OUTCOME ASSESSMENT

The vasculitides are a group of heterogeneous conditions characterized by inflammation of blood vessels. Anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV) are small vessel vasculitides that include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic GPA (EGPA). AAV can affect practically any organ system, with manifestations ranging from diseases of the ears, nose, and sinuses to life-threatening failure of kidneys, lungs, or heart.

Outcome Measures in Rheumatology (OMERACT) is an international organization that strives to develop data-driven, optimal outcome measures for use in clinical trials[1]. In 2010, OMERACT endorsed a core set of outcome measures for ANCA-associated vasculitis[2]. Subsequently, a framework was developed for the selection of areas and domains that should be assessed in clinical trials, referred to as the OMERACT Filter 2.0 framework[1,3]; it calls for inclusion of a range of stakeholders, especially patients, into the process of outcome measure development.

The OMERACT Vasculitis Working Group has conducted several projects aimed at updating and expanding the existing expert-driven OMERACT core set for AAV[4,5], including this project, which uses the International Classification of Function, Disability and Health (ICF). The ICF is a general health status framework[6] that views health as a broad concept shaped by the relationship between various ICF components: impairments of body functions and body structures, limitations of activities, restrictions of participation, and the influence of environmental and personal contextual factors[6]. The ICF also offers a classification system to describe functioning and health using categories organized into a 4-level hierarchically nested structure[6]. The OMERACT initiative endorsed the ICF as a tool to identify and classify (sub)domains relevant to measurement of outcomes for a specific medical condition[1].

This manuscript describes the ICF-based analysis of aspects of health prioritized by patients with AAV.

MATERIALS AND METHODS
The study consisted of 2 parts, both overseen by a steering committee composed of content experts, methodologists (including qualitative experts),

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and patients with AAV. The research received approval from the Ottawa Hospital's Research Ethics Board (protocol #20120604-01H and #20150189-01H), and all participating patients gave informed consent.

The first, qualitative part of the study consisted of a series of individual semistructured interviews conducted with English-speaking adult patients with AAV at the Ottawa Hospital in Ottawa, Ontario, Canada, and the Nuffield Orthopaedic Centre in Oxford, UK. A purposive sampling strategy was used to select interviews for our study and aimed at including patients with each of the 3 types of AAV, with different severities, and at different stages of disease[7]; interviews were performed until saturation of the identified concepts was reached[8].

Interviews were audio recorded, professionally transcribed, and all basic concepts were "linked" to the most precise ICF category according to previously established ICF linking rules by Cieza, et al[9,10], and then summarized on the second ICF level, as we described previously[11]. Because personal factors are currently not classified by the ICF, the general scheme proposed by Geyh, et al[12] was followed. It divides the personal factors into 3 broad groups: (1) "facts" about the individual's position in the physical, social, and temporal context, (2) "experience" of the concept in question (feelings, thoughts, beliefs, and motives), and (3) "patterns" of experience and behavior including personality traits and habits.

In the second part of the study, categories identified through the qualitative analysis were incorporated into an ICF-based questionnaire that was administered to participants of 2 vasculitis patient symposia: the International Vasculitis and ANCA Workshop in London, UK, April 18, 2015, and the Vasculitis Foundation symposium in Jacksonville, Florida, USA, June 19–21, 2015. Participants rated the relevance of each listed category on a standardized ordinal scale associated with the ICF classification[6]. The physiologic effects of vasculitis and its effects on patients' activities were rated on a 5-level scale from 0 to 4 with the following categories: "no effect," "mild," "moderate," "severe," and "complete impairment." The relevance of environmental and personal factors was rated on a 9-level scale from –4 ("extreme negative effect on health"), through the same gradations to 0 ("no effect"), and then to +4 ("extreme positive effect"). Factors that have at least "moderate" effect for at least 5% of respondents were selected, as suggested previously[13].

RESULTS
Fourteen individual interviews (10 from Ottawa, Ontario, Canada, and 4 from Oxford, UK) were available for the qualitative portion of the study. Participants identified a wide range of important aspects of AAV that were linked to 159 ICF categories.

The underlying qualitative findings were incorporated into a questionnaire administered to about 100 participants at each of the 2 vasculitis patient symposia described above; 51 and 74 patients from the United Kingdom and United States returned the questionnaire, and 36 and 63 (respectively) had AAV and were included in this analysis. Participants' demographic and clinical characteristics are summarized in Appendix 1; the respondents' disease spectrum was representative of a general population of patients with AAV.

All the categories presented in the questionnaire were rated as at least "moderately relevant" by at least 5% of subjects. This includes 44 second-level categories in the ICF component body functions, 14 in body structures, 35 in activities and participation, 31 in environmental factors, and 38 in personal factors. A subset of the most relevant categories, ranked as at least "moderately relevant" by at least 30% of participants, is summarized in Table 1, Table 2, and Table 3.

Table 1. Categories from the International Classification of Function (ICF) compenents Body Functions, Body Structures, and Activities and Participation identified as at least moderately important by at least 30% of participants.

ICF Code	ICF Category Description	% Ranking Category as ≥ Moderately Impaired
Body functions		
b1	Mental functions	
b130	Energy and drive	
b1300	• Energy	87
b1301	• Motivation (wanting to do things)	59
b1302	• Appetite	47
b134	Sleep (quality and quantity)	68
b147	Agitation, feeling "jittery"	31
b152	Emotions such as feeling down or depressed, anxious, frustrated	46
b180	Body image (one's satisfaction with their look)	42
b2	Sensory functions, pain, voice and speech	
b230	Hearing	40
b240	Sensations related to the ears — ringing, irritation, pressure	38
b279	Numbness, decreased sensation (peripheral sensory neuropathy)	47
b280	Pain	80
b4	Cardiovascular, hematological, immunological, respiratory systems	
b420	Blood pressure	35
b435	Functions of immune system: protection against infections, hypersensitivity reactions (e.g., allergies)	50
b440	Lung function (breathing, results of lung function tests)	50
b455	Exercise tolerance	67
b460	Shortness of breath, wheezing, chest tightness/other sensations associated with lungs or heart	56
b5	Digestive, metabolic, and endocrine functions	
b530	Weight issues (weight loss or gain)	64
b535	Sensations related to digestive system: nausea, feeling bloated, heartburn, abdominal cramps	40
b550	Fever, chills, sweats	46
Other body functions		
b310	Ability to speak, quality of voice	30
b610	Functions of kidney and bladder (making urine, peeing)	37
b710	Joint functions (moving joints, etc.)	44
b840	Sensation related to the skin: itching, burning, and tingling	34
Body structures		
s310	Nose	55
nc-bs*	Sinuses	59
s430	Lungs and airways (breathing tubes)	53
s6100	Kidneys and urinary bladder	37
s7701	Joints (includes arthritis)	42
s810	Skin — rashes, scarring, thinning, and breaking down	34
Activities and participation		
d4	Mobility	
d430	Lifting and carrying objects	37
d450	Walking	42
d4551	Climbing (e.g., stairs)	52
Other activities and participation		
d920	Recreation and leisurely activities	65

ICF code is a numeric identifier that uniquely identifies each ICF category; it starts with a letter that denotes the ICF component (b: body functions; s: body structures; d: activities and participation) and is followed by numbers that specify progressively more detailed categories; for example, category b1300 (energy) is a subcategory of the broader category b130 (energy and drive). *Not covered – body structures; category not covered by the current ICF classification.

A greater proportion of participants from the United States compared to the United Kingdom reported financial situation and healthcare system issues, such as access to medications, as relevant to their health (38% and 60% vs 19% and 44%, respectively). Similarly, more American participants reported positive effects of having vasculitis (personal factors → experience of vasculitis), including increased appreciation of life, increased sensitivity to other people's misfortunes, and increasing activities related to helping others (72%, 73%, and 64% vs 42%, 36%, and 39%, respectively). In contrast, the effect of the vasculitis on patients' ability to travel (activities and participation → recreation and leisurely activities) was reported as at least moderately relevant by 61% of participants from the United Kingdom compared to 29% of Americans.

Similar analyses by type of AAV demonstrated expected

Table 2. International Classification of Function (ICF) Environmental Factors identified as at least moderately relevant by at least 30% of participants.

ICF Code	ICF Category Description	% Ranking Category as ≥ Moderately Relevant
e1	Products and technology	
e1101	Medications	75
	• Unwanted side effects of medications	64
	• Unwanted side effects of prednisone specifically	73
e130	Products and technology for education (books, computer hardware and software, Internet)	42
e1650	Financial assets (money), tangible assets (houses, land, owned goods, and technology), other assets	31
e3	Support and relationships	
e310	Immediate family	79
e320	Friends	72
e325	Acquaintances, peers, colleagues, neighbours, community members	51
e350	Health professionals	82
nc-cf*	Support from others in a similar situation – e.g., other patients with vasculitis, patients with other chronic conditions, support groups	63
eE4	Attitudes (of family members, friends, colleagues, health professionals, etc.)	
e410	Attitudes of immediate family members	73
e420	Attitudes of friends	61
e425	Attitudes of acquaintances, peers, colleagues, neighbours, and community members	47
e450	Attitudes of health professionals	73
Other factors that may affect health		
e260	Air quality	32
e580	Health-related services, systems and policies including access to medical services and medications, health insurance	55
nc-cf*	Information about disease and drugs, either provided by healthcare providers or researched in journals, books, or Internet	71
nc-cf *	Living arrangement — private house or apartment, amount of external noise, proximity to traffic, to parks or exercise facilities, etc.	50
nc-cf *	Stress – physical or psychological stress from any source	49
nc-cf *	Clinical research in teaching hospitals	33

ICF code is a numeric identifier that uniquely identifies each ICF category; it starts with a letter that denotes the ICF component ("e" for environmental factors) and is followed by numbers that specify progressively more detailed categories; for example, category e310 (family members) is a subcategory of the broader category e3 (support and relationships). *Not covered – contextual factors; category not covered by the current ICF classification.

Table 3. International Classification of Function (ICF) Personal Factors identified as at least moderately relevant by at least 30% of participants.

ICF Code and Category Description	% Ranking Category as ≥ Moderately Relevant
p1: Facts about individual and his/her personal life	
Demographic characteristics	
Marital status	40
Health literacy — one's ability to understand the nature of vasculitis and prescribed treatments	76
Occupation — job or profession	37
Personal history and biography	
Personal and family circumstances — specific events in one's personal life	37
Roles and responsibilities in one's family (dependents to look after, etc.)	40
Financial situation	48
p2: One's experience of vasculitis	
General well-being (how well do you feel overall compared to how you were before the diagnosis of vasculitis?)	67
Mental/psychological well-being	35
Feelings/emotions/mood related to vasculitis or its treatments	68
Thoughts and beliefs related to vasculitis or its treatments	93
Change of potential and goals	61
p3: Personality, habits, and patterns of behavior	
Personality	73
Habits	81
Lifestyle, interests, and hobbies before diagnosis	68
Health-related habits (tendency to look after oneself, compliance with treatments, interest in own health)	72
Adaptation to chronic illness	75

trends: more respondents with EGPA reporting an effect of their disease on the heart and lungs and a prominent effect of air quality (consistent with asthma being a central feature of the disease); subjects with MPA had the most difficulty with blood pressure and kidneys. Further, subjects with MPA seemed to be most affected by the various aspects of their psychosocial functions, including mental functions (motivation, appetite, concentration, and emotions); domestic, community, and social life (activities and participation); and interpersonal interactions and relationships (environmental factors).

DISCUSSION

In our analysis mainly limited by the narrow geographic sampling, the ICF was a useful framework for describing aspects of AAV relevant to patients. Comparisons of prioritized items by country of residence and by diagnosis revealed that while the majority of differences between the 3 different forms of AAV were in keeping with the expected differences in the frequencies of specific organ involvement, most variability between the 2 participating countries was seen in the importance of various contextual factors. As the role of contextual factors in interpreting outcome measures continues to be clarified[14], considering some key contextual factors will deepen the ability to fully assess the effect of AAV and other diseases.

An earlier ICF-based analysis of the current OMERACT Core Set for AAV[11] revealed that it does not measure the whole spectrum of limitations in activities and participation prioritized by patients in this study. In addition, it covers only a small number of environmental and personal factors, likely because contextual factors have only recently become recognized as relevant for interpreting the measured outcomes[14]. The areas under-sampled by the core set were also found to be less important to vasculitis clinical experts in a recent ICF-based analysis[15]; this is not surprising, given that the composite tools that constitute the current OMERACT core set for AAV were designed by the same clinical experts. Notably, the few contextual factors that clinicians did identify as important differ from those prioritized by patients: clinicians focus on hard "objective" factors such as demographics, comorbidities, availability of health services, and social support[15], while the range of factors identified by patients is much broader and dominated by the more subjective factors such as attitudes of other people and patients' own reactions and thoughts. In contrast, several of the more severe disease manifestations of AAV, such as lung and kidney involvement, visual impairment, and hearing loss, which are prioritized by the majority of vasculitis clinical experts[15], were rated as at least "moderately relevant" by < 50% of patient participants, likely reflecting the frequency of these manifestations in the cohort. Along with similar findings in other studies[16], the observed differences in perspectives of patients and clinicians support OMERACT's recommendation to include perspectives of different stakeholders, including patients, into the process of development of core sets of domains and outcome measures[1]. To comply with these standards, the OMERACT Vasculitis Working Group is working to update the current OMERACT core set for AAV.

REFERENCES

1. Boers M, Kirwan JR, Wells G, Beaton D, Gossec L, d'Agostino MA, et al. Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. J Clin Epidemiol 2014;67:745-53.
2. Merkel PA, Aydin SZ, Boers M, Direskeneli H, Herlyn K, Seo P, et al. The OMERACT core set of outcome measures for use in clinical trials of ANCA-associated vasculitis. J Rheumatol 2011;38:1480-6.
3. Boers M, Kirwan JR, Tugwell P, Beaton D, Bingham CO III, Conaghan PG, et al. The OMERACT Handbook. [Internet. Accessed August 24, 2018.] Available from: https://omeract.org/resources
4. Robson JC, Tomasson G, Milman N, Ashdown S, Boonen A, Casey GC, et al. OMERACT endorsement of patient-reported outcome instruments in antineutrophil cytoplasmic antibody-associated vasculitis. J Rheumatol 2017;44:1529-35.
5. Merkel PA, Aydin SZ, Boers M, Cornell C, Direskeneli H, Gebhart D, et al. Current status of outcome measure development in vasculitis. J Rheumatol 2014;41:593-8.
6. World Health Organization. ICF-international classification of functioning, disability and health. Geneva: World Health Organization Library; 2001.
7. Robson JC, Dawson J, Cronholm PF, Milman N, Kellom KS, Ashdown S, 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.
8. Kerr C, Nixon A, Wild D. Assessing and demonstrating data saturation in qualitative inquiry supporting patient-reported outcomes research. Expert Rev Pharmacoecon Outcomes Res 2010;10:269-81.
9. Cieza A, Brockow T, Ewert T, Amman E, Kollerits B, Chatterji S, et al. Linking health-status measurements to the international classification of functioning, disability and health. J Rehabil Med 2002;34:205-10.
10. Cieza A, Geyh S, Chatterji S, Kostanjsek N, Ustün B, Stucki G. ICF linking rules: an update based on lessons learned. J Rehabil Med 2005;37:212-8.
11. Milman N, Boonen A, Merkel PA, Tugwell P. Mapping of the outcome measures in rheumatology core set for antineutrophil cytoplasmic antibody-associated vasculitis to the International Classification of Function, Disability and Health. Arthritis Care Res 2015;67:255-63.
12. Geyh S, Müller R, Peter C, Bickenbach JE, Post MW, Stucki G, et al. Capturing the psychologic-personal perspective in spinal cord injury. Am J Phys Med Rehabil 2011;90:S79-96.
13. Cieza A, Hilfiker R, Boonen A, van der Heijde D, Braun J, Stucki G. Towards an ICF-based clinical measure of functioning in people with ankylosing spondylitis: a methodological exploration. Disabil Rehabil 2009;31:528-37.
14. Finger ME, Boonen A, Woodworth TG, Escorpizo R, Christensen R, Nielsen SM, et al. An OMERACT initiative toward consensus to identify and characterize candidate contextual factors: report from the contextual factors working group. J Rheumatol 2017;44:1734-9.
15. Milman N, Boonen A, Tugwell P, Merkel PA; OMERACT Vasculitis

Working Group. Clinicians' perspective on key domains in ANCA-associated vasculitis: a Delphi exercise. Scand J Rheumatol 2017;46:112-7.

16. 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 2010;62:1639-45.

APPENDIX 1. Demographic characteristics of participants. Values are n (%) unless otherwise specified.

Characteristic	UK Cohort, n = 36	USA Cohort, n = 63	All, n = 99
Age, yrs, mean	60	54	56
Female	21 (58)	40 (64)	61 (62)
Country of residence			
Canada		8 (13)	8 (8)
UK	36 (100)		36 (36)
USA		54 (85.7)	54 (55)
Not answered		1 (2)	1 (1)
Race			
White	36 (100)	62 (98)	99 (99)
Not answered		1 (2)	1 (1)
Highest education			
No formal qualifications	0	1 (2)	1 (1)
School/high school diploma	7 (19.4)	9 (14)	16 (16)
Vocational training	5 (14)	3 (5)	8 (8)
Degree or higher qualifications	23 (64)	50 (79)	73 (74)
Not answered	1 (3)		1 (1)
Employment status			
Employed with income	11 (31)	30 (48)	41 (41)
Employed without income	1 (3)	2 (3)	3 (3)
Homemaker	1 (3)	0	1 (1)
Retired because of vasculitis	5 (14)	7 (11)	12 (12)
Retired not because of vasculitis	16 (44)	20 (32)	36 (36)
Disabled because of vasculitis	2 (6)	4 (6)	6 (6)
Type of vasculitis			
GPA	21 (58)	46 (73)	67 (68)
MPA	7 (19)	7 (11)	14 (14)
EGPA	8 (22)	10 (16)	18 (18)
Duration of disease, mean, yrs	6	8	7
Active vasculitis at time of survey			
(self-reported)	9 (25)	14 (22)	23 (23)
Current medications			
Asthma Inhalers	6 (17)	16(25)	22 (22)
Azathioprine	8 (22)	17(27)	25(25)
Cyclophosphamide	1 (3)	1(2)	2(2)
Cyclosporine	0	0	0
Glucocorticoids	21 (58)	31 (49)	52(53)
Methotrexate	6 (17)	11 (18)	17(17)
Mycophenolate	8 (22)	6 (10)	14(14)
Rituximab	6 (17)	11 (18)	17(17)
Other	12 (33)	14 (22)	26(26)
Organ systems involved (self-reported)			
Aorta or other large blood vessels	0	1 (2)	1(1)
Brain	2 (6)	4 (6)	6 (6)
Ears or sinuses	23 (64)	52 (83)	76 (76)
Eyes	16 (44)	22 (35)	38 (38)
Heart	4 (11)	10 (16)	14 (14)
Joints	13 (36)	32 (52)	46 (47)
Kidneys	14 (39)	29 (46)	43 (43)
Lungs or airways	27 (75)	46 (73)	73 (74)
Nerves	19 (53)	24 (38)	43 (43)
Skin	11 (30)	19 (30)	30 (30)

GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; EGPA: eosinophilic granulomatosis with polyangiitis.