Objective. To develop and validate revised classification criteria for granulomatosis with polyangiitis (GPA).

Methods. Patients with vasculitis or comparator diseases were recruited into an international cohort. The study proceeded in 5 phases: 1) identification of candidate criteria items using consensus methodology, 2) prospective collection of candidate items present at the time of diagnosis, 3) data-driven reduction of the number of candidate items, 4) expert panel review of cases to define the reference diagnosis, and 5) derivation of a points-based risk score for disease classification in a development set using least absolute shrinkage and selection operator logistic regression, with subsequent validation of performance characteristics in an independent set of cases and comparators.

Results. The development set for GPA consisted of 578 cases of GPA and 652 comparators. The validation set consisted of an additional 146 cases of GPA and 161 comparators. From 91 candidate items, regression analysis identified 26 items for GPA, 10 of which were retained. The final criteria and their weights were as follows: bloody nasal discharge, nasal crusting, or sino-nasal congestion (+3); cartilaginous involvement (+2); conductive or sensorineural hearing loss (+1); cytoplasmic antineutrophil cytoplasmic antibody (ANCA) or anti–proteinase 3 ANCA positivity (+5); pulmonary nodules, mass, or cavitation on chest imaging (+2); granuloma or giant cells on biopsy (+2); inflammation or consolidation of the nasal/paranasal sinuses on imaging (+1); pauci-immune glomerulonephritis (+1); perinuclear ANCA or antimiylperoxidase ANCA positivity (–1); and eosinophil count ≥1 × 10⁹/liter (–4). After excluding mimics of vasculitis, a patient with a diagnosis of small- or medium-vessel vasculitis could be classified as having GPA if the cumulative score was ≥5 points. When these criteria were tested in the validation data set, the sensitivity was 93% (95% confidence interval [95% CI] 87–96%) and the specificity was 94% (95% CI 89–97%).

Conclusion. The 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for GPA demonstrate strong performance characteristics and are validated for use in research.
INTRODUCTION

The antineutrophil cytoplasmic antibody (ANCA)–associated vasculitides (AAV) are multisystem disorders involving inflammation of the small blood vessels and include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA) (1). GPA is characterized by necrotizing granulomatous inflammation involving the ears, nose, and upper and lower respiratory tracts, and necrotizing vasculitis affecting predominantly small- to medium-sized vessels, often including necrotizing glomerulonephritis (1).

Unlike diagnostic criteria, the purpose of classification criteria is to ensure that a homogeneous population is selected for inclusion in clinical trials and other research studies of GPA. In 1990, the American College of Rheumatology (ACR) published criteria for the classification of GPA (then named Wegener’s granulomatosis) (2–4). The 1990 criteria were effective and widely accepted, facilitating coordinated approaches to international randomized controlled trials (5,6). In 2011 it was proposed to change the name “Wegener’s granulomatosis” to “granulomatosis with polyangiitis” with subsequent wide adoption of the new terminology (7–9). The 1994 and 2012 publications of the international Chapel Hill Consensus Conference (CHCC) nomenclature for vasculitis clarified and standardized the nomenclature of the systemic vasculitides (1,10). The CHCC is a nomenclature system based on expert consensus rather than a classification system (1).

There are several important reasons for the development of revised classification criteria for the vasculitides, including a decline in the sensitivity of the 1990 ACR classification criteria, particularly for AAV (11); a consensus that any such criteria must now incorporate testing for ANCA; increased and widespread use, since 1990, of cross-sectional diagnostic imaging tools, including magnetic resonance imaging and computed tomography (12,13); and the introduction and adoption of the classification of patients with MPA, a term not in use in the 1990 ACR classification criteria.

There have been methodologic advances in the derivation of classification criteria, moving from the “number of criteria” rule, as used in the ACR 1990 criteria (3), toward weighted criteria with threshold scores, as demonstrated in the 2010 classification criteria for rheumatoid arthritis (14). Weighted criteria improve measurement properties of classification criteria because certain items within a criteria list may be more discriminative. The previous 1990 criteria for vasculitis collected retrospective data from patient files, without specification of which items were relevant at the time of diagnosis compared to those that were important later in the disease process. Criteria based on prospectively collected data sets from newly diagnosed patients should have higher face validity as inclusion criteria for future clinical trials of early-stage disease. This article outlines the development and validation of the revised ACR/European Alliance of Associations for Rheumatology (EULAR)–endorsed classification criteria for GPA.

METHODS

A detailed and complete description of the methods involved in the development and validation of the classification criteria for GPA is provided in Supplementary Appendix 1, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41986/abstract. Briefly, an international Steering Committee comprising clinician investigators with expertise in vasculitis, statisticians, and data managers was established to oversee the overall Diagnostic and Classification Criteria in Vasculitis (DCVAS) project (15). The Steering Committee established a 5-stage plan using data-driven and consensus methodology to develop the criteria for each of 6 forms of vasculitis.

Stage 1: generation of candidate classification items for the systemic vasculitides. Candidate classification items were generated by expert opinion and reviewed by a group of vasculitis experts across a range of specialties using a nominal group technique.

Stage 2: DCVAS prospective observational study. A prospective, international, multisite observational study was conducted (see Appendix A for study investigators and sites). Ethical approval was obtained from national and local ethics committees. Consecutive patients representing the full spectrum of disease were recruited from academic and community practices. Patients were included if they were 18 years or older and had a diagnosis of vasculitis or a condition that mimics vasculitis. Patients with AAV could only be enrolled within 2 years of diagnosis. Only data present at diagnosis were recorded.

Stage 3: refinement of candidate items specifically for AAV. The Steering Committee conducted a data-driven process to reduce the number of candidate items of relevance to cases and comparators for AAV. Items were selected for exclusion if they had a prevalence of <5% within the data set and/or they were not clinically relevant for classification criteria (e.g., related to infection, malignancy, or demographic characteristics). Low-frequency items of clinical importance could be combined, when appropriate.
Stage 4: expert review to derive a gold standard-defined set of cases of AAV. Experts in vasculitis from a wide range of geographic locations and specialties reviewed all submitted cases of vasculitis and a random selection of mimics of vasculitis. Each reviewer was asked to review ~50 submitted cases to confirm the diagnosis and to specify the certainty of their diagnosis as follows: very certain, moderately certain, uncertain, or very uncertain. Only cases agreed upon with at least moderate certainty were retained for further analysis.

Stage 5: derivation and validation of the final classification criteria for GPA. The DCVAS AAV data set was randomly split into development (80%) and validation (20%) sets. Comparisons were performed between cases of GPA confirmed by expert review and a comparator group randomly selected from the DCVAS cohort in the following proportions: another type of AAV (including MPA and EGPA), 64%; another form of small-vessel vasculitis (e.g., cryoglobulinemic vasculitis) or medium-vessel vasculitis (e.g., polyarteritis nodosa), 36%. Least absolute shrinkage and selection operator (lasso) logistic regression was used to identify items from the data set and create a parsimonious model including only the most important items. The final items in the model were formulated into a clinical risk-scoring tool with a threshold that best balanced sensitivity and specificity. A threshold for classifying GPA was identified for AAV.

In sensitivity analyses, the final classification criteria were applied to an unselected population of cases and comparators from the DCVAS data set based on the submitting physician diagnosis. Comparison was also made between the measurement properties of the new classification criteria for GPA and the 1990 ACR classification criteria for GPA using pooled data from the development and validation sets.

RESULTS

Generation of candidate classification items for the systemic vasculitides. The Steering Committee identified >1,000 candidate items for the DCVAS case report form (see Supplementary Appendix 2, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41986/abstract).

DCVAS prospective observational study. Between January 2011 and December 2017, the DCVAS study recruited 6,991 participants from 136 sites in 32 countries. Information on the DCVAS sites, investigators, and study participants is listed in Supplementary Appendices 3, 4, and 5, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41986/abstract.

Refinement of candidate items specifically for AAV. Following a data-driven and expert consensus process, 91 items from the DCVAS case report form were retained for regression analysis, including 45 clinical (14 composite), 18 laboratory (2 composite), 12 imaging (all composite), and 16 biopsy (1 composite) items. Some clinical items were removed in favor of similar but more specific pathophysiologic descriptors. Supplementary Appendix 6, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41986/abstract, lists the final candidate items used in the derivation of the classification criteria for GPA, MPA, and EGPA.

Expert review to derive a gold standard-defined final set of cases of AAV. Fifty-five independent experts reviewed vignettes derived from the case report forms for 2,871 cases submitted with a diagnosis of either small-vessel vasculitis

| Table 1. Demographic and disease features of cases of GPA and comparators* |
|---------------------------------|-------------------|----------------|
| Age, mean ± SD years           | 53.6 ± 16.2       | 56.4 ± 17.1    | 0.001 |
| Sex, no. (%) female            | 340 (47.0)        | 424 (52.2)     | 0.048 |
| Maximum serum creatinine, mean | 168.3 mg/dl       | 185.2          | 0.077 |
| Maximum eosinophil count ≥1 × 10^9/liter, no. (%) | 196 (27)         | 366 (45)       | <0.001 |

* cANCA = cytoplasmic antineutrophil cytoplasmic antibody; pANCA = perinuclear ANCA; anti–PR3-ANCA = anti-proteinase 3–ANCA; anti–MPO-ANCA = anti-myeloperoxidase-ANCA.
† Diagnoses of comparators for the classification criteria for granulomatosis with polyangiitis (GPA) included microscopic polyangiitis (n = 291), eosi

| GPA (n = 724) | Comparators (n = 813) |
|---------------|-----------------------|
| PR3-ANCA positive, no. (%) | 595 (82.2) | 21 (2.6) |
| MPO-ANCA positive, no. (%)  | 59 (8.1)  | 399 (49.1) |
| Maximum eosinophil count ≥1 × 10^9/liter, no. (%) | 196 (27) | 366 (45) | <0.001 |
(90% of case report forms) or another type of vasculitis or a mimic of vasculitis (10% of case report forms). The characteristics of the expert reviewers are shown in Supplementary Appendix 7, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41986/abstract. A flow chart showing the results of the expert review process is shown in Supplementary Appendix 8, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41986/abstract. A total of 2,072 cases (72%) passed the process and were designated as cases of vasculitis; these cases were used for the stage 5 analyses.

After expert review, 724 of 843 cases retained a reference diagnosis of GPA. There were 813 comparators randomly selected for analysis. Table 1 shows the demographic and disease features of the 1,537 cases included in this analysis (724 patients with GPA and 813 comparators), of which 1,230 (80%, 578 patients with GPA and 652 comparators) were in the development set, and 307 (20%, 146 patients with GPA and 161 comparators) were in the validation set.

**Derivation and validation of the final classification criteria for GPA.** Lasso logistic regression analysis using all 91 items resulted in a model of 26 independent items (see Supplementary Appendix 9B, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41986/abstract). The variables “positive test for cytoplasmic ANCA (cANCA)” and “positive test for anti–proteinase 3 (anti-PR3)
antibody" and the variables “positive test for perinuclear ANCA (pANCA)” and “positive test for antitymelperoxidase (anti-MPO) antibody” were strongly co-linear and were combined within the model as “positive test for cANCA or positive test for anti-PR3 antibody” and “positive test for pANCA or positive test for anti-MPO antibody,” respectively. Each item was scrutinized for inclusion based on statistical significance, clinical relevance, and specificity to GPA, resulting in 10 final items. Weighting of an individual criterion was based on logistic regression fitted to the 10 selected items (see Supplementary Appendix 10B, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41986/abstract).

**Model performance.** Use of a cutoff of ≥5 for total risk score (see Supplementary Appendix 11B, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41986/abstract, for different cut points) yielded a sensitivity of 92.5% (95% confidence interval [95% CI] 86.9–96.2%) and a specificity of 93.8% (95% CI 88.9–97.0%) in the validation set. The area under the curve (AUC) for the model was 0.98 (95% CI 0.98–0.99) in the development set and 0.99 (95% CI 0.98–1.00) in the validation set (Supplementary Appendix 12B, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41986/abstract). The final classification criteria for GPA are shown in Figure 1 (for the slide presentation version, see Supplementary Figure 1, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41986/abstract).

**Sensitivity analyses.** The classification criteria for GPA were applied to 2,511 patients randomly selected from the DCVAS database using the original physician-submitted diagnosis (n = 483 GPA and 2,028 comparators). Use of the same cut point of ≥5 points for the classification of GPA yielded a similar specificity of 94.6% but a lower sensitivity of 83.8%. This upheld the a priori hypothesis that specificity would remain unchanged but sensitivity would be reduced in a population with fewer clear-cut diagnoses of GPA (i.e., cases that did not pass expert review).

When the 1990 ACR classification criteria for GPA were applied to the DCVAS data set, the criteria performed poorly due to low sensitivity (69.3%) and moderate specificity (75.8%), with an AUC of 0.73 (95% CI 0.70–0.75).

**DISCUSSION**

Presented here are the final 2022 ACR/EULAR GPA classification criteria. A 5-stage approach has been used, underpinned by data from the multinational prospective DCVAS study and informed by expert review and consensus at each stage. The comparator group for developing and validating the criteria were other forms of AAV and other small- and medium-vessel vasculitides, the clinical entities where discrimination from GPA is difficult, but important. The new criteria for GPA have excellent sensitivity and specificity and incorporate ANCA testing and modern imaging techniques. The criteria were designed to have face and content validity for use in clinical trials and other research studies.

These criteria are validated and intended for the purpose of classification of vasculitis and are not appropriate for use in establishing a diagnosis of vasculitis. The aim of the classification criteria is to differentiate cases of GPA from similar types of vasculitis in research settings. Therefore, the criteria should only be applied when a diagnosis of small- or medium-vessel vasculitis has been made and all potential “vasculitis mimics” have been excluded. The exclusion of mimics is a key aspect of many classification criteria, including those for Sjögren’s syndrome (16) and rheumatoid arthritis (14). The 1990 ACR classification criteria for vasculitis perform poorly when used for diagnosis (i.e., when used to differentiate between cases of vasculitis versus mimics without vasculitis) (17), and it is expected that the 2022 criteria would also perform poorly if used inappropriately as diagnostic criteria in people in whom alternative diagnoses, such as infection or other non-vasculitis inflammatory diseases, are still being considered. The relatively low weight assigned to glomerulonephritis in these classification criteria highlights the distinction between classification and diagnostic criteria. While detection of kidney disease is important to diagnose GPA, glomerulonephritis is common among patients with either GPA or MPA and thus does not function as a strong classifier between these conditions.

These criteria differ from the previous 1990 ACR criteria in that they have been developed using cases presenting prospectively at the start of their disease process. This approach is different from the methods used to generate the 1990 ACR criteria, in which prevalent case records were utilized, potentially including items related to irreversible damage accrued over time. Inclusion of newly diagnosed cases in these criteria should improve their accuracy within the context of early intervention trials as well as refractory disease. The comparators used for these new criteria are also more appropriate and are closer mimics of GPA; for example, comparators with predominantly small-vessel vasculitides rather than predominantly giant cell arteritis were included. The new criteria perform better than previous criteria within this data set (11). ANCA is a major discriminator within these criteria, although patients can be classified as having GPA without having a positive test result for ANCA if they have a sufficient number of other features. These new criteria were validated in an independent data set and are weighted with threshold scores (14,16) to maximize predictive ability.

There are some study limitations to consider. Although this was the largest international study ever conducted in vasculitis, most patients were recruited from Europe, Asia, and North America. The performance characteristics of the criteria should be further tested in African and South American populations, which may have different clinical presentations of vasculitis. These
criteria were developed using data collected from adult patients with vasculitis. Although the clinical characteristics of GPA and the other vasculitides which these criteria were tested against are not known to differ substantially between adults and children, these criteria should be applied to children with some caution. The scope of the criteria is intentionally narrow and applies only to patients who have been diagnosed as having vasculitis. Diagnostic criteria are not specified. The criteria are intended to identify homogeneous populations of disease and, therefore, may not be appropriate for studies focused on the full spectrum of clinical heterogeneity in these conditions. To maximize relevance and face validity of the new criteria, study sites and expert reviewers were recruited from a broad range of countries and different medical specialties. Nonetheless, the majority of patients were recruited from academic rheumatology or nephrology units, which could have introduced referral bias.

A key strength of this study is the use of an independent expert review process to confirm cases of GPA and comparators to avoid the circularity of using predefined criteria to define the gold standard. Approximately one-quarter of cases were excluded via this process, due to either a lack of consensus on exact diagnosis or insufficient data available to make the diagnosis. A limitation of this approach, however, could be the exclusion of true, but less clearcut, cases submitted by the original physicians. It is important that cases are classified accurately for inclusion in clinical trials; therefore, some loss of sensitivity may be appropriate. Importantly, this study also demonstrated that applying the new criteria for GPA to the whole unselected DCVAS data set resulted in a reduction in sensitivity while maintaining specificity. Thus, the criteria should also be useful in a more generalized, “real-world” population.

The 2022 ACR/EULAR classification criteria for GPA are the product of a rigorous methodologic process that utilized an extensive data set generated by the work of a remarkable international group of collaborators. These criteria have been endorsed by the ACR and EULAR and are now ready for use to differentiate one type of vasculitis from another to define populations in research studies.

ACKNOWLEDGMENTS

We acknowledge the patients and clinicians who provided data to the DCVAS project.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Merkel had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Robson, Grayson, Ponte, Suppiah, Craven, Judge, Khalid, Hutchings, Watts, Merkel, Luqmani.

Acquisition of data. Robson, Grayson, Ponte, Suppiah, Craven, Judge, Hutchings, Watts, Merkel, Luqmani.

Analysis and interpretation of data. Robson, Grayson, Ponte, Suppiah, Craven, Judge, Khalid, Hutchings, Watts, Merkel, Luqmani.

REFERENCES

1. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference nomenclature of vasculitides. Arthritis Rheum 2013;65:1–11.
2. Fries JF, Hunder GG, Bloch DA, Michel BA, Arend WP, Calabrese LH, et al. The American College of Rheumatology 1990 criteria for the classification of vasculitis. Arthritis Rheum 1990;33:1135–6.
3. Bloch DA, Michel BA, Hunder GG, McShane DJ, Arend WP, Calabrese LH, et al. The American College of Rheumatology 1990 criteria for the classification of vasculitis: patients and methods. Arthritis Rheum 1990;33:1068–73.
4. Leavitt RY, Fauci AS, Bloch DA, Michel BA, Hunder GG, Arend WP, et al. The American College of Rheumatology 1990 criteria for the classification of Wegener’s granulomatosis. Arthritis Rheum 1990;33:1101–7.
5. Jones RB, Tervaert JW, Hauser T, Luqmani R, Morgan MD, Peh CA, et al. Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis. N Engl J Med 2010;362:211–20.
6. Stone JH, Merkel PA, Spiera R, See P, Langford CA, Hoffman GS, et al. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. N Engl J Med 2010;363:221–32.
7. Falk RJ, Gross WL, Guillevin L, Hoffman GS, Jayne DR, Jennette JC, et al. Granulomatosis with polyangiitis (Wegener’s): an alternative name for Wegener’s granulomatosis. Arthritis Rheum 2011;63:863–4.
8. Falk RJ, Gross WL, Guillevin L, Hoffman G, Jayne DR, Jennette JC, et al. Granulomatosis with polyangiitis (Wegener’s): an alternative name for Wegener’s granulomatosis. Ann Rheum Dis 2011;70:704.
9. Falk RJ, Gross WL, Guillevin L, Hoffman G, Jayne DR, Jennette JC, et al. Granulomatosis with polyangiitis (Wegener’s): an alternative name for Wegener’s granulomatosis. J Am Soc Nephrol 2011;22:587–9.
10. Jennette JC, Falk RJ, Andryassy K, Bacon PA, Chung J, Gross WL, et al. Nomenclature of systemic vasculitides: proposal of an international consensus conference. Arthritis Rheum 1994;37:187–92.
11. Seelig B, Sznajd J, Robson JC, Judge A, Craven A, Grayson PC, et al. Are the 1990 American College of Rheumatology vasculitis classification criteria still valid? Rheumatology (Oxford) 2017;56:1154–61.
12. Watts RA, Suppiah R, Merkel PA, Luqmani R, Systemic vasculitis—is it time to reclassify? Rheumatology (Oxford) 2011;50:643–5.
13. Basu N, Watts R, Bajema I, Baslund B, Bley T, Boers M, et al. EULAR points to consider in the development of classification and diagnostic criteria in systemic vasculitis. Ann Rheum Dis 2010;69:1744–50.
14. Atalanta D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO III, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum 2010;62:2569–81.
15. Craven A, Robson J, Ponte C, Grayson PC, Suppiah R, Judge A, et al. ACR/EULAR-endorsed study to develop Diagnostic and Classification Criteria for Vasculitis (DCVAS). Clin Exp Rheumatol 2013;31:619–21.
16. Shiboski SC, Shiboski CH, Criswell L, Baer A, Challacombe S, Lanfranchi H, et al. American College of Rheumatology classification criteria for Sjögren’s syndrome: a data-driven, expert consensus approach in the Sjögren’s International Collaborative Clinical Alliance cohort. Arthritis Care Res (Hoboken) 2012;64:475–87.
17. Rao JK, Allen NB, Pincus T. Limitations of the 1990 American College of Rheumatology classification criteria in the diagnosis of vasculitis. Ann Intern Med 1998;129:345–52.
APPENDIX A: The DCVAS Investigators

The DCVAS study investigators are as follows: Paul Gatensby (ANU Medical Centre, Canberra, Australia); Catherine Hill (Central Adelaide Local Health Network: The Queen Elizabeth Hospital, Australia); Dwaraka-nathan Ranganathan (Royal Brisbane and Women’s Hospital, Australia); Andreas Krontzichier (Medical University Innsbruck, Austria); Daniel Blockmans (University Hospitals Leuven, Belgium); Lillian Barra (Lawson Health Research Institute, London, Ontario, Canada); Simon Carette, Christian Pagnoux (Mount Sinai Hospital, Toronto, Canada); Navjot Dhindsa (University of Manitoba, Winnipeg, Canada); Aurore Fifi-Mah (University of Calgary, Alberta, Canada); Nader Khalidi (St Joseph’s Healthcare, Hamilton, Ontario, Canada); Patrick Liang (Sherrbrooke University Hospital Centre, Canada); Nataliya Milman (University of Ottawa, Canada); Christian Pineau (McGill University, Canada); Xiping Tian (Peking Union Medical College Hospital, Beijing, China); Guochun Wang (China-Japan Friendship Hospital, Beijing, China); Tian Wang (Arzhen Hospital, Capital Medical University, China); Ming-hui Zhao (Peking University First Hospital, China); Vladimir Tesar (General University Hospital, Prague, Czech Republic); Bo Baslund (University Hospital, Copenhagen Rigshospitalet, Denmark); Nevin Hammam (Assiut University, Egypt); Amira Sharih in (Cairo University, Egypt); Laura Pirula (Turku University Hospital, Finland); Jukka Putaala (Helsinki University Central Hospital, Finland); Bernhard Hellmich (Kreiskliniken Essen, Germany); Jörg Henes (Universitätsklinikum Tübingen, Germany); Peter Lamprech (Klinikum Bad Bramstedt, Germany); Thomas Neumann (Universitätsklinikum Jena, Germany); Wolfgang Schmidt (Immanuel Krankenhaus Berlin, Germany); Cord Sunderkoetter (Universitätsklinikum Münster, Germany); Zoltan Szekanecze (University of Debrecen Medical and Health Science Center, Hungary); Debashish Danda (Christian Medical College & Hospital, Vellore, India); Siddharth Das (Chatrapathi Shawali Maharaj Medical Center, Lucknow, India); Rajiva Gupta (Medanta, Delhi, India); Liza Rajasekar (NIMH, Hyderabad, India); Aman Sharma (Postgraduate Institute of Medical Education and Research, Chandigarh, India); Shrikant Waghi (Jehangir Clinical Development Centre, Pune, India); Michael Clarkson (Cork University Hospital, Ireland); Eamonn Molloy (St. Vincent’s University Hospital, Dublin, Ireland); Carlo Salvarani (Santa Maria Nuova Hospital, Reggio Emilia, Italy); Franco Schiavon (L’Azienda Ospedaliera di University of Padua, Italy); Enrico Tombetti (Università Vita-Salute San Raffaele, Milano, Italy); Augusto Vaglio (University of Parma, Italy); Koichi Amano (Saitama Medical University, Japan); Yoshihiro Airmura (Kyorin University Hospital, Japan); Hiroaki Dobashi (Kagawa University Hospital, Japan); Shouichi Fujimoto (Miyazaki University Hospital, Japan); Masayoshi Harigai, Fumio Hirano (Tokyo Medical and Dental University Hospital, Japan); Junichi Hirashishi (University Tokyo Hospital, Japan); Sakae Homma (Toho University Hospital, Japan); Tamihiro Kawakami (St. Marianna University Hospital Dermatology, Japan); Shigeto Kobayashi (Kojo University Keio Hospital, Japan); Hajime Kono (Keio University Hospital, Japan); Hiroaki Dobashi (Kagawa University Hospital, Japan); Hirofumi Makino (Okayama University Hospital, Japan); Kazuo Matsui (Kameda Medical Centre, Kamogawa, Japan); Eri Muso (Kitamin Hospital, Japan); Kazuo Suzuki, Kei Ikeda (Chiba University Hospital, Japan); Tsutomu Takeuchi (Keio University Hospital, Japan); Tatsuo Tsukamoto (Kyoto University Hospital, Japan); Shunya Uchida (Teikyo University Hospital, Japan); Takashi Wada (Kanazawa University Hospital, Japan); Hidehiro Yamada (St. Marianna University Hospital Internal Medicine, Japan); Kunihiro Yamagata (Tsukuba University Hospital, Japan); Wiako Yumura (UHMW Hospital [Jichi Medical University Hospital], Japan); Kan Sow Lai (Penang General Hospital, Malaysia); Luís Felipe Flores-Suarez (Instituto Nacional de Enfermedades Respiratorias, Mexico City, Mexico); Andrea Hinojosa (Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico); Bram Rutgers (University Hospital Groningen, Netherlands); Paul-Peter Tak (Academic Medical Centre, University of Amsterdam, Netherlands); Rebecca Grainger (Wellington, Otago, New Zealand); Vicki Quincey (Waikato District Health Board, New Zealand); Lisa Stamp (University of Otago, Christchurch, New Zealand); Ravi Suppiah (Auckland District Health Board, New Zealand); Emilie Besada (Tromso, Northern Norway, Norway); Andreas Diamantopoulos (Hospital of Southern Norway, Kristiansand, Norway); Jan Szrajd (University of Jagiellonian, Poland); Elsa Azevedo (Centro Hospitalar de São João, Porto, Portugal); Ruth Gardenes (Hospital de Santa Maria, Lisbon, Portugal); Miguel Rodrigues (Hospital Padua, Almada, Portugal); Ernestina Santos (Hospital Santo Antonio, Porto, Portugal); Yeong-Wook Song (Seoul National University Hospital, Republic of Korea); Sargey Moiseev (First Moscow State Medical University, Russia); Alczija Hocevar (University Medical Centre Ljubljana, Slovenia); Maria Cinti Ciò (Hospital Clinic de Barcelona, Spain); Xavier Solanich Moreno (Hospital de Bellvitge Ictiòbel, Spain); Inoshi Atukorala (University of Colombo, Sri Lanka); Ewa Berglin (Umeå University Hospital, Sweden); Aladdin Mohammed (Lund-Malmö University, Sweden); Mårtén Segelmark (Linköping University, Sweden); Thomas Daikeler (University Hospital Basel, Switzerland); Haner Direskeneli (Marmara University Medical School, Turkey); Gullen Hatemi (istanbul University, Cerrahpasa Medical School, Turkey); Sevl Kamali (istanbul University, Istanbul Medical School, Turkey); Ömer Karadag (Haceteppe University, Turkey); Seval Pehlevan (Feth University Medical Faculty, Turkey); Matthew Adler (Frimley Health NHS Foundation Trust, Wexham Park Hospital, UK); Neal Basu (NIH-SGramian, Aberdeen Royal Infirmary, UK); Iain Bruce (Manchester University Hospitals NHS Foundation Trust, UK); Kuntal Chakraborty (Barking, Havering and Redbridge University Hospitals NHS Trust, UK); Bharatk Dasgupta (Southend University Hospital NHS Foundation Trust, UK); Oliver Flossmann (Royal Berkshire NHS Foundation Trust, UK); Nagui Gendi (Basildon and Thurock University Hospitals NHS Foundation Trust, UK); Aala Hassan (North Cumbria University Hospitals, UK); Rachel Hoyles (Oxford University Hospitals NHS Foundation Trust, UK); David Jayne (Cambridge University Hospitals NHS Foundation Trust, UK); Colin Jones (York Teaching Hospitals NHS Foundation Trust, UK); Rainer Klocke (The Dudley Group NHS Foundation Trust, UK); Peter Lanyon (Nottingham University Hospitals NHS Trust, UK); Cathy Laversuch (Traunton & Somerset NHS Foundation Trust, Musgrove Park Hospital, UK); Raashid Lugmani, Joanna Robson (Nuffield Orthopaedic Centre, Oxford, UK); Malgorzata Magliano (Buckinghamshire Healthcare NHS Trust, UK); Justin Mason (Imperial College Healthcare NHS Trust, UK); Win Win Maw (Mid Essex Hospital Services NHS Trust, UK); Iain McInnes (NHS Greater Glasgow & Clyde, Gartnavel Hospital & GRI, UK); John Mclaren (NHS Fife, Whyteman’s Brae Hospital, UK); Matthew Morgan (University Hospitals Birmingham NHS Foundation Trust, Queen Elizabeth Hospital, UK); Ann Morgan (Leeds Teaching Hospitals NHS Trust, UK); Chetan Mukhtyar (Norfolk and Norwich University Hospitals NHS Foundation Trust, UK); Edmond O’Riordan (Salford Royal NHS Foundation Trust, UK); Sanjeev Patel (Epsom and St Heller University Hospitals NHS Trust, UK); Adrian Peall (Wye Valley NHS Trust, Hereford County Hospital, UK); Joanna Robson (University Hospitals Bristol NHS Foundation Trust, UK); Vinodan Venkatesh (The Royal Wolverhampton NHS Trust, UK); Erin Vermaak, Aij Menon (Staffordshire & Stoke on Trent Partnership NHS Trust, Haywood Hospital, UK); Richard Watts (East Suffolk and North Essex NHS Foundation Trust, UK); Chee-Seng Yeo (Doncaster and Bassetlaw Hospitals NHS Foundation Trust, UK); Daniel Albert (Dartmouth-Hitchcock Medical Center, US); Leonard Calabrese (Cleveland Clinic Foundation, US); Sharon Chung (University of California, San Francisco, US); Lindsey Forbes (Cedars-Sinai Medical Center, US); Angelo Gaffo (University of Alabama at Birmingham, US); Ora Gewurz-Singer (University of Michigan, US); Peter Grayson (Boston University School of Medicine, US); Kimberly Liang (University of Pittsburgh, US); Eric Matteson (Mayo Clinic, US); Peter A. Merkel (University of Pennsylvania, US); Jason Springer (University of Kansas Medical Center Research Institute, US); and Antoine Sreih (Rush University Medical Center, US).