Unmet need in rheumatology: reports from the Targeted Therapies meeting 2018

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Handling editor Dimitrios T Boumpas

To cite: Winthrop KL, et al. Ann Rheum Dis 2019;78:872–878. doi:10.1136/annrheumdis-2018-214280

ABSTRACT

To develop a comprehensive listing of the greatest unmet scientific and clinical needs in rheumatology. The 20th annual international Targeted Therapies meeting brought more than 100 leading basic scientists and clinical researchers in rheumatology, immunology, epidemiology, molecular biology and other specialties. During the meeting, breakout sessions were convened, consisting of five disease-specific groups with 20–30 experts assigned to each group based on expertise. Specific groups included rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis, systemic lupus erythematosus, connective tissue diseases and a basic science immunology group spanning all of these clinical domains. In each group, experts were asked to consider recent accomplishments within their clinical domain in the last year and update the unmet needs in three categorical areas: basic/translational science, clinical science and therapeutic development, and clinical care. While progress was noted among some of previously identified needs, both new needs were identified and themes from prior meetings were re-iterated: the need for better understanding the heterogeneity within each disease, and for identifying preclinical states of disease allowing treatment and prevention of disease in those at risk, and the elusive ability to cure disease. Within the clinical care realm, improved comorbidity management and patient-centred care continue to be unmet needs, and the need for new and affordable therapeutics was highlighted. Unmet needs for new and accessible targeted therapies, disease prevention and ultimately cure remain a priority in rheumatology.

BACKGROUND

The Targeted Therapies meeting has met annually for 20 years, with experts in the fields of clinical rheumatology, infectious diseases, epidemiology and basic scientific areas including immunology and molecular biology, presenting research developments in their fields. The meeting focuses on medicine and translational research, and stimulates collaboration between basic scientists and clinicians. The meeting’s objective is to update participants regarding the latest insights regarding disease mechanism(s) and pathophysiology, and recent developments with both existing and novel targeted therapies in rheumatology. Previously, a consensus document describing the recommended use of targeted therapies within rheumatology was produced from this meeting.1 However, with the expance of biologic therapies and the recent clinical recommendations published from both American College of Rheumatology and the European Union League Against Rheumatism,2,3 a single consensus document covering all targeted therapies across all disease indications became too complex and voluminous as a single manuscript. Accordingly, the annual meeting’s output was modified to debate and formulate a list of key unmet needs within the field, consistent with the meeting’s underlying objective of promoting innovation and collaboration within all areas of rheumatology.1 With the 2018 meeting, we conducted a similar process to review and update these unmet needs, with the goal of producing a roadmap for research in the future.

METHODS

We assigned conference participants to disease-specific breakout groups which included Psoriatic Arthritis (PsA), Rheumatoid Arthritis (RA), Axial Spondyloarthritis (axSpA), Systemic Lupus Erythematosus (SLE) and Connective Tissue Diseases (CTD). The CTD group was charged with specifically discussing Sjögren’s syndrome, myositis, systemic sclerosis, IgG4-related disease and vasculitis including Behçet’s disease. Experts in each group were tasked with identifying unmet needs in three categorical areas: clinical care, clinical science and therapeutic development, and basic/translational science. A ‘facilitator’ and ‘rapporteur’ lead each group’s discussion and summarised their results. The groups were asked to highlight notable progress made towards previously identified needs,5 identify new areas of need, and categorise all unmet needs as either primary or secondary. Subject-matter groups did not pursue formal measures of agreement or consensus, and needs were not ranked or further prioritised.

RESULTS

The RA group (table 1) reiterated the progress made to date with treatment of RA, including the strategy of ‘treat to target’ with rapid dose escalation of methotrexate followed by addition of either biologic disease-modifying antirheumatic drugs (DMARDs) or targeted small molecules. However, the committee also recognised that a significant proportion of patients continue to have moderate to high disease activity despite these therapeutic approaches, and the group highlighted the need...
Table 1. Primary and secondary unmet scientific needs within rheumatoid arthritis with regard to translational science, clinical science and therapeutic strategies, and clinical care.

| Primary unmet needs | Secondary unmet needs |
|---------------------|-----------------------|
| Understanding the role of the microbiome in disease development, causation and modulation | Identifying patients who can taper their treatment without a flare of articular or extra-articular disease |
| Continued need for treatment withdrawal studies and long-acting therapies for these consequences | Identifying patients who should be able to dose reduce without a risk for flare remains challenging, and will require further development of biomarkers, particularly within target tissues, and imaging programmes. |
| Development of new non-conventional disease-modifying anti-rheumatic drugs (DMARDs) for post-marketing surveillance | Identifying sites beyond the joint (eg, gut) that may be driving disease |
| Identifying sites beyond the joint (eg, gut) that could be driving joint inflammation were re-identified as areas of research needs. | Development of infrastructure for using electronic health records in clinical research. This includes the development of approaches to prevent RA (eg, screening, tolerisation, vaccination) |

Clinical science and therapeutic trials

- Achieving cure and defining this as long-term remission off drug therapy
- Identifying and defining the role of the vascular and lymphatic systems in the development of RA in the joint
- Identifying the need for RA classification to extend beyond predefined clinical definitions; for example, using clinical phenotypes (eg, treatment response (ie, TNF vs B-cell responsive disease)) or developing a new mechanism-based taxonomy of disease.
- The role of the microbiome in RA development and natural history, the development of animal models more reflective of human disease, and the identification of extra-articular sites (eg, the gut) that could be driving joint inflammation were re-identified as areas of research needs.

For PsA (table 2), advances have been escalating due to the convergence of greater understanding of the pathophysiology of PsA's varied clinical domains and the coming to fruition of numerous therapeutic clinical trials. Whereas a core set of clinical domains to be assessed in PsA clinical trials and long-term observational studies was recently revised and updated, the identification of a core outcome measure set for clinical trials is in process. New therapies have been approved for PsA, confirming the importance of several pathophysiological pathways including the cytokines TNF, IL-17 and IL-23, as well as various T-cell subset pathways. TNF inhibitors continue to represent standard of care, including one new approval—intra-venuous golimumab. Other approvals include two additional oral agents, the JAK inhibitors tofacitinib and baricitinib, an additional IL-17 inhibitor ixekizumab, and the T-cell modulator abatacept. Numerous other agents which exploit these and other pathways are in phase II and III trials, including the IL-23 inhibitors guselkumab, risankizumab and tildrakizumab, and JAK inhibitors filgotinib and upadacitinib. Country-based or regional-based clinical registries around the world are maturing with substantial numbers of patients with clinically well-characterised PsA to further define 'treatment-resistant disease'. These patients should be the priority for study with new molecules, as they remain the most difficult to treat. On the other hand, another unmet need highlighted the necessity of better identifying patients in low disease activity/remission in whom dose reduction could be considered and, accordingly, highlighted a need for clinical trials to evaluate dose reduction strategies and their impact on both joint and extra-articular disease. There is also a need for a registry or other population-based observational studies for postmarketing surveillance of biologics including originators and biosimilars, as well as newly approved small molecules. Identifying patients who should be able to dose reduce without a risk for flare remains challenging, and will require further development of biomarkers, particularly within target tissues, and imaging programmes. Future clinical trials should use such biomarkers to stratify patients.

Pain and fatigue were also recognised as important components of disease morbidity in a substantial portion of patients, despite there being numerous efficacious therapies for decreasing inflammation. Specific research regarding the multifactorial origin of fatigue and pain in RA should be developed using new methods of neuroimaging and ideally used to further the development of novel, non-opioid analgesics. Another domain of therapeutic unmet need was highlighted again this year: specifically the evaluation and treatment of extra-articular disease including RA lung disease. The impact of DMARD therapy and low disease activity on cardiovascular disease was also highlighted as a continued important area of study. A major challenge remains access to care due to the high cost of biologic and new small-molecule DMARDs. This was a universal concern of group members independent of country of origin, as many patients fear the loss of access to treatment. The potential ability of biosimilars to allow for greater access to biologics was debated, although it remains unclear whether this will occur.

The group also identified the need for RA classification to extend beyond predefined clinical definitions; for example, using clinical phenotypes (eg, treatment response (ie, TNF vs B-cell responsive disease)) or developing a new mechanism-based taxonomy of disease. The role of the microbiome in RA development and natural history, the development of animal models more reflective of human disease, and the identification of extra-articular sites (eg, the gut) that could be driving joint inflammation were re-identified as areas of research needs.
with, in some cases, paired biorepositories to pursue clinical and translational science in ‘real world’ settings distinct from clinical trial populations. Efforts to standardise clinical assessments have occurred in recent years, and publications regarding disease natural history, clinical features and treatment outcomes, and comorbidities are now emerging from these registries. The heterogeneous clinical domains include arthritis and skin manifestations, and also enthesitis, dactylitis, spondylitis, enthesitis, uveitis, nail disease, and colitis are being studied translationally and clinically.22 Research on how to optimally assess these various clinical domains both individually and as part of composite measures is proceeding. This is important to holistically evaluate PsA when targeting remission or low disease activity during treatment, but also to recognise how treatments may differentially affect different domains, raising the need for combination therapy and/or therapy intensification.20 21 23 24 At the moment, several composite measures, both categorical to measure multi-domain response, and continuous to measure disease activity as well as response, are being used in clinical trials and registries. There is not yet a consensus on which measure(s) will be the optimal one to use as a target of treatment.24 Numerous questions remain at a basic science level. What mechanisms underlie the pathogenesis of different clinical domains; how similar and different? In situations where it is difficult to interrogate mechanisms by tissue biopsy (eg, enthesitis), can advanced imaging techniques serve as a useful tool? There is a need to understand the transition from having just skin disease to the development of musculoskeletal features at the translational level; can arthritis development be preventable in those with skin psoriasis? Needed are serum biomarkers which predict that transition, as well as assessment of disease activity and predicting progressive structural damage in those with established PsA. Conversely, many patients with PsA have little or no skin involvement and do not even know they have skin psoriasis—this raises the question as to whether this group of patients is fundamentally different than those with significant skin disease. Biomarkers should be developed using well-characterised clinical cohorts with appropriate imaging, tissue and fluid samples. An expert group has initiated a project to fund a collaborative consortium of centres to collect such samples.25 There is increasing understanding about genetic, gastrointestinal and skin microbiome profiles in PsA.26 It is associated with a number of comorbidities, including metabolic syndrome (obesity, hypertension, hyperlipidaemia), which increases the risk for early cardiovascular disease.27 A common but inadequately recognised comorbidity, the phenomenon of central sensitisation, which overlaps with fibromyalgia, characterised by augmented pain and fatigue, can have a significant impact on disease assessment and therapeutic response. There is a need for greater understanding of the impact of comorbidities, especially if modifiable, on disease course and outcomes through registry-based studies.28

Unlike RA, there have been a paucity of PsA studies evaluating combined or sequential therapies, controlled withdrawal and treatment of early or ‘pre-disease’. As more therapies with different mechanisms of action are proven efficacious in PsA, head-to-head comparisons are needed; several trials are underway, including comparison of TNF and IL-17 inhibition.29 It was highlighted in deliberations that ‘it takes a village’ to care for a patient with PsA. Optimal care teams include rheumatologists and also dermatologists, ophthalmologists and geneticists, gastroenterologists and other specialists.

Table 2 Primary and secondary unmet scientific needs within psoriatic arthritis with regard to translational science, clinical science and therapeutic trials, and clinical care

| Primary unmet needs                                                                 | Secondary unmet needs                                                                 |
|-------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|
| **Translational science**                                                           | Development of appropriate animal models for pathogenesis                            |
| Understanding how to use molecular imaging modalities to interrogate tissue         | Understanding various mechanisms of pain, including central sensitisation              |
| pathophysioloogy, especially the enthesis                                            | Understanding the progression of skin psoriasis to that of associated arthritis.      |
| Better understanding the effect of genetic markers, skin and gut microbiome          | Understanding at the molecular level similarities or differences in inflammation      |
| patterns, metabolic syndrome and central sensitisation (fibromyalgia) on disease     | between affected joints and skin                                                     |
| subtypes and their outcomes                                                          |                                                                                       |
| Further development of longitudinal, clinically well-characterised cohorts with      |                                                                                       |
| appropriate imaging, tissue and fluid samples; improved data-sharing among          |                                                                                       |
| investigators; these relate to inception cohorts as well as cohorts of patients with |                                                                                       |
| patients with long-standing disease                                                  |                                                                                       |
| **Clinical science and therapeutic trials**                                         | Development/validation of advanced imaging and other biomarkers including patient-    |
| Standardisation of enthesitis and dactylitis measures                                 | reported outcomes to assess disease activity and clinical outcomes in the different  |
| Reliable and feasible imaging assessment of new bone formation                       | clinical domains of PsA                                                               |
| Testing the benefits and risks of scores that use multiple disease domains vs        | Use of NMR spectroscopy and other advanced imaging for metabolic syndrome             |
| scores that use single domains for approval of drugs                                 | Specific interventions related to microbiome                                          |
| Understanding differential therapeutic effects on different clinical domains in PsA  |                                                                                       |
| Further evaluation of combination therapies and strategic trials including the use   |                                                                                       |
| of sequential therapies, controlled withdrawal, the treatment of early disease, and  |                                                                                       |
| the treatment of monarticular or oligoarticular disease                               |                                                                                       |
| Head-to-head comparison of therapies with different mechanisms of action             |                                                                                       |
| **Clinical care**                                                                   | Use of serum and other types of biomarkers for diagnosis, disease severity             |
| Standardisation in the characterisation and measurement of PsA clinical domains      | categorisation and identifying structural damage                                      |
| The development of a clinician-feasible measure(s) of PsA remission or low disease   | The development of guidance regarding therapeutic choice based on patient factors,    |
| activity as a target of therapy                                                     | clinical presentations and ‘to be developed’ biomarkers                              |
| Developing better knowledge, communication and screening approaches (including the   |                                                                                       |
| development of educational initiatives and cross-specialty clinics) for rheumatologists, dermatologists and primary care providers caring for patients with PsA to facilitate earlier diagnosis |                                                                                       |
| Improved clinical attention to PsA-related comorbidities, especially metabolic       |                                                                                       |
| syndrome and central sensitisation                                                  |                                                                                       |

*Sequence of needs within the table is random and is not meant to imply order of importance.

PsA, psoriatic arthritis.
gastroenterologists with the ability to closely communicate their care of the disease’s key clinical features and associated conditions. Professional societies are nurturing the development of ‘combined’ clinics staffed by rheumatologists and dermatologists, especially in academic centres for teaching as well as clinical consultation purposes. Similar efforts in the community among private practitioners are also occurring to improve communication and collaboration between specialists caring for these patients. Education of dermatologists, primary care providers and others who may see patients with PsA prior to the rheumatologist should be focused on screening patients with skin psoriasis for inflammatory musculoskeletal symptoms.

In axSpA (table 3), there is an urgent need to increase our knowledge of the intestinal microbiome and pathology and their influence on the development of SpA. Clinical and subclinical inflammation is a major feature of SpA, and there is increasing evidence of intestinal dysbiosis in SpA.

Biomarkers for early disease stages (or ‘pre-disease’) are lacking, as is the clinical and pathophysiological understanding of the processes that characterise SpA at the time of onset or before. To accomplish these aims, international collaborations in terms of registries and bio-banks need to be established, integrated with the exploration of novel imaging modalities like enhanced MRI and PET scanning to detect early pathology. To improve clinical care, education should focus on early referral and diagnosis. This includes the appropriate use of imaging for both correctly interpreting disease classification criteria as well as making a correct diagnosis. Moreover, identifying patient subsets that can be best treated with a specific biologic agent could tremendously enhance treatment effectiveness.

In the domain of clinical research and trials, peripheral SpA remains relatively unstudied, and there are little data to guide the treatment choice. For axial SpA, although current biologics have demonstrated efficacy, our knowledge of which biologics to choose is unsatisfactory, and head-to-head trials as well as treatment strategy trials are needed to guide clinicians. Ideally, such studies should be complemented by detailed biomarker and genetic analyses in order to identify predictive factors associated with treatment response, as well as to understand the mechanisms of inadequate response to a biologic. Such studies will likely require international collaboration in order to be successful.

SLE (table 4), with its protean yet heterogeneous clinical manifestations as well as extensive autoimmunity and immune cell dysfunction, remains a disease that requires deeper insights into its aetiology and mechanisms in addition to more effective therapies. The breakout group discussing unmet needs and research priorities related to SLE noted considerable progress in those areas of scientific and clinical need that had been identified in 2017. Technological advances continue to allow dissection of the phenotypes and mechanisms of regulating T and B lymphocytes, including the important role of cell metabolism and effector cell populations. The significance of nucleic acid triggers of innate immune responses and type I interferon production continues to gain strong support. New insights regarding the contribution of brain microglial cells and transcriptome analysis of kidney tissue from patients with lupus nephritis, particularly data generated through the Accelerating Medicines Partnership programme, highlight the importance of tissue-specific mechanisms that contribute to the various disease phenotypes. The growing understanding of epigenetic alterations and correlation of genome-wide association studies with clinical phenotypes have identified new genes and loci associated with risk of developing lupus, extending these analyses to include more samples from patients of African-American and Asian ethnicities. Metabolic studies and studies of perturbations of signalling pathways, such as mTOR, have extended understanding of disease pathophysiology. Despite these advances addressing factors impacting susceptibility and immune and tissue-specific mechanisms, the group reiterated the view that the current classification criteria for SLE contribute to the observed heterogeneity of disease. Effective bioinformatics tools, including machine learning, will be required to effectively interpret in an unbiased manner the extensive and growing datasets derived from patient cohorts followed longitudinally, which include genetic, epigenetic, transcriptomic, serological, immunological and microbiome data. These comprehensive analyses will likely yield actionable insights into the clinical heterogeneity of SLE. Despite continued progress in basic and clinical research, the group articulated the reality that the ‘cause’ of SLE remains elusive. Understanding the core aetiology of SLE, as well as the continued dissection of its disease mechanisms, were identified as the highest priority challenges for the research community.

Clinical trial design has been supported by the general acceptance of SLE Responder Index 4 as an informative measure of response to therapy; novel outcome measures also have been developed. Industry-sponsored clinical trials have generated valuable samples to be analysed for biologic factors associated with clinical response to therapy. Patients have identified ‘lupus fog’ and fatigue as the disease manifestations of greatest concern,
Improved identification and use of biomarkers within clinical practice and trials.

- Broaden membership of groups designing trials.
- Better understanding of the natural history of disease flares.
- Better understanding of the role of T and B lymphocytes (and subsets), the epigenetic modification of various cell types (in connexion with environmental factors) and metabolic perturbations in the pathophysiology of disease.

Clinical trials that incorporate IFN signature and emphasise responder analyses.

Identification of socioeconomic factors that contribute to long-standing disease.

Identification of factors that lead to tissue specificity of SLE disease manifestations.

Further development of longitudinal, clinically well-characterised cohorts (immunologically, genetically and metabolically).

Clinical science and therapeutic trials.

Large pragmatic trials of existing and emerging therapies. These trials should focus also on prevention of disease in those identified to be at risk.

Establish patient support groups and guides/advocates to improve adherence to medical regimen.

Small proof of mechanism trials for emerging therapies.

Clinical care.

Better characterise patient concerns (vs provider concerns).

Optimisation of steroid-sparing approaches to treatment including the development of toxicity scoring systems, the development of improved understanding of targeting specific therapies to specific disease clinical manifestations.

Small proof of mechanism trials for emerging therapies.

Table 4: Primary and secondary unmet scientific needs within systemic lupus erythematosus with regard to translational science, clinical science and therapeutic trials, and clinical care.

Proritary unmet needs

Better understanding of the role of T and B lymphocytes (and subsets), the epigenetic modification of various cell types (in connexion with environmental factors) and metabolic perturbations in the pathophysiology of disease.

Identification of biomarkers that contribute to long-standing disease.

Identification of socioeconomic factors that contribute to long-standing disease.

Identification of factors that lead to tissue specificity of SLE disease manifestations.

Clinical science and therapeutic trials.

Large pragmatic trials of existing and emerging therapies. These trials should focus also on prevention of disease in those identified to be at risk.

Establish patient support groups and guides/advocates to improve adherence to medical regimen.

Small proof of mechanism trials for emerging therapies.

Clinical care.

Better characterise patient concerns (vs provider concerns).

Optimisation of steroid-sparing approaches to treatment including the development of toxicity scoring systems, the development of improved understanding of targeting specific therapies to specific disease clinical manifestations.

Small proof of mechanism trials for emerging therapies.

This area is changing rapidly and is of increasing need for rheumatological input.

In ANCA-associated vasculitis, there is a need to profile the genomic, proteomic ANCA subtypes MPO, PR3 and EGPA before therapy initiation as markers of prognosis. It is important to assess the use of these subtypes to ascertain whether they can be used as therapeutic guides with current and novel treatments in patients with new onset and remission induction. Such therapies include rituximab, anti IL-6, JAK inhibitors, anti granulocyte-macrophage colony-stimulating factor and synthetic chemotherapies (eg, cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil) and anti-IL5/anti-IL5Ra (EGPA) as well as randomised control trials targeting the complement pathway. Secondary unmet needs include understanding the relationship between disease pathophysiology and autoantibody states, as well as the patterns of disease regarding organ involvement and treatments, and identification of strategies to predict when (if ever) ANCA vasculitis treatment can be discontinued without risk of recurrence.

Giant cell arteritis (GCA) and Takayasu arteritis (TAK) were representative types of large vessel vasculitis (LVV) considered. Recognising the important differences in the clinical features and response to various therapies used and in development, as well as effect on life expectancy and need for vascular surgery, the role, use and cost-effectiveness of approved IL-6 antagonist therapy in GCA, as well as its potential role in TAK are primary unmet needs. Other unmet secondary needs are efforts to understand the effects of anti-IL6 on the fundamental disease pathophysiology. The efficacy of abatacept in GCA requires ongoing study. Better outcome measures and disease activity measures and strategies for their use are needed for all forms of LVV, including improved biomarkers and imaging (PET, US, MRI, CT). For all forms of vasculitis, international prospective observational studies of patient cohorts that include clinical imaging and bio-banking are needed.

For systemic sclerosis, similarly, the potential use of IL-6 inhibition remains important to further evaluate, as well as challenging the research community to identify instruments that are sensitive and specific in their measure of these symptoms, and to design trials to test candidate therapeutic interventions.

Clinical trials should be conducted in distinct clinical subpopulations to optimise the likelihood of detecting a significant clinical response. Development of practical interventions that might improve access to care, compliance with treatment and clinical outcomes represents yet another priority area to address the unmet needs of patients with lupus.

The CTD portion of this exercise included a number of diseases, including Sjogren’s syndrome, systemic sclerosis, inflammatory myopathies and vasculitides (Table 5 and online supplementary table 5a–d). The unmet need in this group of diseases mirrored their inherent heterogeneity. The group agreed that compared with the prior year, little had changed with regard to identified unmet needs.

Emerging checkpoint inhibitor adverse events dominated the groups’ conversation early on, as these malignancy therapies can trigger severe rheumatic manifestations even among individuals who lack a history of CTD. Understanding most aspects of these events was highlighted again as an important unmet need including basic questions regarding incidence, risk factors, and optimal clinical management with glucocorticoids and other immunosuppressives. The ramifications of instituting immunosuppression in these cases, in terms of the ability to continue using checkpoint inhibitors and control of the underlying malignancy, represent important and challenging clinical questions. This area is changing rapidly and is of increasing need for rheumatological input.

Winthrop KL, et al. Ann Rheum Dis 2019;78:872–878. doi:10.1136/annrheumdis-2018-214280
identifying those patients at high risk for lung cancer within the clinical care of patients with scleroderma. Unmet needs continue to include means for earlier diagnosis and consideration of haematopoietic stem cell transplantation for treatment. In Sjögren’s syndrome, lymphoma aetiology and pathophysiology remain poorly understood, although a recently developed algorithm is said to be able to predict this complication with high predictive value. This remains to be validated in a large multicentre multinational cohort. For inflammatory myositis, identified unmet needs from the prior year were reiterated this year as unchanged. Questions remain regarding the association of anti-TIF1 and NXP2 antibodies with cancer-associated myositis, as well as the optimal management of these malignancies and associated myositis.

SUMMARY

The convening of the 20th annual Targeted Therapies meeting afforded the possibility to discuss and articulate major unmet needs in the field of rheumatology, and across domains there were several overarching perceived unmet needs. These included the need for the infrastructure necessary to study heterogeneity within each disease and develop predictive tools for therapeutic response. This would best be facilitated by creation, or further development, of well-characterised, longitudinal patient cohorts (preferably inception cohorts) paired with biorepositories of patient specimens. Within clinical care, a commonly identified unmet need was improved management of comorbidities as well as patient-centred care. Within clinical science and therapeutic development, the abilities to identify ‘pre-disease’ with subsequent prevention in those at risk, and to cure disease were identified. Other primary unmet needs included accessible and affordable new therapeutics including the development of non-opioid therapies for pain control. Issues of improved management of comorbidities and cross-specialty training/education and co-management continued to be a theme, although progress has been made in some disease areas. Finally, despite the relatively rapid evolution of new therapies for some rheumatic diseases, continued development of new therapeutics across all disease states, better access and better targeting of existing therapies continues to represent a major unmet need for patients and rheumatologists.

Table 5  Primary and secondary unmet scientific needs within other connective tissue disorders/vasculitis with regard to translational science, clinical science and therapeutic trials, and clinical care (these are overarching needs in common across individual diseases (including Sjögren’s syndrome, systemic sclerosis, inflammatory myopathies and vasculitides, including IgG4-related disease); individual diseases are presented in online supplementary appendices)"
