Online supplement to: Identifying Provisional Generic Contextual Factor Domains for Clinical Trials in Rheumatology: Results from an OMERACT Initiative. *The Journal of Rheumatology*. doi:10.3899/jrheum.181081

ONLINE DATA SUPPLEMENT

Supplementary Table 1: Case scenarios involving contextual factors from study 1a

	Working Group (self-reported name)	Trial settings (Population, Intervention, Outcome, Reference, Study type)	Contextual factors (Personal, Environmental)	Explanation
1	**Chronic Pain**	P: Rheumatoid arthritis I: Rituximab O: DAS28ESR (Isaacs et al. 2013) *Meta-analysis of RCTs*	RF or ACPA NA	This is a meta-analysis of 4 RCTs showing seropositivity influence response to rituximab.
2		P: Rheumatoid arthritis I: Abatacept and Adalimumab O: NA (Sokolove et al. 2016) *RCT*	ACPA NA	In AMPLE, baseline anti-CCP2 positivity was associated with a better response for Abatacept and Adalimumab. Patients with the highest baseline anti-CCP2 antibody concentrations had better clinical response with Abatacept.
3		P: Rheumatoid arthritis I: Biologics O: Fatigue (Almeida et al. 2016) *Meta-analysis of RCTs*	Early rheumatoid arthritis trial vs trial in established rheumatoid arthritis NA	In this meta-analysis, there was statistically significant heterogeneity. Sensitivity analysis showed that early RA trials produced larger effect size than trials in patients with established disease.
4	**Gout**	P: Gout I: Urate-lowering treatment O: Serum urate (Becker et al. 2005) *RCT*	Baseline serum urate level NA	The highest baseline, the lowest rate of target sUa (< 6 mg/dl or 0.36 mmol/L) achieved with a specific dose of any arm of medication assignment.
5		P: Gout I: Urate-lowering treatment O: Flares (Schumacher et al. 2009) *Observational study*	Presence of subcutaneous tophi NA	Patients with the highest burden of disease (tophi) showed higher rate of flares (at 12-mo after stopping prophylaxis).
6		P: Patients with gout I: Urate-lowering treatment O: Rate of flares (Becker et al. 2010) *RCT*	Previous urate-lowering vs. ULT-naïve NA	In the CONFIRMS trial, patients previously treated (even in a previous trial) showed lower rate of flares.
7	**Hand OA**	P: Patients with erosive hand OA I: Adalimumab vs. placebo O: Radiological erosive progression (scoring method: GUSS) (Verbruggen et al. 2012; Kloppenburg et al. 2016) *RCT*	Presence of joint inflammation (soft swelling at physical examination) NA	In this study, radiological erosive progression was slowed in joints with soft tissue swelling at baseline that were treated with adalimumab compared to placebo, while in joints without soft tissue swelling at baseline no difference in radiological erosive progression could be demonstrated between adalimumab and placebo. An abstract of another trial showed the same result.
8	**Medication Adherence**	P: Patients with any rheumatic condition I: Any drug trial for a rheumatic condition O: ACR or other core set for the specific condition	Medication adherence NA	Poor medication adherence in clinical trials can lead to failure to confirm efficacy of the intervention, underestimate efficacy, underestimate harms and lead to inaccurate dosing recommendations post trial.

		(Breckenridge et al. 2017; Blaschke et al. 2012) *Narrative review*		
9		P: Patients with any rheumatic condition I: Interventions (RCTs) aimed to improve medication adherence O: Adherence, clinical outcomes (Allemann et al. 2017) *Meta-analysis of RCTs*	Baseline medication adherence (prior to starting the trial) NA	Baseline medication adherence (including non-adherent patients) was found to be a feature significantly associated with effective interventions regarding adherence.
10	**Myositis**	P: Patients with inflammatory myopathies I: Health-enhancing physical activity (HEPA) intervention consisting of physical activity in group, education, motivating conversation. The control group will receive only education. O: Level of physical activity and comorbidities [no publication]	Motivation, knowledge, self-efficacy Support at work, family, friends, availability of facilities/environment for being physically active.	This would be an interesting study as patients with inflammatory rheumatic disease are less physically active than the population. Sustained HEPA can markedly reduce risk of cardiovascular disease, some cancer diagnosis and diabetes. Patients with myositis have a higher risk to develop cardiovascular disease and diabetes.
11	**PsA Outcome Measure Working Group**	P: Psoriatic arthritis I: Secukinumab O: ACR20 response (Mease et al. 2015) *RCT*	Comorbid fibromyalgia, comorbid depression, pain sensitization, BMI NA	This is a phase 2 RCT to evaluate the efficacy and safety of secukinumab, an anti–interleukin-17A monoclonal antibody in psoriatic arthritis. Patients in the placebo group were switched to subcutaneous secukinumab at a dose of 150 mg or 75 mg at week 16 or 24, depending on clinical response. 606 patients with psoriatic arthritis were randomly assigned in a 1: 1: 1 ratio to receive intravenous secukinumab (at a dose of 10 mg per kilogram) at weeks 0, 2, and 4, followed by subcutaneous secukinumab at a dose of either 150 mg or 75 mg every 4 weeks, or placebo. The primary end point was the proportion of patients with an American College of Rheumatology 20 (ACR20) response at week 24. Comorbid fibromyalgia affect pain perception and tender joint count which is component of ACR20 response have less pain but not related to intervention. Depressive mood, pain sensitization and BMI may also affect pain perception. All these were not measured and difficult to controlled for and may affect pain perception as an outcome in trials. However, in trial setting set for comparison between interventions, randomization has taken care of some of the above contextual factors. Assuming that equal proportion of subjects with contextual factors may have been randomized to both interventional and placebo arms.
12	**Shoulder Pain**	P: Patients with rotator cuff tears I: Surgical repair and rehabilitation O: Western Ontario Rotator Cuff (WORC) index (Gagnier et al. 2017) *Observational study*	Medical Comorbidities as measured by the functional comorbidity index (FCI) NA	The study is a cohort study within an established registry. Quote ”Across the entire sample, regression analysis revealed that increased FCI score was associated with worse baseline WORC score”
13	**Stiffness**	P: Patients with RA I: NA O: Development of new stiffness PROM (Halls et al. 2018; Halls et al. 2015; Orbai et al. 2014) *Observational study*	Physical function, quality of life, psychological well-being, activities of daily living and participation in work and leisure activities	In UK and US based qualitative work, patients highlighted that stiffness impacted on their daily lives in a range of domains, including physical function, quality of life, psychological well-being, activities of daily living and participation in work and leisure activities. ‘Impact on daily life’ was one of six themes in the resulting conceptual model of the patient experience of stiffness in the UK work. This led to the development and testing of a set of candidate items

			NA	for a new RA stiffness PROM that captured the patient perspective i.e. including 'impact' based questions.
14	**Synovial tissue**	P: Patients with RA I: Adalimumab or tocilizumab therapy O: ACR50 (Dennis et al. 2014) *[Also reported by Hand OA and Myositis]* *Observational study*	Type of synovial tissue infiltrate NA	In this study, patients with myeloid vs lymphoid gene-expression responded better to adalimumab vs tocilizumab, respectively; i.e. myeloid and lymphoid patterns were important in achieving ACR50 in response to adalimumab and tocilizumab, respectively
15	**TJR**	P: Black patients with knee osteoarthritis I: Total knee arthroplasty O: WOMAC pain and function 2 years after surgery (Goodman et al. 2016) *Observational study*	NA Community poverty	Observational study linking individuals to community socioeconomic factors including poverty, demonstrating that blacks in wealthy neighbourhoods have the same outcomes as their white peers, but have worse outcomes if they live in impoverished neighbourhoods
16		P: Patients with knee osteoarthritis I: Arthroplasty O: WOMAC pain and function at 2 years (Goodman et al. 2017) *Observational study*	Education college or above Community poverty	Patients undergoing knee arthroplasty with < college education from impoverished neighbourhoods have worse 2 year outcomes, but those with at least some college do as well as those from wealthier neighbourhoods
17	**Vasculitis**	P: ANCA-Associated Vasculits I: Trials of new therapies to induce remission in ANCA-associated vasculitis O: Rate of remission at X months (usually 6 or 12) "Multiple trials for personal contextual factors" [no publication]	New vs. relapsing disease; MPO vs. PR-3 ANCA type Experience of investigator	Patients with New vs. relapsing disease and MPO vs. PR-3 ANCA type are well known to have differing rates of relapse and these factors are use for stratification in randomization and analysis. Experience of investigator may influence how subjects are evaluated.
18	**Extra I***	P: NA I: Systemic sclerosis O: Combined Response Index for Systemic Sclerosis (CRIS) [no publication]	Race (AA vs Hispanic vs Caucasia Disease duration	Ethnicity is associated with more severe disease and worse outcome; disease duration is associated with responsiveness
19	**Extra II***	P: Patients with Knee Osteoarthritis I: Colchicine vs placebo O: 30% improvement in WOMAC pain (Leung et al. 2018) *RCT*	Pattern of NSAIDs usage (regular use/ intermittent use), NSAIDs usage before outcome assessment, depression, anxiety, pain sensitization, patient expectation Physical activity before outcome assessment	This is a RCT on short term pain relieving response of using colchicine versus placebo for 4 months for treatment of symptomatic knee OA. Pain response can be affected by NSAIDs use, e.g. patients who took NSAIDs before outcome assessment have less pain but not related to intervention. Anxiety and depression affect pain perception. Patients with pain sensitization may have more pain and less pain relief from intervention. Patients with higher expectation may have less pain relief. Patients who had increased physical activity right before endpoint assessment may have more pain that is not related to treatment at all. All these were not measured and difficult to controlled for and may affect pain perception as an outcome in OA trials. However, in trial setting set for comparison between interventions, randomization has taken care of some of the above contextual factors. Assuming that equal proportion of subjects with contextual factors may have been randomized to both interventional and placebo arms.

*Extra examples of case-scenarios provided from individual members not representing the relevant working group.

AA, African Americans; ACPA, anti-citrullinated protein antibodies; ACR, American College of Rheumatology; ANCA, anti-neutrophil cytoplasmic antibody; BMI, body mass index; CRIS, Combined Response Index for Systemic Sclerosis; DAS28ESR, Disease Activity Score - Erythrocyte Sedimentation Rate; FCI, functional comorbidity index; HEPA, Health-enhancing physical activity ; NSAIDs, nonsteroidal anti-inflammatory drugs; OA, osteoarthritis; PROM, patient reported outcome measures; PsA, psoriatic arthritis; RA, rheumatoid arthritis; RCT, randomized controlled trial; RF, rheumatoid factor; TJR, Total Joint Replacement; WOMAC, The Western Ontario and McMaster Universities Osteoarthritis Index; WORC, Western Ontario Rotator Cuff.

Full references for case scenarios

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Supplementary Table 2: Contextual factors mentioned in study 1a and study 1b

1. Activities of daily living
2. Adherence to treatment
3. Age
4. Anti–citrullinated protein antibody (ACPA)
5. Anxiety
6. Availability of facilities/environment for being physically active
7. Baseline state (of the outcome of interest)
8. BMI
9. Body weight
10. Community poverty
11. Comorbid depression
12. Comorbid fibromyalgia
13. Comorbidities
14. Country
15. Disability
16. Disease duration
17. Disease severity
18. Drug history
19. Early vs established rheumatoid arthritis
20. Education
21. Education college or above
22. Ethnicity
23. Exercise
24. Exercise level
25. Experience of investigator
26. Function
27. Gender
28. Genetics
29. Health care system
30. Household (living alone or in a family)
31. Knowledge
32. Lifestyle
33. Medical Comorbidities measured by functional comorbidity index (FCI)
34. Medication Adherence
35. Medication adherence at baseline (prior to starting the trial)
36. Mental health
37. Motivation
38. New vs. relapsing disease
39. NSAIDs usage before outcome assessment
40. NSAIDs usage pattern (regular use/intermittent use)
41. Occupation
42. Pain sensitization

43. Participation in work and leisure activities
44. Patient education/health literacy
45. Patient expectation
46. Patient expectation of outcome
47. Physical activity before outcome assessment
48. Physical function
49. Place of residence
50. Placebo characteristics
51. Presence of joint inflammation (soft swelling at physical examination) (/synovitis)
52. Presence of subcutaneous tophi
53. Previous exposure to drugs/therapeutics
54. Previous urate-lowering vs. ULT-naive
55. Psychological well-being
56. Quality of healthcare system
57. Quality of life
58. Quality of sleep
59. Race (African American vs Hispanic vs Caucasia)
60. Race
61. Religion
62. Rheumatoid Factor (RF)
63. Self-efficacy
64. Serum urate level at baseline
65. Sex
66. Sexual orientation
67. Smoking
68. Social capital
69. Social class
70. Social system
71. Socioeconomic class/status
72. Stress level
73. Support at work, family, friends
74. Temperature/climate
75. Time of day
76. Type of synovial tissue infiltrate
77. Type of vasculitis (Myeloperoxidase [MPO] type vs. Proteinase 3 anti-neutrophil cytoplasmic antibody [PR-3 ANCA] type)
78. Weather
79. Year of study

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Supplementary Table 3: Detailed results from group-based exercise

		Generic	Important
		Grp A	Grp A
1	Activities of daily living	X	
2	Adherence to treatment	X	3
3	Age	X	4
4	Anti–citrullinated protein antibody (ACPA)		
5	Anxiety	X	
6	Availability of facilities/environment for being physically active		
7	Baseline state (of the outcome of interest)		
8	BMI	X	
9	Body weight	X	
10	Community poverty	X	
11	Comorbid depression	X	
12	Comorbid fibromyalgia	X	
13	Comorbidities	X	2
14	Country	X	
15	Disability		
16	Disease duration	X	5
17	Disease severity		
18	Drug history		
19	Early vs established rheumatoid arthritis		
20	Education	X	
21	Education college or above		
22	Ethnicity	X	
23	Exercise	X	
24	Exercise level		
25	Experience of investigator		
26	Function		
27	Gender	X	1
28	Genetics		
29	Health care system	X	
30	Household (living alone or in a family)		
31	Knowledge		
32	Lifestyle		
33	Medical Comorbidities measured by functional comorbidity index (FCI)		
34	Medication Adherence		
35	Medication adherence at baseline (prior to starting the trial)		
36	Mental health	X	
37	Motivation		
38	New vs. relapsing disease		
39	NSAIDs usage before outcome assessment		
40	NSAIDs usage pattern (regular use/intermittent use)	X	

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		Generic		Important	
		Grp B-I	Grp B-II	Grp B-I	Grp B-II
41	Occupation	X	X		
42	Pain sensitization	X		6	
43	Participation in work and leisure activities	X	X		
44	Patient education/health literacy	X	X	3	7
45	Patient expectation	X			
46	Patient expectation of outcome	X			
47	Physical activity before outcome assessment	X	X		
48	Physical function	X	X		
49	Place of residence	X	X		
50	Placebo characteristics	X			
51	Presence of joint inflammation (soft swelling at physical examination) (/synovitis)	X			
52	Presence of subcutaneous tophi	X			
53	Previous exposure to drugs/therapeutics	X	X		2
54	Previous urate-lowering vs. ULT-naive				
55	Psychological well-being	X	X	2	3
56	Quality of healthcare system	X			
57	Quality of life	X	X		
58	Quality of sleep	X	X		
59	Race (African American vs Hispanic vs Caucasia)	X			
60	Race	X	X	5	5
61	Religion	X			
62	Rheumatoid Factor (RF)				
63	Self-efficacy	X	X		
64	Serum urate level at baseline				
65	Sex	X	X	1	4
66	Sexual orientation	X			
67	Smoking	X		4	
68	Social capital	X			
69	Social class	X			
70	Social system	X			
71	Socioeconomic class/status	X	X		
72	Stress level	X	X		
73	Support at work, family, friends	X	X		6
74	Temperature/climate	X	X		
75	Time of day	X			
76	Type of synovial tissue infiltrate				
77	Type of vasculitis (Myeloperoxidase [MPO] type vs. Proteinase 3 anti-neutrophil cytoplasmic antibody [PR-3 ANCA] type)				
78	Weather	X	X		
79	Year of study	X			
	Extra factors suggested by the group(s)				
	Health care system		X		1
	Age		X		
	Drug mix (current)		X		
	Exercise level		X		
	Diet		X		

	Duration of disease	X
	Time at work – work flexibility	X
	Comorbidities	X