

## APPENDIX

### Supplementary file 1. Written questionnaire capturing patient voice

#### FSR Endpoints Initiative

The members of the Endpoints Steering Committee for the Endpoints Initiative are committed to ensure that both the physicians and the patients have a voice in determining which Core Outcomes are important based on life experience alongside data. The purpose of this questionnaire is to hear from you, as a pulmonary sarcoidosis patient, and learn how the disease impacts your life. This will help to identify Core Outcomes that are important to pulmonary sarcoidosis patients.

**What is a Core Outcome?** A Core Outcome is something that physicians and researchers use to measure how well a treatment or an assessment is working. Research studies testing treatments often measure different outcomes. For example, one pulmonary sarcoidosis trial might use a CT scan to track improvements, while another might use a 6-minute walk test. For patients, outcomes related to pain and fatigue might be of great importance, but can be hard to measure. If researchers measure different things, it makes it difficult to compare and combine the results. But if all future research studies measure the same important outcomes, then the results will be combined and new treatments that work will be available for people with pulmonary sarcoidosis more quickly. The information you provide in this questionnaire will help to decide what outcomes are the most important and should be measured in all future pulmonary sarcoidosis research. Your opinion is very important.

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### Written Questionnaire

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#### Topic 1: Symptoms That Matter Most to Patients

Of all the symptoms you have experienced with pulmonary sarcoidosis, which do you consider to have the most significant impact on your daily life?
How often do these symptoms affect you, using scale - never, sometimes, often, always?

Rank the top three aspects/symptoms of the disease that impact your daily life.

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How has your condition and its symptoms changed over time?

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How much of your day is spent thinking and planning activities because of shortness of breath? (0-25%, 25 – 50%, 50 – 75%, or >75%) Please explain.

*Things to consider when answering: Planning steps and routes in order to get from one place to the next. Avoiding stairs or inclines, and looking for elevators or escalators. Planning meals around times you know you have to walk.*

## **Topic 2: Daily Impacts That Matter Most to Patients**

Are there specific activities that are important to you, but you can't do at all or as fully as you would like because of your condition?

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How do your symptoms and their negative impacts affect your daily life on the best days? On the worst days?

*Things to consider when answering: How do your symptoms impact you at work? How do they impact you at home? How do they impact you with your relationships or social activities?*

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How has your condition and its symptoms impacted you emotionally?

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How often do you avoid interactions with people or feel embarrassed due to the breathlessness brought on by sarcoidosis? Use the scale - never, sometimes, often, always. Please explain.

*Things to consider when answering: Trouble walking at a "normal" pace with others, trouble walking and talking at the same time, and inability to participate in activities.*

How fearful has sarcoidosis caused you to become? Use the scale – not at all fearful, somewhat fearful, often fearful, very fearful. Please explain.

*Things to consider when answering: Fear of contracting infections, impact on your financial future, declining health, and dying.*

How often has sarcoidosis made you feel guilty? Use the scale – never, sometimes, often, always. Please explain.

*Things to consider when answering: Not being able to fulfill responsibilities at work or home, and the perception of being a burden to family and friends.*

In addition to the care you receive from your doctors, what else or who else has helped you manage the disease? How important are they to you?

*Things to consider when answering: support groups, family, friends, spirituality, and faith.*

**Topic 3: Outcomes That Matter Most to Patients**

In your own words, describe a core outcome?

What outcomes do you think are the most critical to measure during a pulmonary sarcoidosis clinical trial?

Supplementary file: R1 consensus matrix

Outcome ID	Outcome name	%1-3	%4-6	%7-9	HCP result	%1-3	%4-6	%7-9	Patient Result	Number of groups reaching consensus in
2	Death - pulmonary sarcoidosis	4	9	87	In	3	5	92	In	2
3	Disease activity	0	24	76	In	1	9	90	In	2
5	Extra pulmonary organ involvement	2	22	76	In	2	13	86	In	2
6	Dyspnoea	2	16	82	In	2	19	79	In	2
10	Pulmonary function	0	29	71	In	1	11	88	In	2
11	Oxygenation	0	25	75	In	2	15	84	In	2
20	Functional exercise capacity	0	24	76	In	1	29	70	In	2
33	Health related quality of life	4	16	80	In	1	21	78	In	2
43	Adherence to treatment	0	27	73	In	2	20	79	In	2
45	Tolerability of treatment	0	20	80	In	0	15	85	In	2
46	Treatment failure	2	13	85	In	1	11	87	In	2
48	Need for hospitalisation because of	2	16	82	In	5	24	72	In	2
49	Side effects of treatment	0	15	85	In	1	19	80	In	2
1	Death - any cause	4	24	72	In	7	25	68	Medium	1
4	Systemic inflammation	4	42	55	Medium	1	11	88	In	1
13	Infection	6	57	37	Low	2	21	77	In	1
14	General Health	4	47	49	Low	2	27	72	In	1
16	Pain	6	54	41	Low	3	27	70	In	1
17	Chest pain	7	57	35	Low	5	22	73	In	1
18	Joint pain or muscle pain	5	65	29	Low	3	27	70	In	1
21	Mobility	2	51	47	Low	2	22	76	In	1
23	Fatigue	0	40	60	Medium	1	16	83	In	1
26	Cognitive Function	5	51	44	Low	3	19	77	In	1
34	Overall quality of life	5	29	65	Medium	1	22	77	In	1
35	Activities of daily living	2	33	65	Medium	2	23	75	In	1
37	Ability to take part in usual family lif	5	47	47	Low	4	26	70	In	1
44	Satisfaction with treatment	0	44	56	Medium	1	16	82	In	1
7	Wheeze	7	62	31	Low	6	31	62	Medium	0
8	Chest tightness	11	58	31	Low	4	26	69	Medium	0
9	Cough	4	42	55	Medium	4	30	66	Medium	0
12	Radiographic outcomes	5	53	42	Low	3	31	66	Medium	0
15	Perceived health status	5	35	60	Medium	5	35	59	Medium	0
19	Body weight	7	53	40	Low	7	43	51	Medium	0
22	Strength	0	62	38	Low	1	33	65	Medium	0
24	Quality of sleep	9	69	22	Low	3	29	68	Medium	0
25	Disease knowledge	20	53	27	Low	5	33	62	Medium	0
27	Anxiety	6	70	24	Low	10	40	49	Low	0
28	Depression	6	59	35	Low	10	36	54	Medium	0
29	Emotional wellbeing	7	55	38	Low	7	33	60	Medium	0
30	Fear of disease progression	16	58	25	Low	9	33	59	Medium	0
31	Feelings of isolation	20	59	20	Low	21	43	36	Low	0
32	Community awareness of condition	31	44	24	Low	24	43	33	Low	0
36	Ability to take part in social/leisure a	5	53	42	Low	5	33	62	Medium	0
38	Ability to undertake usual role/respc	7	42	51	Medium	4	27	69	Medium	0
39	Ability to work or study	0	42	58	Medium	6	25	68	Medium	0
40	Impact on personal finances	9	48	43	Low	11	28	60	Medium	0
41	Impact on relationships	9	50	41	Low	6	34	60	Medium	0
42	Social support (including from family	13	48	39	Low	8	42	49	Low	0
47	Healthcare resource use	4	54	43	Low	5	41	54	Medium	0
				Total outcomes "in"	14					Total outcomes "in" 26

			Patients				HCPs			
			Not that important	Important but not critical	Critically Important	Patient Result	Not that important	Important but not critical	Critically Important	HCP result
Outcome	Overall result	Help Text	%1-3	%4-6	%7-9		%1-3	%4-6	%7-9	
Death	Death - any cause	In		5	14	81 In		0	20	80 In
	Death - pulmonary sarcoidosis	In	Death as a result of having pulmonary sarcoidosis	2	3	95 In		0	8	92 In
Physiological	Disease activity	In	A measure of current, active, inflammation index	0	6	93 In		0	12	88 In
	Extra pulmonary organ involvement	In	Having sarcoidosis in other organs as well as the lungs	1	8	92 In		0	18	82 In
	Extra pulmonary organ impairment	In	When sarcoidosis causes problems in other organs	1	15	85 In		0	26	74 In
	Dyspnoea	In	Shortness of breath/being unable to catch breath	1	11	88 In		2	8	90 In
	Pulmonary function	In	How well someone's lungs are working	1	7	92 In		2	20	78 In
	Oxygenation	In	How well oxygen is being sent to parts of the body	0	8	92 In		2	14	84 In
	Functional exercise capacity	In	Includes what day to day activities someone is able to do	0	18	82 In		0	20	80 In
	Systemic inflammation	Discuss	An immune response resulting in inflammation	0	8	92 In		6	40	54 Medium
	Recurrence of sarcoidosis	Discuss	Sarcoidosis coming back after a period of remission	0	14	86 In		8	24	69 Medium
	Fatigue	Discuss	An overwhelming, sustained sense of extreme tiredness	0	12	88 In		0	39	61 Medium
	Cough	Discuss	Cough	2	28	70 In		6	35	59 Medium
	Pain	Discuss	A feeling of noticeable discomfort or an unpleasant sensation	3	24	73 In		2	69	29 Out
	Chest pain	Discuss	Pain specifically in the chest	4	18	78 In		6	67	27 Out
	Mobility	Discuss	Includes ability to walk, climb, run, stand, sit with ease	0	22	78 In		2	53	45 Out
	Infection	Discuss	The presence of an unexpected and unwanted virus/bacteria	1	19	79 In		6	68	26 Out
	Radiographic outcomes	No consensus	How someone's lungs look including parts of the chest	3	32	65 Medium		8	57	35 Out
	Joint pain or muscle pain	No consensus	Pain specifically in the joints and/or muscles	2	29	69 Medium		2	76	22 Out
	Strength	No consensus	Includes ability to grasp large heavy objects, lift	1	36	63 Medium		4	59	37 Out
	Quality of sleep	No consensus	Including sleep disruption, early awakening, poor sleep	1	33	66 Medium		10	71	20 Out
	Wheeze	No consensus	Experiencing a high pitched sound that comes from the chest	5	36	59 Medium		6	75	20 Out
Chest tightness	No consensus	Experiencing tightness in the chest	2	31	67 Medium		14	67	20 Out	
Health and quality of life	Health related quality of life	In	An overall measure of how a person's health affects their quality of life	1	11	88 In		4	12	84 In
	Overall quality of life	Discuss	A state of health, happiness, comfort and well-being	0	12	88 In		2	31	67 Medium
	General Health	Discuss	Someone's general health	1	25	74 In		4	51	45 Out
	Perceived health status	Discuss	How someone thinks their overall health is	3	34	63 Medium		4	41	55 Medium
Wellbeing	Depression	No consensus	Persistent feelings of sadness/low mood/unhappiness	9	37	55 Medium		6	66	28 Out
	Emotional wellbeing	No consensus	Emotional wellbeing includes lots of things like happiness	4	34	62 Medium		8	57	35 Out
	Fear of disease progression	No consensus	Feelings of fear around pulmonary sarcoidosis getting worse	7	38	55 Medium		20	59	22 Out
	Anxiety	Out	Feelings of worry or deep concern or uneasiness	8	51	41 Out		8	75	18 Out
	Feelings of isolation	Out	Feelings of isolation, being alone and lacking in connection	17	55	28 Out		22	68	10 Out
Life Impact	Activities of daily living	Discuss	Being able to take care of oneself and complete tasks	1	15	83 In		0	31	69 Medium
	Ability to work or study	Discuss	Someone's ability to work or study, ability to gain education	2	21	78 In		0	37	63 Medium
	Ability to undertake usual role/responsibilities	Discuss	Being able to manage personal role and responsibilities	2	24	75 In		0	51	49 Out
	Ability to take part in usual family life/activities	Discuss	Being able to take part in family life and activities	3	28	70 In		4	53	43 Out
	Cognitive Function	Discuss	Mental abilities/mental processes, including memory	2	18	80 In		2	53	45 Out
	Ability to take part in social/leisure activities	No consensus	How able someone feels to join in social or leisure activities	2	35	63 Medium		2	57	41 Out
	Disease knowledge	No consensus	How knowledgeable someone is about their condition	4	37	59 Medium		18	59	24 Out
	Impact on personal finances	No consensus	The impact of someone's pulmonary sarcoidosis on their finances	6	33	60 Medium		12	50	38 Out
	Impact on relationships	No consensus	The impact of someone's pulmonary sarcoidosis on their relationships	3	34	63 Medium		10	54	36 Out
Community awareness of condition	Out	How aware someone's community is of sarcoidosis	25	47	28 Out		38	50	12 Out	
Social support (including from family and friends)	Out	The support that is available to someone from their community	5	51	44 Out		12	56	32 Out	
Treatment	Adherence to treatment	In	The degree to which someone follows medical advice	1	10	89 In		0	12	88 In
	Tolerability of treatment	In	How tolerable the treatment is, for example, burden of treatment	0	6	94 In		0	12	88 In
	Treatment failure	In	When the current treatment is no longer working	0	6	93 In		2	6	92 In
	Side effects of treatment	In	When the treatment given causes unwanted/undesired effects	0	8	91 In		0	6	94 In
	Satisfaction with treatment	Discuss	How satisfied someone is with the treatment/symptoms	0	14	85 In		2	49	49 Out
	Body Weight	Out	How much someone weighs	6	48	46 Out		4	61	35 Out
Resource use	Need for hospitalisation because of pulmonary sarcoidosis	In	How often someone is admitted to hospital because of their condition	2	16	82 In		0	10	90 In
	Healthcare resource use	Out	Total cost of health care (includes the time of healthcare professionals)	5	48	48 Out		2	64	34 Out
Total "In"			15							
Out			6							
Total to discuss			17							

**Supplementary file: Feedback questionnaire**

The questions below was provided to participants using Google Forms and were answered anonymously.

**Which best describes how you voted at the meeting?**

**Response options**

As a patient  
As a health professional

**Please tell us how much you agree with each of the following statements**

1 strongly disagree, 2 - disagree, 3 neither agree nor disagree, 4 - agree, 5 - strongly agree

**Response options**

The information that the organisers provided me with in advance of the meeting was helpful.

1-5 Likert scale

I was satisfied with the amount of background to the study presented on the day

1-5 Likert scale

I was satisfied with the information, presented at the meeting, about how the day was going to work

1-5 Likert scale

I was satisfied with the process used to discuss and vote on outcomes

1-5 Likert scale

I was satisfied with the way the meeting was facilitated

1-5 Likert scale

I felt able to contribute to the meeting

1-5 Likert scale

I felt comfortable communicating my views

1-5 Likert scale

The workshop produced a fair result

1-5 Likert scale

The meeting length was just right

1-5 Likert scale

I was satisfied with the number of comfort breaks

1-5 Likert scale

I was satisfied with the use of Zoom to conduct the meeting

1-5 Likert scale

Was there anything that could have been done to improve the workshop

free text

Is there anything else that you would like to tell us

free text

Name	HelpText	DomainName
Death - any cause	Death from any cause	Death
Death - pulmonary sarcoidosis	Death as a result of having pulmonary sarcoidosis	Death
Disease activity	A measure of current, active, inflammation indicating active sarcoidosis.	Physiological/clinical
Systemic inflammation	An immune response resulting in inflammation in the whole body, including the lungs	Physiological/clinical
Extra pulmonary organ involvement	Having sarcoidosis in other organs as well as the lungs	Physiological/clinical
Extra pulmonary organ impairment*	When sarcoidosis causes problems in other organs meaning that they don't function properly and/or may worsen over time.	Physiological/clinical
Recurrence of sarcoidosis*	Sarcoidosis coming back after a period of remission	Physiological/clinical
Dyspnoea	Shortness of breath/being unable to catch breath	Physiological/clinical
Wheeze	Experiencing a high pitched sound that comes from the chest when breathing out	Physiological/clinical
Chest tightness	Experiencing tightness in the chest	Physiological/clinical
Cough	Cough	Physiological/clinical
Pulmonary function	How well someone's lungs are working	Physiological/clinical
Oxygenation	How well oxygen is being sent to parts of the body	Physiological/clinical
Radiographic outcomes	How someone's lungs look including parts of the lung affected by sarcoidosis	Physiological/clinical
Infection	The presence of an unexpected and unwanted virus, bacteria, fungus or mycobacteria anywhere in the body	Physiological/clinical
General Health	Someone's general health	Physiological/clinical
Perceived health status	How someone thinks their overall health is	Physiological/clinical
Pain	A feeling of noticeable discomfort or an unpleasant physical sensation, in general, experienced anywhere in the body.	Physiological/clinical
Chest pain	Pain specifically in the chest	Physiological/clinical
Joint pain or muscle pain	Pain specifically in the joints and/or muscles	Physiological/clinical
Body weight	How much someone weighs	Physiological/clinical
Functional exercise capacity	includes what day to day activities someone is able to do including the ability to do complete physical activity and exercise. This includes the ability to walk (including, for example, walking up an incline, walking a long distance and walking whilst talking)	Life impact
Mobility	Includes ability to walk, climb, run, stand, sit without difficulty, taking into account stiffness.	Life impact
Strength	Includes ability to grasp large heavy objects, lift or carry groceries, overall weakness, lower extremity weakness, and muscle weakness	Life impact
Fatigue	An overwhelming, sustained sense of extreme tiredness or lethargy resulting in physical and/or mental weariness	Life impact
Quality of sleep	Including sleep disruption, early awakening, problems getting to sleep	Life impact
Disease knowledge	How knowledgeable someone is about their condition.	Life impact
Cognitive Function	Mental abilities/mental processes, including memory, concentration, language and thinking.	Life impact
Anxiety	Feelings of worry or deep concern or uneasiness that may also cause physical feelings such as nausea, stomach upset, dizziness, dry mouth.	Life impact
Depression	Persistent feelings of sadness/low mood/unhappiness often with decreased energy and loss of interest in usual activities. Constant feelings of guilt, doubt or self-blame, worthlessness and hopelessness; times of feeling very sad, despairing and hopeless.	Life impact
Emotional wellbeing	Emotional wellbeing includes lots of things like your mood, how often you worry, how often you get angry or upset, feelings of embarrassment and your self esteem.	Life impact
Fear of disease progression	Feelings of fear around pulmonary sarcoidosis getting worse	Life impact
Feelings of isolation	Feelings of isolation, being alone and lacking in close relationships, because of pulmonary sarcoidosis impacting on ability to contact/engage with other people	Life impact
Community awareness of condition	How aware someone's community is of sarcoidosis and the impact it can have	Life impact
Health related quality of life	An overall measure of how a person's health affects their general wellbeing; perceived physical, mental and social health over time	Life impact
Overall quality of life	A state of health, happiness, comfort and well-being	Life impact
Activities of daily living	Being able to take care of oneself and complete usual daily activities/tasks, for example, eating, bathing and dressing oneself	Life impact
Ability to take part in social/leisure activities	How able someone feels to join in social or leisure/recreational activities (e.g., sports, do-it-yourself, playing instruments, or outdoor life).	Life impact
Ability to take part in usual family life/activities	Being able to take part in family life and activities	Life impact
Ability to undertake usual role/responsibilities	Being able to manage personal role and responsibilities	Life impact
Ability to work or study	Someone's ability to work or study, ability to gain or keep employment, influence of pulmonary sarcoidosis on the type of job or study undertaken, time off from work or study, impact on career.	Life impact
Impact on personal finances	The impact of someone's pulmonary sarcoidosis on their personal finances	Life impact
Impact on relationships	The impact of someone's pulmonary sarcoidosis on their relationships, including relationship with partner or family member, neglect of family, poor understanding of disease by family.	Life impact
Social support (including from family and friends)	The support that is available to someone from their family, friends, peers and workplace	Life impact
Adherence to treatment	The degree to which someone follows medical advice or guidance from their doctor, for example, taking their prescribed medications.	Life Impact
Satisfaction with treatment	How satisfied someone is with the treatment/s they are receiving including satisfaction with its effectiveness (how well it's working) and the time spent on treatment.	Life Impact
Tolerability of treatment	How tolerable the treatment is, for example, burden of treatment, side effects etc.	Life Impact
Treatment failure	When the current treatment is no longer working to control pulmonary sarcoidosis symptoms	Life Impact
Healthcare resource use	Total cost of health care (includes the time of healthcare staff, facilities and medicines/treatments)	Resource Use
Need for hospitalisation because of pulmonary sarcoidosis	How often someone is admitted to hospital because of pulmonary sarcoidosis	Resource Use
Side effects of treatment	When the treatment given causes unwanted/unintended effects	Adverse Events

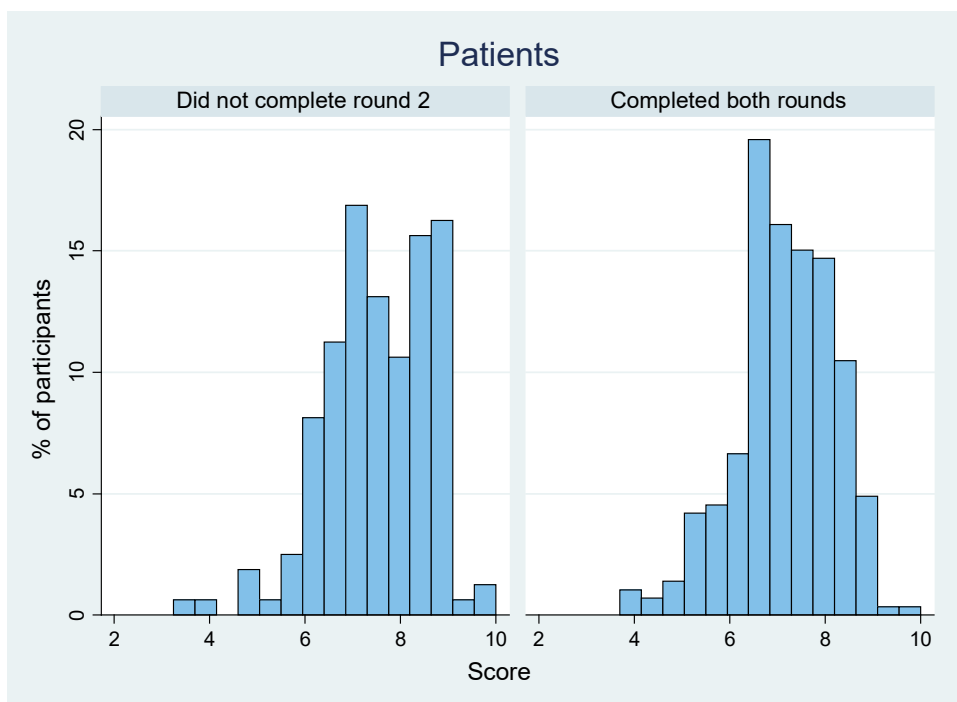
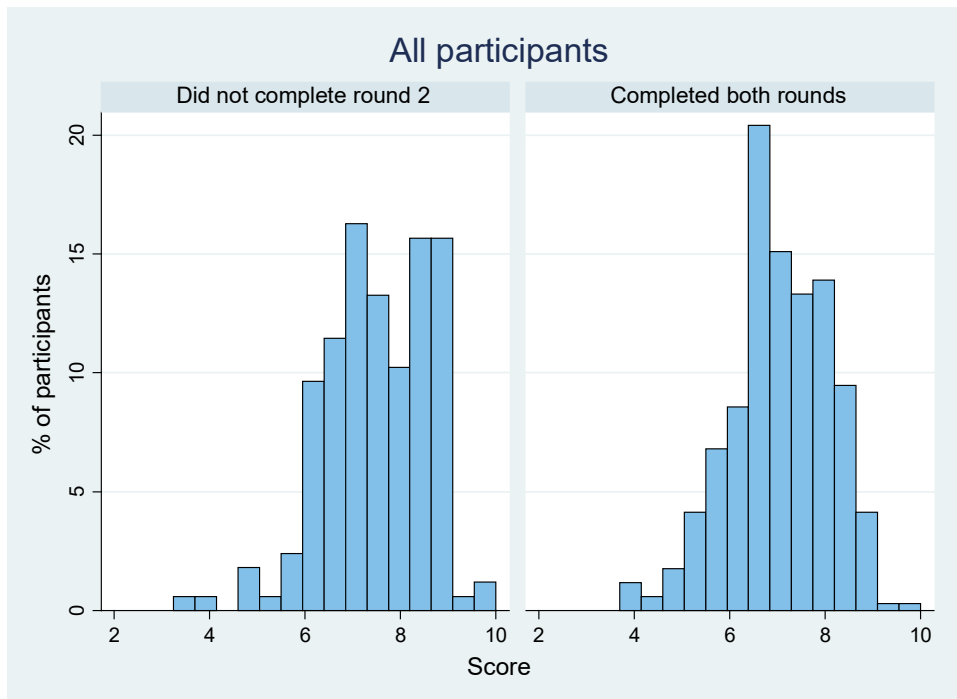
\*outcomes rated in R2 of the Delphi survey only



### Supplementary file 5. Attrition bias analysis

- 166 (32.9%) of 504 participants with data in round 1 did not provide any scores in round 2
  - In round 1, participants provided a mean (SD) of 45 (12.2) outcome ratings (median 49, IQR = 49,49) (range = 1,51).
  - In round 2, participants provided a mean (SD) of 32 (24.4) outcome ratings (median 51, IQR = 0,51) (range = 0,51).

Histograms are shown below for all participants combined, and for patients (including carers);



## Foundation for Sarcoidosis Research – Sarcoidosis Clinical Outcomes Taskforce (FSR-SCOUT) – Consensus meeting report



**Meeting date and time: 16<sup>th</sup> October 2020**

**Location: Online**

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### 1 Summary

Following a two round online Delphi survey an online consensus meeting was held on the 16<sup>th</sup> October 2020 to discuss outcomes where, according to the pre-agreed definition of consensus, consensus for inclusion in, or exclusion from, the core outcome set had not been reached. This report summarises these discussions and the resulting core outcome set.

### 2 Consensus meeting participants

Twenty-five participants, who had completed both rounds of the online Delphi survey, attended the online meeting (7 health professionals, 17 patients) (Table 1). In addition, nine pharmaceutical

company representatives attended the meeting and were invited to contribute to discussions but were not eligible to rate the inclusion of outcomes in the core outcome set.

### **3 The average R2 ratings for participants of the consensus meeting compared to all participants is shown in table 2. Outcomes**

At the end of round 2 of the Delphi survey the definition of consensus was applied to the responses for each stakeholder group (Supplementary file 1 – consensus matrix). Fifteen outcomes met the definition for “consensus in” to be included in the core outcome set and six met the definition of “consensus out” and were excluded from the core outcome set, the remaining outcomes had no consensus. Seventeen outcomes were prioritised for discussion at the consensus meeting as either 70% or more of participants in one stakeholder group, or 50-69% of participants in both stakeholder groups, had rated the outcome 7-9.

For the purpose of the consensus meeting the 17 outcomes, prioritised for discussion, were grouped into four domains, physiological/clinical (8 outcomes), health and quality of life (3 outcomes), life impact (5 outcomes) and treatment (1 outcome). All outcomes in a particular domain were presented, alongside those outcomes already included in the COS, and participants of the meeting invited to provide comments for inclusion of outcomes followed by comments against. After discussion of outcomes in that domain participants rated each outcome, that had been discussed, using the 1-9 scale (1 not that important – 9 critically important). Patients and health professionals voted separately, for an outcome to be included in the core outcome set 70% or more of participants in both groups were required to give a rating of 7-9. The results of consensus meeting ratings are provided in Table 3.

#### **3.1 Physiological/clinical outcomes**

Eight outcomes were prioritised for discussion in the physiological/clinical domain. These were described and presented alongside outcomes in the same domain that had reached “consensus in” in the Delphi surveys.

No participant offered reasons for inclusion of the outcomes “systemic inflammation”, “pain”, “chest pain”, “mobility” or “infection” as such these outcomes were not discussed or rated.

### 3.1.1 Outcome Discussion and rating

**Cough** – the impact of cough on quality of life was discussed, with patients explaining that this was one of the worst, most debilitating symptoms. A different view held was that cough is not necessarily specific to pulmonary sarcoidosis and should only be measured as an outcome if it is attributed to sarcoidosis. However, it was also raised that the cause is irrelevant and what matters to patients is the cough and how debilitating it is. It was noted that it would be important to measure whether a cough gets better but also if a cough gets worse.

**Result of voting: Not included in the core outcome set**

**Fatigue** – the prevalence of fatigue was discussed together with the impact of fatigue on quality of life and on other aspects like the ability to work. It was raised that fatigue can be present when there is no granulomatous inflammation and so whilst it is important it might not be a core outcome for every trial. It was also discussed that fatigue might be a side effect of some treatments and that side effects of treatment is already an included outcome domain.

**Result of voting: Not included in the core outcome set**

**Recurrence** – pulmonary sarcoidosis is characterised by remission and relapse. Patients agreed that it is important to measure “recurrence of sarcoidosis” to know whether a treatment is effective long term. However, patients also commented that it makes the assumption that the sarcoidosis goes away at some point but this may not be the same for everyone. It may also take a number of months/years for patients to go into remission and this outcome could only be measured in studies with a long follow up period. It was noted that if there is a positive effect of treatment then it is important to know if this effect is maintained long term.

**Result of voting: Not included in the core outcome set**

### 3.2 Health and quality of life outcomes

All three outcomes in the health and quality of life outcomes domain were discussed together. There was a comment that health professionals may have rated these outcomes less important as they felt that the concepts would already be covered by “health related quality of life”. The meeting facilitator reminded participants that this meeting would recommend the overall core outcome set but future

research would be needed to decide how to measure each outcome. Participants were asked to consider whether specific additional outcomes should be included alongside “health related quality of life” as this would then contribute to the outcome measurement tool chosen. After discussion participants were asked to rate the outcomes based on whether it was critical to include these as part of the “health related quality of life” assessment.

**Overall quality of life/General health/Perceived health status** – Some patients felt that specific symptoms affected their quality of life and so measuring those specific symptoms was more important. Some felt that they considered “health related quality of life” to be the most important whilst others felt that an overall quality of life measure, which assessed usual day to day activities and mental health issues, was important to consider but that this was also correlated to health. It was noted that it was important for this to be assessed from the patient perspective rather than the health professionals’ opinion.

**Result of voting: Not included in the core outcome set**

### **3.3 Life impact outcomes**

All outcomes in the life impact domain were discussed. Clarification was sought on whether the “health related quality of life” outcome would include assessment of these life impact outcomes. The meeting facilitator clarified that it should not be assumed that these are included and if these individual outcomes are critically important to measure then they should be voted in individually.

#### **Activities of daily living/ Ability to work or study/ Ability to undertake usual role/responsibilities/Ability to take part in usual family life/activities/Cognitive Function**

For some patients these outcomes were considered to be secondary to symptoms i.e. specific symptoms have a life impact and so it is those that are critically important to measure. Discussion also took place around the impact on the ability to work/study and that this can have a major impact on a patient’s life. There was some discussion that patients would want their doctor to ask these questions but that they may not be critical to measure in a trial.

Outcomes were discussed together but voted on individually.

**Result of voting: Not included in the core outcome set**

### 3.4 Treatment outcomes

Participants were asked if “satisfaction with treatment” was critical to include alongside the other treatment outcomes that were already in the core outcome set.

**Satisfaction with treatment** – clarification was sought that this outcome was for clinical trials and that these might be for new or established treatments. Some felt that this was important as it gave the perspective of the treatment in terms of side effects of treatment and tolerability which, although included, might not capture the patient perspective. Others felt that this outcome did not add anything to the outcomes already included.

**Result of voting: Not included in the core outcome set**

## 4 Discussion

Fifteen outcomes were included, in the core outcome set, after the two round online Delphi survey and no further outcomes were added at the consensus meeting – the core outcome set is reported in Table 4.

Review and discussion of the outcomes with “no consensus” highlighted the different stakeholder viewpoints in relation to each outcome. Patients and health professionals agreed that five of the 17 outcomes did not need further discussion at the consensus meeting and would not be included in the core outcome set. Of the 12 outcomes that were discussed patients and health professionals both agreed that six of these should not be included in the core outcome set with 50% or less of participants in both groups rating the outcome 7-9. However, for the remaining outcomes there were differences of opinion between the stakeholder groups. There were four outcomes (recurrence of sarcoidosis, cognitive function, satisfaction with treatment and activities of daily living) that did not reach the definition of consensus “in” for either group but were rated more highly by patients (rated 7-9 by 50-67%) than health professionals (rate 7-9 by 0-29%).

Two outcomes “cough” and “fatigue” were rated critically important by patients (70% and 80% of patients rating the outcome 7-9 respectively) but not by health professionals (57% and 14% of health professionals rating 7-9). Discussions and comments from patients highlighted the impact that cough and fatigue have on everyday life, with comments being made that these were the most important symptoms of pulmonary sarcoidosis. Existing patient reported outcome measures for “health related quality of life” include questions relating to these items. Future work to identify a suitable health

related quality of life measurement instrument (the ‘how’ to measure) may also want to consider whether items relating to “cough” and “fatigue” are included.

**Table 1. Consensus meeting participants**

		N (%)
<b>Healthcare professionals</b>		<b>7 (100%)</b>
<b>Role</b>		
	Sarcoidosis specialist	3 (43%)
	Researcher in the field	1 (14%)
	Industry representative	3 (43%)
<b>Country of residence</b>		
	United States	5 (71%)
	India	1 (14%)
	The Netherlands	1 (14%)
<b>Patients with pulmonary sarcoidosis</b>		17 (100%)
<b>Country of residence</b>		
	United States	14 (82%)
	UK	3 (18%)

**Table 2. Delphi round 2 ratings for participants of the consensus meeting versus all participants.**

	Average R2 rating of all participants	Average R2 rating of those attending the consensus meeting	Average R2 rating for Cough All participants	Average R2 rating for cough – Consensus meeting participants	Average R2 rating for Fatigue – all participants	Average R2 rating for fatigue – consensus meeting participants
Health professionals	6.5	5.8	6.6	6.6	6.1	5.4
Patients	7.3	7.4	7.1	6.9	6.9	8.5

Supplementary file 6: Consensus meeting report.

**Table 3. Summary of outcome discussed and rated during the consensus meeting**

Domain	Outcome		% patients rating 7-9 in online Delphi	% HCPS voting 7-9 in online Delphi	% Patients voting 7-9 in consensus meeting	% HCPs voting 7-9 in consensus meeting	Result
<b>Physiological/clinical</b>	Cough	Cough	70	59	70%	57%	Not included in the COS
	Fatigue	An overwhelming, sustained sense of extreme tiredness or lethargy resulting in physical and/or mental weariness	88	61	80%	14%	Not included in the COS
	Recurrence of sarcoidosis	Sarcoidosis coming back after a period of remission	86	69	50%	29%	Not included in the COS
	Systemic inflammation	An immune response resulting in inflammation in the whole body, including the lungs	92	54	Not discussed or rated	Not discussed or rated	Not included in the COS
	Pain	A feeling of noticeable discomfort or an unpleasant physical sensation, in general, experienced anywhere in the body.	73	29	Not discussed or rated	Not discussed or rated	Not included in the COS
	Chest pain	Pain specifically in the chest	78	27	Not discussed or rated	Not discussed or rated	Not included in the COS
	Mobility	Includes ability to walk, climb, run, stand, sit without difficulty, taking into account stiffness.	78	45	Not discussed or rated	Not discussed or rated	Not included in the COS
	Infection	The presence of an unexpected and unwanted virus, bacteria, fungus or mycobacteria anywhere in the body	79	26	Not discussed or rated	Not discussed or rated	Not included in the COS
<b>Quality of life/general health</b>	Overall quality of life	A state of health, happiness, comfort and well-being	88	67	47	0	Not included in the COS
	General Health	Someone's general health	74	45	44	0	Not included in the COS
	Perceived health status	How someone thinks their overall health is	63	55	25	0	Not included in the COS
<b>Life impact outcomes</b>	Activities of daily living	Being able to take care of oneself and complete usual daily activities/tasks, for example, eating, bathing and dressing oneself	83	69	58	17	Not included in the COS
	Ability to work or study	Someone's ability to work or study, ability to gain or keep employment, influence of pulmonary sarcoidosis on the type of job or study undertaken, time off from work or study, impact on career.	78	63	17	17	Not included in the COS



Supplementary file 6: Consensus meeting report.

	Ability to undertake usual role/responsibilities	Being able to manage personal role and responsibilities	75	49	33	17	Not included in the COS
	Ability to take part in usual family life/activities	Being able to take part in family life and activities	70	43	42	17	Not included in the COS
	Cognitive Function	Mental abilities/mental processes, including memory, concentration, language and thinking.	80	45	67	0	Not included in the COS
<b>Treatment outcomes</b>	Satisfaction with treatment	How satisfied someone is with the treatment/s they are receiving including satisfaction with its effectiveness (how well it's working) and the time spent on treatment.	85	49	50	0	Not included in the COS

**Table 4. Outcomes included in the Core Outcome Set**

<b>Domain</b>	<b>Outcome</b>	<b>Outcome description</b>
Physiological/Clinical	Disease activity	A measure of current, active, inflammation indicating active sarcoidosis.
Physiological/Clinical	Extra pulmonary organ involvement	Having sarcoidosis in other organs as well as the lungs
Physiological/Clinical	Extra pulmonary organ impairment	When sarcoidosis causes problems in other organs meaning that they don't function properly and/or may worsen over time.
Physiological/Clinical	Dyspnoea	Shortness of breath/being unable to catch breath
Physiological/Clinical	Pulmonary function	How well someone's lungs are working
Physiological/Clinical	Oxygenation	How well oxygen is being sent to parts of the body
Physiological/Clinical	Functional exercise capacity	Includes what day to day activities someone is able to do including the ability to do complete physical activity and exercise. This includes the ability to walk (including, for example, walking up an incline, walking a long distance and walking whilst talking)
Quality of Life	Health related quality of life	An overall measure of how a person's health affects their general wellbeing; perceived physical, mental and social health over time
Treatment	Adherence to treatment	The degree to which someone follows medical advice or guidance from their doctor, for example, taking their prescribed medications.
Treatment	Tolerability of treatment	How tolerable the treatment is, for example, burden of treatment, side effects etc.
Treatment	Treatment failure	When the current treatment is no longer working to control pulmonary sarcoidosis symptoms
Treatment	Side effects of treatment	When the treatment given causes unwanted/unintended effects
Resource Use	Need for hospitalisation because of pulmonary sarcoidosis	How often someone is admitted to hospital because of pulmonary sarcoidosis
Death	Death - any cause	Death from any cause
Death	Death - pulmonary sarcoidosis	Death as a result of having pulmonary sarcoidosis