Qualitative Assessment of Health-Related Quality of Life Impacts Associated with Sickle Cell Disease in the United States and United Kingdom

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Supplementary Information

Supplementary Table 1 Moderation guide for interview sessions with participants (or their caregivers) living with SCD

FOCUS GROUP MODERATION GUIDE: EXAMINING PERSPECTIVES ON HRQoL WITH SCD
Individuals with SCD (aged ≥18 years) and caregivers or parents of adolescents (aged 12–17 years) with SCD • Focus group number: • Date: • Location: • Name of interviewer: • Supervisor: • Starting time: • Ending time:
INTRODUCTION • Thank you for taking the time to meet with us today. My name is [*name of interviewer*] (and my [*supervisor's name – if present*] will also be present today) and we'll be moderating today's focus group. • Before we get started, has everyone reviewed and signed the informed consent form? o Yes: Proceed. o No: This must be completed and signed before the focus group can start. If not: do not go further with the focus group until the consent form is signed. • Thank you for consenting to participate in this study. The goal of today's focus group session is to better understand the disease burden of people living with SCD from your own perspective as a person diagnosed with SCD or how you perceive the impact of SCD on the adolescent in your care who has been diagnosed with SCD. We wish to understand how SCD affects your health-

related quality of life or the health-related quality of life of your adolescent. This study is conducted by QC Medica, a research agency based in the United Kingdom, for Vertex Pharmaceutical Incorporated, the sponsor of this study. For this study, we are working together with different organizations including the SCD patient organization, "[*insert name*]" and on behalf of a pharmaceutical company.

- For the purpose of today's focus group session some of you are participating as individuals with SCD and others are participating as caregivers or parents of adolescents with SCD. For those participating as caregivers or parents when we use "you" or "your" we are asking about your adolescent. We would like you to provide how you think his or her life has been affected, unless we state otherwise. Is that clear?
- Today's focus group will be divided into two 30-minute sections.
    - During our first 30-minute section, we will ask you about:
        - Your SCD symptoms (or your adolescent's SCD symptoms).
        - Your quality of life due to your SCD (or your adolescent's quality of life due to his or her SCD).
        - Your current treatment (or your adolescent's current treatment).
    - In the last 30 minutes of our session, we will review and ask for your feedback on the survey provided prior to today's session. We will also ask for your feedback on whether the information we found in the literature on disease impacts reflects the impacts of SCD on you or your adolescent's experience. Specifically, we will talk about:
        - The signs, symptoms, and life impacts that SCD patients may experience.
        - The survey questions.
        - The answer choices to the survey questions.
        - The design, format, and how we intend to administer the survey.
        - The timing and duration of the survey.
- Before we start, I want to clarify some aspects of the focus group:
    - As we begin our discussion today, please know that there are no right or wrong answers to any of my questions.
    - The information gathered today will be used for research purposes only. Your responses will be grouped and summarized so that no information will be shared that can be used to identify you or your adolescent.

- This focus group will take about 60 minutes.
- You are not obligated to answer questions that you do not wish to respond to. You can stop being in the study and the focus group session at any time without having to give a reason.
- If you do not understand a question, you may always ask for more explanation.

- Please note that as outlined in the consent forms this focus group will be recorded for transcription and analysis. Do I have your consent to begin recording?
  - Yes: Proceed.
  - No: Again, explain to participants the need to record the session. Excuse those participants that opt-out of the audio recording. Proceed with participants who do not object to have the session recorded.
- I'm going to now press record. Thank you for consenting to participate in the study and also for allowing this focus group session to be recorded to help us analyze the results.

A. THE FIRST HALF OF THE INTERVIEW

This brings us to the first 30-minute section. For this session, we'll talk about the symptoms you or your adolescent currently experience with SCD, health-related quality of life, current treatment, and aims for new treatment therapies.

Introduction	
Introductory question	• My first question to the group and we can all take turns is: Why did you choose to participate in this study?
Symptomatic experience of SCD	
Thank you. I'd like to shift gears to talk about the symptoms and experience with SCD.	
Symptomatic experience	• What symptoms do you or your adolescent generally experience? • What makes it better or worse?

	• Prompt: If relevant, please can you describe:
	  ○ Vaso-occlusive or pain crises due to SCD?
	  ○ Anemia symptoms experienced?
	  ○ Symptoms prior to needing a transfusion, if needed?
	  ○ Complications around when you received transfusions and other medications?
	  ○ Any potential iron-induced complications? Complications relating to potential iron overload?
	  ○ Any other symptoms experienced?

Daily activity and living	• How does your SCD affect your ability to do day-to-day activities? (or) How does your adolescent's SCD affect his or her ability to do day-to-day activities?
	  ○ Day-to-day activities include: your ability to perform household activities such as food preparations, housework, gardening, etc.; your ability to take care of yourself; the ability to take care of others.
	• Are there specific activities of daily living you or your adolescent avoid or can't be done because of the impact of SCD?
	  ○ Probe: Please tell me more [if elicits yes or no answers].
	• Are there times when SCD is worse than usual? Can you walk me through one of those days, what is it like in the morning/afternoon/evening?

Physical health	• How does your SCD affect your physical health? (or) How does your adolescent's SCD affect his or her physical health? • Are there specific physical activities you or your adolescent avoid or can't do because of the impact of SCD?
Psychological health	• How does your SCD affect your mental/psychological wellbeing? (or) How does your adolescent's SCD affect his or her mental/psychological wellbeing?

Social and family life	• How does your SCD affect social and family life? (or) How does your adolescent's SCD affect social and family life?
	  ○ What aspects of social and family life does it impact the most?
	  ○ Probe:
	  ▪ Does it affect relationships with your spouse/partner? In what ways?
	  ▪ Does it affect relationships with your or your adolescent's friends? In what ways?

Work or school (college or university) life	• How does your SCD affect work or school life? (or) How does your adolescent's SCD affect his or her work or school life?
	  ○ Probe:
	  ▪ Does it cause work or school to be missed?
	  • If yes:
	  ○ In the past 6 months, how many days have you (or your adolescent) been absent from work or school because of SCD?
	  ▪ Have you missed part of the workday or left early from school because of your SCD? Has your adolescent with SCD left early from school because of his or her SCD?
	  • If yes:
	  ○ In the past 6 months, how many days have you missed part of the workday because of SCD? Why have you had to miss part of the day due to SCD?
	  ▪ In general, how has your SCD affected your ability to get work done? (or) In general, how has your adolescent's SCD affected his or her ability to get work done?

Pain crises	• How do vaso-occlusive crises or pain crises due to SCD affect your life or your adolescent's life? • What makes these worse or more frequent?

	• How frequently do these occur? How often do you treat them at home? How often do you need to seek medical attention? • How bothersome are these impacts to you [with SCD] or your adolescent with SCD?
Transfusions	• How does the need for blood transfusions for your SCD affect your life or your adolescent's SCD affect his or her life? How bothersome are these impacts to you [participant with SCD] or your adolescent [with SCD]?
Overall quality of life	• Are there any other ways that your SCD impacts your life or your adolescent's SCD affects his or her quality of life that we have not discussed?
Ranking exercise	
• On average, how do the following disease impacts of your SCD affect aspects of your health-related quality of life? (or) On average, how do the following disease impacts of your adolescent's SCD affect aspects of his or her health-related quality of life? • Please rank the impacts from 1 to 6, where 1 is the <u>least impact</u> and 6 is the <u>most impact.</u> o Daily activities and living o Physical health o Psychological health o Social and family life o Work or school (college or university) life o Other • Please explain why you have ranked these in such an order.	
Current treatment	
• Now let's talk about current treatment.	

- What treatments are you or your adolescent currently receiving for SCD?
    - Probe: How many of you or your adolescents are currently taking:
        - Hydroxyurea
        - Hydroxycarbamide
        - Iron chelation therapy (ICT)
        - Crizanlizumab (Adakveo)
        - Voxelotor (Oxbryta)
        - Pain medications
        - Other
            - Please tell me more.
- How easy is it to take the medication as instructed?
- If you could, is there one thing about your current treatment(s) that you wish you could change?

Thank you. This completes the first half of the focus group session. We will now proceed to the second half of the session.

B. THE SECOND HALF OF THE INTERVIEW

- This half will be sub-divided into two parts.
    - First, I'd like us to discuss your SCD symptoms and disease impacts (or your adolescent's SCD symptoms and disease impacts) that we pulled from the scientific literature.
    - Second, we will discuss the survey questions we all received and reviewed a few days ago.

1. SCD symptoms and disease impacts section

- We have identified some concepts from the literature that we think may be important to you or your adolescent's disease experience of SCD.

Symptoms associated with SCD
Anemia symptoms: • Tiredness and fatigue • Body weakness
Episodes of pain: • Pain crises with varied intensity, frequency, and duration (hour to weeks) • Chronic pain associated with bone and joint damage, ulcers, and other • Swelling of hands and feet
Frequent infections: • Damage to spleen increases vulnerability to infections • Pneumonia risk
Potential sickle cell anemia complications: • Stroke, acute chest syndrome, pulmonary hypertension, organ damage, blindness, leg ulcers, gallstones, priapism, pregnancy complications
Potential medication and transfusion complications: • Infection • Allomimmunity (immune response)

• Transfusion-related acute lung injury • Allergic, febrile, and delayed hemolytic reactions • Nausea, joint pain, back pain and fever
Potential iron-induced complications: • Heart complications (heart failure, left ventricular dysfunction, and arrhythmias) • Liver complications (increased ALT and AST, fibrosis, and cirrhosis) and risk of hepatocellular carcinoma • Endocrine complications (hypogonadism, diabetes, hypothyroidism, hypoparathyroidism, and calcium metabolism abnormalities)
Other symptoms: • Delayed growth or puberty • Vision problems

- Can everyone see the list of symptoms I'm currently showing on my screen?
    - Yes: Great, thank you.
    - To create this list, we reviewed studies that have been conducted in SCD patients. These studies outlined or reviewed the symptoms and disease impacts that may affect your quality of life due to your SCD or your adolescent's quality of life due to his or her SCD.
    - We would like to elicit your opinion on this list and discuss how relevant these symptoms are to you or your adolescent's experience of SCD.
- We are going to work our way down the table, starting first with the row on anemia symptoms.
    - Can everyone see where I've placed my cursor on my screen?
        - Yes: Great. We'll start from here.

- Are these symptoms relevant to you or your adolescent's experience of SCD?
- Did we correctly capture all the relevant symptoms and how you would describe the symptoms?
  - Are there additional symptoms which we have missed?
    - Yes: Please tell me more.
  - What about how we categorized the symptoms?
    - Yes: Please tell me more.
  - Would you describe the symptoms differently or use different words or names for these symptoms?
    - Yes: Please tell me more.

To moderator: Use the same approach to review and discuss all the other symptoms.

- Thank you for a productive discussion. We will now shift gears to discuss broad categories that researchers suggest may impact you or your adolescent's health.
- Again, to create this table, we reviewed many scientific studies that have been conducted with patients and caregivers with SCD. These studies outlined broad ways that SCD may impact one's health-related quality of life.
- Can everyone see the table on my screen?

Health-related quality of life impacts due to SCD
Emotional and psychological: • Depression and anxiety (increased with severity) • Frustration with symptoms • Worry about the future and death • Stress • Mental impairment and inability to focus

	• Insomnia and trouble sleeping • Low self-esteem	
	Physical functioning: • Fatigue and tiredness • Pain: aching, throbbing, sharp, stabbing, hammering, pounding • Limitations to activities of daily life • Body issues (appearance) • Weight management	
	Social functioning and family life: • Having to plan around SCD • Household functions and relationships with others • Intimate relationships challenging • Limited active lifestyle	
	Other: • Impact on work and school • Time sacrifice • Travel restrictions • Possible stigma • Treatment financial concerns • Mistrust of healthcare professionals	

- We would like to elicit your opinion on these categories. Specifically, we would like to know if these categories are relevant to your SCD experience or your adolescent's experience of SCD.
- We will work our way down this list by first starting with the Emotional and Psychological disease impact category.
    - Can everyone see where I've placed my cursor on my screen?
    - Yes: Great, we'll start from here.
- What do you think about this category?
    - Have we missed anything?
    - What do you think about the sub-definitions and sub-bullets? For this, we have included high resilience, low mood and irritability, anxiety. . .
        - Do these correctly capture everything you would put under the emotional and psychological disease impact?
            - Yes: Please tell me more.
            - No: What is missing?
        - Would you describe the impacts differently or use different words or names to describe them?
            - Yes: Please tell me more.

To moderator: Use the same approach to review and discuss all the other disease impacts.

2. Review of survey questions/operationalization

Format and mode of survey delivery

Next, we would like to discuss the survey questions we all received and reviewed a few days ago.

- The survey can be taken online either using a computer or smartphone.
- We think the survey will take no longer than 30 minutes to complete.
    - What do you think about this?

- In your opinion, are there any specific requirements that we should consider to support survey completion:
    - Prompt: We plan to send reminders to let participants know when to take the survey. If you were taking the survey, how would you like to be reminded?
        - Probe:
            - Phone text-messaging
            - Phone call
            - Email

Timing and duration of the survey

We plan to collect the survey information across three timepoints: when the participant enters the study, at 3 months, and again at 6 months.

- What do you think about these data collection time periods?
- In your opinion, would administering the survey when the participant enters the study, 3 months and 6 months be appropriate to capture the symptomatic experience and changes in health-related quality of life due to SCD?
    - Yes: Please tell me more.
    - No: Please tell me more.

Other

- Is there anything else we should consider when administering the survey?

WRAP-UP. FINISHING THE INTERVIEW.

- Thank you. This brings us to the end of our session today.
- Is there anything you would like to share that we did not discuss?
- Do you have any questions for me? Can I contact you if I have any follow-up questions?

- We would like to follow-up and provide a summary of our focus group findings to share with you to ensure we have correctly interpreted our discussion. Is this acceptable?

Thanks a lot for your participation in this interview. Our team will be in touch via email to share with you an Amazon voucher as a thank you for your participation. Please do not hesitate to contact me if you have any further questions in the meantime.

ALT, alanine transaminase; AST, aspartate transferase; HRQoL, health-related quality of life; SCD, sickle cell disease

Supplementary Table 2a Saturation table and codebook development

		Interview or focus group							
	Code*	1	2	3	4	5	6	7	8
Impacts on daily activities	Limitations in daily functioning	X							
	Ability to cook		X						
	Ability to walk		X						
	Ability to shower		X						
	Unpredictability of condition impacting functioning	X							
	Maintaining an active lifestyle	X							
Sickle cell crisis	Frequency	X							
	Triggers	X							
Psychological impact	Depression and low mood	X							
	Anxiety	X							
	Insomnia	X							
	Resentment	X							
	Concerns about future	X							

	Isolation	X							
	Self-harm and suicide	X							
	High resilience	X							
	Time sacrifice		X						
	Dealing with unpredictability	X							
	Mourning members of the community				X				
Social life	Communicating about condition to friends			X					
	Ability to participate in social activities	X							
	Friends not being understanding			X					
	Feeling like a burden on friends	X							
	Positive effects of sickle cell disease on friendships				X				
Family life	Communicating about condition to family			X					
	Family acting as carers	X							
	Burden on family	X							
	Missing out on family activities		X						

	Family planning				X				
	Impact on romantic relationships	X							
Impact on work	Ability to work	X							
	Communicating about condition at work			X					
	Financial concerns		X						
Impact on education	Education impact	X							
	Missed time from education	X							
Treatment	Planning around treatment	X							
	Treatment side effects	X							
	Lack of knowledge by healthcare professionals	X							
	Being ignored	X							
	Trauma and anxiety from bad care	X							
Prejudice and stigma	Racism and prejudice	X							
	Being treated like a drug addict				X				
Cumulative data saturation, n (%)		28/42 (66.7)	34/42 (81.0)	38/42 (90.5)	42/42 (100)	42/42 (100)	42/42 (100)	42/42 (100)	42/42 (100)

*An “X” indicated the interview in which the code was first applied

Supplementary Table 2b Timings of the interview sessions

Order	Interview	Individual or caregiver (age group [years], gender)	Setting	Duration (hours: minutes: seconds)	Date (day/month/year)
1	Interview 1	Individual 1 (18–35, female)	United Kingdom	53:35	20/01/2022
2	Interview 2	Individual 1 (18–35, male)	United Kingdom	1:08:16	21/01/2022
3	Interview 3	Individual 1 (18–35, female)	United Kingdom	58:31	24/01/2022
4	Interview 4	Individual 1 (18–35, female) Individual 2 (18–35, female) Individual 3 (18–35, female) Caregiver 1 (12–17, female)	United States	1:04:57	03/02/2022
5	Interview 5	Individual 1 (18–35, male)	United Kingdom	31:54	08/02/2022
6	Interview 6	Individual 1 (36–49, female) Individual 2 (36–49, male) Individual 3 (36–49, female) Individual 4 (36–49, female) Individual 5 (36–49, female) Individual 6 (36–49, female) Individual 7 (36–49, female)	United States	1:15:06	17/02/2022
7	Interview 7	Individual 1 (36–49, female)	United States	48:53	18/02/2022
8	Interview 8	Individual 1 (>50, male)	United Kingdom	1:17:46	22/02/2022

		Individual 2 (36–49, female) Individual 3 (>50, female)			

Supplementary Table 3 COREQ checklist

Topic	Item no.	Guide questions/description	Reported on page no.
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author(s) conducted the interview or focus group?	9-10
Credentials	2	What were the researcher's credentials? e.g., PhD, MD	N/A
Occupation	3	What was their occupation at the time of the study?	N/A
Gender	4	Was the researcher male or female?	N/A
Experience and training	5	What experience or training did the researcher have?	N/A
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	9
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g., personal goals, reasons for doing the research	Supplementary Table 1
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g., bias, assumptions, reasons, and interests in the research topic	Supplementary Table 1
Domain 2: Study design			
Theoretical framework			
Methodological orientation and theory	9	What methodological orientation was stated to underpin the study? e.g., grounded theory, discourse analysis, ethnography, phenomenology, content analysis	10
Participant selection			

Sampling	10	How were participants selected? e.g., purposive, convenience, consecutive, snowball	9
Method of approach	11	How were participants approached? e.g., face-to-face, telephone, mail, email	9
Sample size	12	How many participants were in the study?	12
Non-participation	13	How many people refused to participate or dropped out? Reasons?	12
Setting			
Setting of data collection	14	Where was the data collected? e.g., home, clinic, workplace	9
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	9
Description of sample	16	What are the important characteristics of the sample? e.g., demographic data, date	Tables 1 and 2
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	10; Supplementary Table 1
Repeat interviews	18	Were repeat interviews carried out? If yes, how many?	12
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	10
Field notes	20	Were field notes made during and/or after the interview or focus group?	10
Duration	21	What was the duration of the interviews or focus group?	Supplementary Table 2b
Data saturation	22	Was data saturation discussed?	10

Transcripts returned	23	Were transcripts returned to participants for comment and/or correction?	10
Domain 3: Analysis and findings			
Data analysis			
Number of data coders	24	How many data coders coded the data?	10
Description of the coding tree	25	Did authors provide a description of the coding tree?	10
Derivation of themes	26	Were themes identified in advance or derived from the data?	10
Software	27	What software, if applicable, was used to manage the data?	10
Participant checking	28	Did participants provide feedback on the findings?	10
Reporting			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g., participant number	13–20
Data and findings consistent	30	Was there consistency between the data presented and the findings?	12–20; Tables 1 and 2
Clarity of major themes	31	Were major themes clearly presented in the findings?	12–20
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	12–20

COREQ, consolidated criteria for reporting qualitative research

Supplementary Table 4 NICE methodology checklist: Qualitative studies

	Circle or highlight one option for each question
1.1 Is a qualitative approach appropriate? *For example:* Does the research question seek to understand processes or structures, or illuminate subjective experiences or meanings (in healthcare this would apply to how care is organized and patient experiences of care)? Or could a quantitative approach better have addressed the research question?	Appropriate Inappropriate Not sure
1.2 Is the study clear in what it seeks to do? *For example:* Is the purpose of the study discussed – aims/objectives/research question(s)? Are the values/assumptions/theory underpinning the purpose of the study discussed?	Clear Unclear Mixed
2.1 How defensible/rigorous is the research design/methodology? *For example:* Are there clear accounts of the rationale/justification for the sampling, data collection, and data analysis techniques used?	Defensible Not defensible Not sure
3.1 How well was the data collection carried out? *For example:* Are the data collection methods clearly described? Were the data collected appropriate to address the research question?	Appropriate Inappropriate Not sure/inadequately reported
4.1 Is the context clearly described? *For example*: Are the characteristics of the participants and settings clearly defined? Were observations made in a variety of circumstances and from a range of respondents? Was context bias considered (that is, did the authors consider the influence of the setting where the study took place)?	Clear Unclear Not sure
4.2 Were the methods reliable? *For example:* Were data collected by more than one method? Were other studies considered with discussion about similar/different results?	Reliable Unreliable Not sure
5.1 Are the data "rich"? *For example:* How well are the contexts of the data described? Has the diversity of perspective and content been explored? Has the detail of the data that were collected been demonstrated? Are responses compared and contrasted across groups/sites?	Rich Poor Not sure/not reported

5.2 Is the analysis reliable? *For example:* Did more than one researcher theme and code transcripts/data? If so, how were differences resolved? Were negative/discrepant results addressed or ignored? Is it clear how the themes and concepts were derived from the data?	Reliable Unreliable Not sure/not reported
5.3 Are the findings convincing? *For example:* Are the findings clearly presented? Are the findings internally coherent (that is, are the results credible in relation to the study question)? Are extracts from the original data included (for example, direct quotes from participants)? Are the data appropriately referenced so that the sources of the extracts can be identified? Is the reporting clear and coherent?	Convincing Not convincing Not sure
5.4 Are the conclusions adequate? *For example:* How clear are the links between data, interpretation, and conclusions? Are the conclusions plausible and coherent? Have alternative explanations been explored and discounted? Are the implications of the research clearly defined? Is there adequate discussion of any limitations encountered?	Adequate Inadequate Not sure
6.1 Was the study approved by an ethics committee?	Yes No Not sure/not reported/not applicable
6.2 Is the role of the researcher clearly described? *For example*: Has the relationship between the researcher and the participants been adequately described? Is how the research was explained and presented to the participants described?	Clear Not clear Not sure/not reported

NICE, National Institute for Health and Care Excellence