



What matters most to sepsis survivors: a qualitative analysis to identify specific health-related quality of life domains

Christian König^{1,2} · Bastian Matt¹ · Andreas Kortgen¹ · Alison E. Turnbull^{3,4,5} · Christiane S. Hartog^{1,2}

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Abstract

Purpose It is unknown how sepsis survivors conceptualize health-related quality of life (HRQL). We aimed to identify important HRQL domains for this population.

Methods A literature search was performed to inform an interview guide. Open-ended interviews were held with 15 purposefully sampled sepsis survivors. Interview transcripts were analyzed by interpretative phenomenological analysis to allow themes to develop organically. Resulting codes were reviewed by an independent expert. The preliminary list of domains was rated in a two-round Delphi consensus procedure with therapists and survivors.

Results Eleven domains emerged as critically important: Psychological impairment, Fatigue, Physical impairment, Coping with daily life, Return to normal living, Ability to walk, Cognitive impairment, Self-perception, Control over one's life, Family support, and Delivery of health care. Sepsis survivors want a "normal life," to walk again, and to regain control without cognitive impairment. Family support is essential to overcome sepsis aftermaths.

Conclusions Survivors described many HRQL domains which are not captured by the QoL instruments that have traditionally been used to study ICU survivorship (i.e., SF-36 and EQ-5D). Future studies of QoL in ICU survivors should consider using both a traditional instrument so that results are comparable to previous research, as well as a more holistic QoL measurement instrument like the WHOQOL-BREF.

Keywords Sepsis · Health-related quality of life domains · Qualitative research · Patient-reported outcome

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✉ Christiane S. Hartog
christiane.hartog@mailbox.org

¹ Department of Anesthesiology and Intensive Care Medicine, Jena University Hospital, Am Klinikum 1, 07747 Jena, Germany

² Integrated Research and Treatment Center for Sepsis Control and Care (CSCC), Jena University Hospital, Am Klinikum 1, 07747 Jena, Germany

³ Outcomes After Critical Illness and Surgery (OACIS) Group, Johns Hopkins University, Baltimore, MD, USA

⁴ Division of Pulmonary and Critical Care Medicine, School of Medicine, Johns Hopkins University, Baltimore, MD, USA

⁵ Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA

Abbreviations

ARDS	Acute respiratory distress syndrome
EQ-5D	EuroQoL-5D
HRQL	Health-related quality of life
ICU	Intensive care unit
IPA	Interpretative phenomenological analysis
PROM	Patient-reported outcome measurement
RNL	Return to normal living
SF-36	Short Form 36 Health Survey
WHOQOL-BREF	Short version of the World Health Organization Quality of Life assessment (WHOQOL-100)

Introduction

Sepsis is a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs. With an incidence rate of 270 per 100,000 person-years

[1], sepsis is common and often fatal with hospital mortality of 26% [1]. Half of patients recover, but among those who survive sepsis, one-sixth have permanent organ damage [2], cognitive impairment, and physical disability [3]. The number of sepsis patients who survive intensive care is growing due to a rise in the incidence of sepsis [1, 4], a general increase in the number and use of intensive care unit (ICU) beds [5], as well as progress in the treatment of sepsis [6]. There is growing recognition among critical care clinicians and researchers that the health-related quality of life (HRQL) of sepsis survivors is an important endpoint for evaluating critical care [7].

While researchers in other fields of health care use both specific and generic measures of HRQL, critical care researchers have hitherto only used generic tools, mainly the Short Form 36 Health Survey (SF-36) and the EuroQoL-5D (EQ-5D). These two tools have been declared by experts to be the most appropriate instruments for ICU survivors [8], have been used extensively in studies of sepsis or ICU survivors [9–12], and are included in a core outcome measurement set to evaluate outcomes of acute respiratory failure survivors [13]. Table 1 shows domains included in these HRQL measures.

However, SF-36 and EQ-5D were developed without input from intensive care survivors [14, 15]. The underlying domains are based on the perspective of the general population and may fail to reflect the specific experiences and concerns of sepsis survivors [16, 17]. Disease-specific measures intend to explore issues which are of most relevance to the people affected by this disease and these tools are generally more responsive to small changes in condition. However, no specific tools exist to assess health-related quality of life in sepsis survivors [17].

Therefore, our goal was to understand how HRQL is perceived by sepsis survivors. We conducted semi-structured interviews with sepsis survivors and developed HRQL domains that matter most to sepsis survivors according to their own perception and priorities. Our study results are an initial step towards the development of a patient-reported outcome measurement (PROM). We followed established reporting standards as applicable [18]. A PROM measures the state of a patient's health condition by the patient himself, without interpretation by a clinician or anyone else. PROMs are disease-specific and responsive measures with a high content validity. PROMs are now considered by regulatory and quality assurance agencies as mandatory for clinical trials [19].

Methods

Development of the preliminary interview guide

A review of the literature was performed to identify measures and domains of health-related quality of life (HRQL)

which were used in clinical trials of ICU and sepsis survivors. From the original publications, instruments which measured HRQL were identified and a list of HRQL domains and items (questions) was extracted to develop a preliminary interview guide. We added the question: What matters most to you in life?

Participants and interview procedure

To achieve a reasonably representative sample, we recruited participants from a sepsis registry derived from interdisciplinary ICUs of a German university hospital (DRKS0000834). Because quality of life may be affected by origin of sepsis, gender, and time interval after sepsis, we purposefully selected participants according to the following criteria: 18 years and older, diagnosis of severe sepsis or septic shock, ICU survival, male or female gender, and type of sepsis (community or hospital acquired) in equal proportion. Published study results obtained from sepsis [10] and ICU survivors [20] suggest that quality of life stabilizes after 6 months. We therefore selected survivors between 6 and 36 months after sepsis. Survivors with a tracheotomy who could not speak for themselves were excluded. During interviews we found it necessary to exclude one survivor because he could not understand the interview questions. Relatives could be present if survivors wished them to be. Eligible participants were invited by mail and received information about the study and written consent forms. Interviews were carried out face-to-face or by telephone. Written informed consent was obtained from all participants before interviews were conducted. The study was approved by the ethics committee of Jena University Hospital (IRB number 4392-04/15).

Data collection

Medical data were obtained from the electronic patient data management system. All interviews were conducted by CK. The preliminary interview guide was continuously revised to include new questions about themes which came up during interviews. When possible, interviews were conducted face-to-face in the patient's home or at the hospital. Patients who declined a face-to-face interview were offered a telephone interview, considering that the quality of data obtained by these two forms of interviews is comparable [21, 22]. Interviews were recorded digitally and transcribed verbatim. See Online Resource 1 for more details about transcription process.

Qualitative analysis of interview transcripts

Interview transcripts were analyzed using the interpretative phenomenological analysis (IPA) approach [23]. IPA

Table 1 HRQL domains in SF-36, EQ-5D, and WHOQOL-BREF

HRQL tool	Explanation
SF-36	
Physical functioning	Limited in performing all physical activities including bathing or dressing
Role limitations due to physical problems	Problems with work or other daily activities as a result of physical health
Social functioning	Interference with normal social activities due to physical and emotional problem
Bodily pain	Severe and extremely limiting pain
General mental health	Feelings of nervousness and depression
Role limitations due to emotional problems	Problems with work or other daily activities as a result of emotional problems
Vitality	Feeling tired and worn out
General health perceptions	Belief that personal health is poor and likely to get worse
EQ-5D ^a	
Mobility	Problems in walking about or being confined to bed
Self-care	Problems with self-care, i.e., washing or dressing
Usual activities	Problems with work, study, housework, family, or leisure activities
Pain/discomfort	Having pain or discomfort
Anxiety/depression	Being anxious or depressed
WHOQOL-BREF	
General health	Overall general health
Physical health	Pain and discomfort Energy and fatigue Sleep and rest Dependence on medication Mobility Activities of daily living Working capacity
Psychological	Negative feelings Positive feelings Self-esteem Thinking, learning, memory, and concentration Body image Spirituality, religion, and personal beliefs
Social relations	Personal relationships Practical social support Sexual activity
Environment	Financial resources Information and skills Recreation and leisure Home environment Access to health and social care Freedom, physical safety, and security Physical safety and security Physical environment Transport

^aThe EQ-5D also contains a visual analogue scale for self-rating of overall health status

is an inductive approach that avoids seeking to confirm prior themes and allows themes to emerge organically [24]. Themes are identified through an iterative cycle of reading transcripts, identifying themes, and applying codes to the data and—as the analysis continues—reviewing earlier transcripts in the light of findings of later transcripts [25]. One researcher (CK) analyzed all transcripts and developed the preliminary codebook. The qualitative analysis software f4analyse v1 was used. A second experienced independent researcher (BM) evaluated the codebook. To ensure that the analysis was exhaustive and no further interviews were necessary, a saturation table of all codes was developed and constantly updated during analysis [26, 27]. After saturation was reached, the codes were clustered into domains. See Online Resource 1 for more details about the qualitative analysis.

Development of the final domains

To validate the findings from our qualitative analysis by an independent panel of experts, we conducted a modified Delphi consensus process with web-based communication and anonymous voting [28]. The Delphi panel consisted of therapists with experience in treating sepsis survivors (physicians, nurses, psychologists, clergy), and sepsis survivors or caregiving relatives. Panelists were recruited through the German Sepsis Aid and personal networks. Panelists received an email or letter with information about the study, detailed instructions on the process, and a list of preliminary domains with explanations and verbatim expressions of interviewees. Panelists were asked to evaluate these domains according to how important they considered them to be for sepsis survivors on a scale from 1 to 9 (1–3 not important, 4–6 important but not critical, 7–9 critically important). Panelists could also comment on or modify a domain and could add a domain which they found missing. In the following round, each panelist who participated in the previous round received detailed information about the process and the results of ratings and respective modifications, specifically the number of respondents, distribution of scores for each item for each stakeholder group separately, and their own score from the previous round. Consensus was defined a priori as $\geq 80\%$ participant agreement on the critical importance of a domain (7–9 points). In case of divergent ratings of therapists compared to survivors and relatives, we defined that consensus criteria were met if $\geq 80\%$ of survivors or relatives agreed on the critical importance of a domain. Domains which did not reach this threshold were not further considered. Voting was conducted online using a LimeSurvey tool. Response rates were reported as proportion of panelists who completed a survey.

Results

Studied population

Sixty-seven consecutive registry patients received invitation letters. Among 27 surviving patients or relatives who responded to the invitation, six patients had died in the interim and four were excluded for cognitive impairment or having a tracheostomy. One respondent was unavailable for interview due to a traffic accident and one respondent was not considered due to gender balance and because thematic saturation had been reached. The group of invited survivors was comparable to the group of responding survivors regarding sex, age, and time after onset of sepsis (Online Resource 2). Fifteen interviews were analyzed (Table 2). Four were conducted in the presence of close relatives. Eight interviewees were male. Mean age was 62 years (range 27–87), mean time after onset of sepsis was 11 months (range 5–40). Mean duration of the interview was 67 min (range 34–95).

Qualitative analysis

To ensure rigorousness in the qualitative analysis, a codebook was developed containing the name of the code, subcodes, when to use and when not to use the code, a verbatim expression of the transcript that exemplified the code, and the number of revisions made to this code (more details in Online Resource 3). After iterative analysis of all transcripts and evaluation by an independent experienced researcher, the final codebook comprised 16 codes and 99 subcodes (see Online Resource 4 and Online Resource 5 for coding and code distribution). Data saturation was already 95% after the first seven interviews. The following eight interviews only added 5% of codes and subcodes (Fig. 1). Online Resource 6 provides details of qualitative analysis. Finally, codes and subcodes were clustered into ten preliminary domains for the Delphi consensus process.

First Delphi round

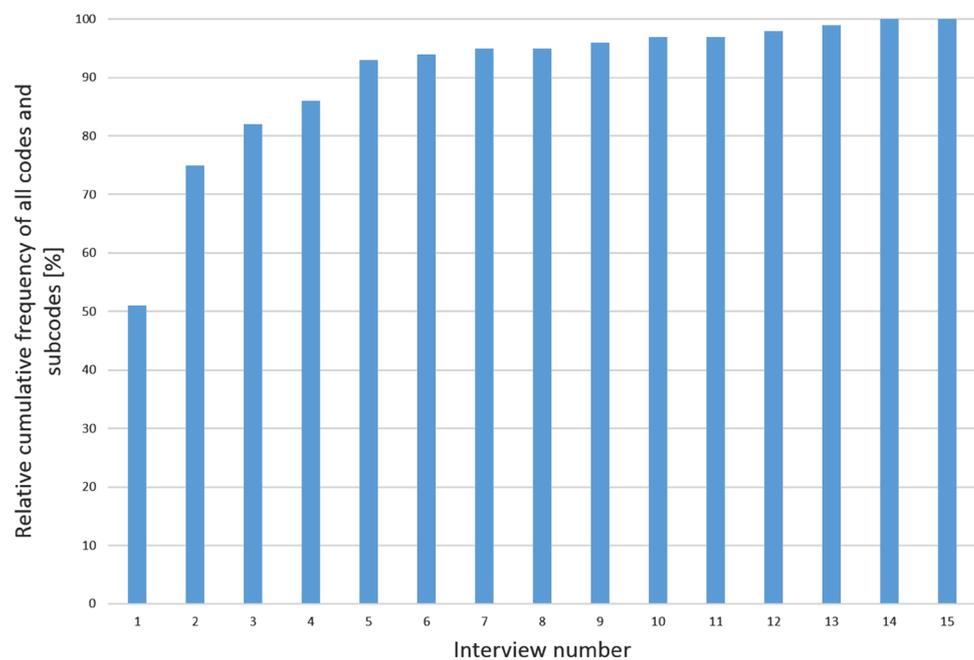
In the first round, 13 panelists took part (Online Resource 7). The median rating for all domains was between 7 and 9 points (Table 3), corresponding to critically important. Consensus (as defined by 80% agreement) was achieved for all domains except the domain “Problems with the health care system/bureaucracy/financial burden” (only 69% of participants agreed on the critical importance of this domain). Domains “Self-perception,” “Fatigue,” and “Importance of family” received consensus from survivors or relatives (83% each) but not from therapists (71% each). As defined previously, these domains were kept for the second round. Due to

Table 2 Characteristics of participants

No.	Gender	Age (years)	Months after onset of sepsis	type of sepsis	Focus of sepsis	Hospital length of stay (days)	ICU length of stay (days)	Type of interview	Interview duration (min)
1	f	59	12	c	Pneumonia	49	34	Telephone	80
2	f	47	40	c	Primary bacteremia	34	26	Face-to-face	68
3	m	48	5	h	Gastro-intestinal	35	5	Face-to-face	34
4	m	57	5	h	Abdominal	33	33	Face-to-face	69
5	m	27	5	c	ARDS	28	28	Face-to-face	45
6	m	63	5	c	Pleural empyema	36	24	Face-to-face	95
7	m	51	6	h	Urosepsis	43	2	Face-to-face	78
8	m	78	5	h	Pneumonia	52	48	Face-to-face	78
9	f	87	12	c	Abdominal	28	7	Face-to-face	71
10	f	78	12	c	Abdominal	22	4	Telephone	51
11	m	64	13	h	Pneumonia	44	44	Face-to-face	81
12	f	79	11	h	Penetrating atherosclerotic ulceration	27	27	Telephone	57
13	m	67	13	h	Endocarditis	35	6	Telephone	62
14	f	59	14	h	Abdominal	65	18	Telephone	54
15	f	68	14	h	Endocarditis	27	9	Face-to-face	85

Type of sepsis: *c* community acquired, *h* hospital acquired, *ARDS* acute respiratory distress syndrome, *m* male, *f* female

Fig. 1 Relative cumulative frequency of all codes and subcodes per interview. As the analysis progresses, saturation is reached as few new codes or subcodes are added. Data saturation was already 95% after the first seven interviews. Later interviews only contributed 5% to the total number of codes and subcodes



comments, the following modifications were made: domain “Importance of family” was renamed “Family support”; “Problems with the health care system/bureaucracy/financial burden” was renamed “Delivery of health care.” The domain “Physical and cognitive impairment” was split into two domains “Physical impairment” and “Cognitive impairment.” A novel domain “Practice of religion or spirituality”

was suggested and added. In addition, participants were asked if they would agree with the following statement: “The overarching goal for all sepsis survivors is to return to a normal life in the sense of what was normal before sepsis or what is considered normal for their age, regardless of specific impairment.” Ten of 13 experts in the first Delphi round agreed with this statement.

Table 3 Results of the first Delphi round

Domain	Median ratings All (<i>n</i> = 13) [range]	Percentage of participants rating domain as “critically important”		
		All (<i>n</i> = 13)	Therapists (<i>n</i> = 7)	Survivors or relatives (<i>n</i> = 6)
Psychological impairment	9 [8–9]	100.00	100.00	100.00
Control over one’s life	9 [6–9]	92.31	100.00	83.33
Ability to walk	8 [6–9]	92.31	85.71	100.00
Coping with daily life	8 [6–9]	92.31	85.71	100.00
Physical and cognitive impairment	8 [5–9]	92.31	85.71	100.00
Return to normal living	8 [4–9]	84.62	85.71	83.33
Fatigue	8 [5–9]	76.92	71.43	83.33
Importance of family	8 [4–9]	76.92	71.43	83.33
Self-perception	7.5 [5–9]	76.92	71.43	83.33
Problems with health care system/ bureaucracy/financial burden	7 [5–9]	69.23 ^a	85.71	50.00

^aConsensus not achieved

Second Delphi round

Twelve members of the first round also participated in the second round (Online Resource 7). Twelve domains which originated from the first round were presented to participants. Eleven of these reached consensus (Table 4): The 12th domain “Practice of religion or spirituality” did not achieve consensus and was therefore omitted. Panelists’ individual comments confirmed the importance of the final domains. All 12 panelists agreed that the domain “Return to normal living” was a domain of overarching importance. Table 5 shows the 11 final HRQL domains.

Description of final HRQL domains

Psychological impairment

Survivors suffer a great deal from psychological impairment. They are anxious and afraid of new diseases or another sepsis episode. They suffer from flashbacks, nightmares, and memories of “coma dreams.” They feel depressed, helpless, and misunderstood, are nervous and restless. They suffer from sleeplessness.

‘During rehab, my nightmares were so intense I couldn’t sleep at all. I woke up every morning dripping in sweat.’ – (Female, 59 years, previously healthy,

Table 4 Results of the second Delphi round

Domain	Median ratings All (<i>n</i> = 12) [range]	Percentage of participants rating domain as “critically important”		
		All (<i>n</i> = 12)	Therapists (<i>n</i> = 6)	Survivors or relatives (<i>n</i> = 6)
Psychological impairment	9 [8–9]	100.00	100.00	100.00
Control over one’s life	9 [7–9]	100.00	100.00	100.00
Ability to walk	9 [6–9]	91.67	83.33	100.00
Return to normal living	8 [7–9]	100.00	100.00	100.00
Cognitive impairment	8 [7–9]	100.00	100.00	100.00
Family support	8 [7–9]	100.00	100.00	100.00
Coping with daily life	8 [6–9]	91.67	83.33	100.00
Delivery of health care	8 [6–9]	91.67	100.00	83.33
Fatigue	8 [5–9]	83.33	83.33	83.33
Physical impairment	8 [5–9]	83.33	83.33	83.33
Self-perception	7.5 [5–9]	83.33	83.33	83.33
Practice of religion or spirituality	5.5 [2–8]	41.67 ^a	50.00	33.33

^aConsensus not achieved

Table 5 Final HRQL domains

Domain	Explanation
Psychological impairment	<i>Psychological symptoms such as fears, anxiousness, depressions, or nightmares</i>
Control over one's life	Loss of control over one's life and the feeling of helplessness and dependency
Ability to walk	Being able to walk independently with or without assisting devices
Return to normal living	Overarching domain describing the ability to go back to the previous 'normal' life
Cognitive impairment	Symptoms such as concentration disorders, loss of memory, disturbance of speech, and disorientation
Family support	Being supported by one's family
Coping with daily life	<i>Performing basic activities of daily living and participating in social activities</i>
Delivery of health care	No access to or lack of post-sepsis health care services and bureaucratic obstacles to obtain help or benefits
Fatigue	<i>Lack of motivation, weakness, and the feeling of weakness</i>
Physical impairment	<i>All physical symptoms and limitations including pain</i>
Self-perception	Discordance between the inner representation of survivor's self and the actual self

Domains in italics overlap with domains from SF-36 or EQ-5D questionnaires; domains in roman are not covered

12 months after sepsis. She describes herself as a fighter and wants to regain her previous health so that she can take care of her old mother and return to work.)

Control over one's life

Survivors often mentioned feelings of helplessness and dependency on others. They lack control over what is going on around them and are unable to actively influence the situation. Physical and cognitive impairments also contribute to the feeling of lack of control.

'Then you realize that you are completely helpless...'
– (Male, 27 years, pre-existing lung disease, five months after sepsis due to pneumonia. He suffered intensely from nightmares and feelings of helplessness during intensive care. He dreams of returning to work and start a family.)

Ability to walk

Being able to walk stuck out from other physical abilities by the degree to which it affected personal freedom and the ability of being active. It was a major concern for all survivors and the main focus during rehabilitation.

'And then I sat at the edge of my bed and said to myself: 'Today I will walk!' There was a really good nurse, together we did three steps and I was so happy that I could stand on my own feet again.' – (Male, 57 years, previously healthy, five months after sepsis due abdominal infection after a car accident. During the interview he was sitting in a wheelchair.)

Return to normal living

"Return to normal living" (RNL) is a global assessment of how completely survivors achieve a state which they consider comparable to what was normal before sepsis or normal in regard to their age. For most survivors, sepsis signified a sudden, extraordinary deterioration of health and functioning. They refused to accept the current state as "normal" compared to their previous state. Survivors want to return to their previous roles and activities; they want to go back to their "normal" everyday life. At the same time, they do not expect extraordinary things and are realistic about what they can do in regard to their age.

'Nobody expected... I haven't realized that I was almost dead because I was in a coma. I have come a long way from there, I almost live a normal life with all its positive and negative parts. That I managed to do so makes me happy. I'm optimistic and look forward.' – (Female, 47 years, 40 months after sepsis from overwhelming infection due to a dysfunctional spleen. Today, after having basically re-learned to swallow, speak and walk, and cope with multiple finger amputations, she has returned to work, enjoys swimming and walking with her husband and daughter.)

Cognitive impairment

Many survivors also suffer from cognitive deficits. Main symptoms are lack of concentration, loss of memory, speech disturbance, and disorientation.

'I can't concentrate anymore. I read a lot, mostly detective stories. But it doesn't work. I read three pages and then I have to put the book aside.' – (Female, 59 years,

14 months after sepsis from peritonitis. Previously independent and physically active, she is now affected every day by loss of concentration and short-time memory. She feels depressed, lonely, misunderstood, and lacks energy.)

Family support

All sepsis survivors pointed out the importance of their family. They could rely on them and were supported by them. In many cases, family ties became stronger after sepsis.

‘All the family things are now way closer and intense.’ – (Male, 48 years, five months after sepsis following chemotherapy for multiple myeloma. Slowly, joy returns to his life. His partnership and family solidarity are stronger than before. He would like to be more of a help at home to unburden his wife.)

Coping with daily life

Being able to deal with daily requirements is essential. Survivors need to perform activities such as washing, eating, putting on clothes, be able to use means of transport, take up some meaningful occupation, or social activity even if impairments make those activities challenging.

‘Some things I can do now on my own, for instance washing myself, taking a shower, prepare my drugs. I do this on my own at home now. Before, the nursing assistant had do this.’ – (Female, 47 years, previously healthy, 40 months after sepsis, suffered from multiple physical sequelae and spent many months in rehab. She grew to accept help from others but still comes up daily against her physical limits.)

Delivery of health care

Sepsis survivors complained about a lack of specific health care services tailored to their needs. There was nobody they could turn to. They stated that General Practitioners do not understand sepsis sequelae. The path from the ICU, hospital, and rehab center back home was full of bureaucratic obstacles and difficult for patients with health problems.

‘The way from hospital and rehab center and the discharge back home was a constant struggle. You had to handle everything on your own.’ – (Female, 47 years, 40 months after sepsis. She had to argue with her insurance company to get all therapies and medical aids she needed. But fighting was almost impossible because she lacked the mental energy to

do so. She wishes that there would be more support and less bureaucratic obstacles for patients after a life-threatening disease.)

Fatigue

Survivors describe a lack of motivation to do something, a general feeling of listlessness (not caused by muscle weakness). Many days, they are unable to do anything and feel passive all the time.

‘I was just sitting there and waited and waited... until it was 12 o’clock again... that he [the nurse] would come back. And give me the injection and prepare some food. And then I was waiting again for the next meal.’ – (Female, 78 years, 12 months after sepsis due to an infected gallbladder. This elderly lady experienced severe fatigue. With time she overcame her lethargy, regained physical strength and is again living independently. She does not want to be a nursing case ever again.)

Physical impairment

Survivors can experience many different physical problems, for instance, amputations, shortness of breath, kidney failure, muscle loss, polyneuropathy, vomiting, nausea, or pain.

‘The kidneys lost their function. It was horrible. I had to get dialysis and I’m very grateful that they could get them working again.’ – (Male, 57 years, five months after sepsis. During rehab, his kidneys failed, and he required dialysis. He still suffers from pain, polyneuropathy, ICU acquired weakness, depends on oxygen supply, and must use a wheelchair.)

Self-perception

The combination of physical changes and psychological impairment often leads to a stressful discordance between a survivor’s inner representation and the actual self.

‘Suddenly I saw myself in the mirror and I thought: That’s not me!’ – (Male, 78 years, previously healthy, five months after sepsis following kidney surgery. He required more than two months intensive care with mechanical ventilation and dialysis. Today, he is almost fully recovered and has kept his sense of humor.)

See Online Resource 8 for more detailed verbatim expressions.

Discussion

This study identified 11 domains which sepsis survivors consider important to describe their quality of life after sepsis. Four domains overlap with generic SF-36 or EQ-5D domains (Table 5): Psychological impairment, Fatigue, Physical impairment, Coping with daily life. Seven domains were not covered by these instruments (Return to normal living, Ability to walk, Cognitive impairment, Self-perception, Control over one's life, Family support, and Delivery of health care). A subsequent modified Delphi procedure with different survivors, relatives, and therapists confirmed the critical importance of all 11 domains. In addition, panel members consented unanimously that the domain "Return to normal living" is an overarching domain regardless of any co-existing impairment.

This study shows that 7 of 11 domains are not addressed by the widely used SF-36 or EQ-5D. Three other research groups which have recently evaluated HRQL domains in survivors of critical care came to similar conclusions. Lim et al. developed a framework based on qualitative analysis of interviews with ICU survivors [29]; Singer et al. identified HRQL domains based on interviews with recipients of lung transplants and healthcare practitioners [30]; and Eakin et al. described ARDS survivors' experience within the context of the PROMIS framework using qualitative interview analysis [31]. All groups identified substantial gaps in generic HRQL tools, which limits their use in clinical practice and research. Thus, use of SF-36 as primary endpoint may be partly responsible for the failure of an intervention study to achieve improved outcomes after sepsis by managed care [10]. In contrast, the WHOQOL-BREF questionnaire [32] (Table 1) includes domains "Level of independence," "Social relationships," or "Thinking, learning, memory, and concentration." It merits further studies in the field.

An important specific domain for sepsis survivors is cognitive impairment. Surviving sepsis more than triples the risk of moderate to severe cognitive impairment [3]. Survivors described these deficits as severely crippling, especially the loss of concentration. Sepsis survivorship is also associated with a high rate of functional limitations. In a prospective cohort of elderly US American sepsis survivors, Iwashyna et al. reported that those with no limits before sepsis experienced a mean 1.57 new limitations and those with moderate limitations before sepsis, a mean of 1.50 new limitations [3]. In our study, the ability to walk emerged as a major HRQL domain. Walking differs from mobility which can also be achieved with a wheelchair. Walking conveys a sense of independence and control over one's body. Loss of the ability to walk was experienced as a major life changing event by survivors who could walk normally before sepsis. Likewise, the domain control over one's life emerged

as an important concept related to loss of independency and inability to make plans for the future.

Critical care researchers worldwide have realized the need to develop core outcome sets, defined as agreed, standardized collection of outcomes measured, and reported in all trials for a specific clinical area [33]. This is a challenge because ICU survivors suffer from a multitude of symptoms, reflected by the development of seven core domains including physical function, cognition, mental health, survival, pulmonary function, pain, and muscle and/or nerve function [34], and the use of 250 different outcome measures [11]. In contrast, our study suggests that there may be one overarching domain—Return to normal living describes the degree to which survivors achieve a life they consider normal relative to their state before sepsis or their age. RNL seems to be of general importance, regardless of other physical, mental, or emotional deficits. Thus, RNL has promise for a core domain which can be applied uniformly to survivors with a broad range of physical and mental outcomes. More research is necessary to develop or refine valid measurement tools.

This study has both limitations and strengths. Our patients were recruited from multidisciplinary ICUs of a single hospital, thus findings may not be generalizable to patients from other hospitals, countries, or health care systems. In countries with a larger proportion of religious inhabitants, the vote of Delphi panel members on the domain "spirituality or religiousness" may have been different. Sepsis patients are a heterogeneous group; despite purposeful sampling which considered factors associated with outcomes (gender, age, and type of sepsis), our sample is not representative for sepsis survivors. We excluded patients with cognitive impairment or who could not speak, which may have excluded the sickest patients. However, this is a well-known limitation of studies of ICU survivors [35]. We followed established rules to identify patient-reported outcomes by using an interview guide developed from a literature review to conduct open-ended interviews. Methodical rigor was maintained by setting up fixed transcription rules, developing a detailed codebook, and reviewing of the codebook by an experienced independent researcher. However, a residual element of subjectivity cannot be ruled out in qualitative analysis. We included 15 interviews which is comparable to sample sizes in other qualitative exploratory phenomenological studies [24, 26, 36–38] and found 95% of data saturation already after seven interviews. Thus, we are confident that we achieved comprehensive coverage of the topic 'quality of life after sepsis' from different survivors' perspectives. The Delphi panel was small; however, there was a good balance between medical and lay experts and 11 out of 12 domains met the consensus criteria defined a priori as 80% agreement. Therefore, we believe a larger panel would not have changed our findings.

Conclusion

Sepsis survivors described many HRQL domains which are not captured by the QoL instruments that have traditionally been used to study ICU survivorship (i.e., SF-36 and EQ-5D). Future studies of QoL in ICU survivors should consider using both a traditional instrument so that results are comparable to previous research, as well as a more holistic QoL measurement instrument like the WHOQOL-BREF. One domain—return to normal living—seems to be an overarching domain. Further research is needed to develop valid and responsive patient-reported measures for these outcomes.

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Author contributions CK and CSH planned the study and drafted the manuscript. CK conducted the study and gathered data. CK, BM, and CSH analyzed and interpreted the data. AET and AK revised the work for important intellectual content. All authors gave final approval of the version to be published.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study was approved by the ethics committee of Jena University Hospital (IRB No. 4392-04/15). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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