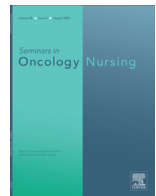




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A Delphi Study of Core Patient-Reported Outcomes for Advanced Renal Cell Carcinoma and Advanced Hepatocellular Carcinoma

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ABSTRACT

Objectives: There is little research to help health care professionals understand what patient outcomes are considered a priority in advanced liver or kidney cancer. Knowing what is important to patients can help promote person-centered approaches to treatment and disease management. The aim of this study was to identify those patient-reported outcomes (PROs) that patients, carers, and health care professionals consider as “core” when providing care to those with advanced liver or kidney cancer.

Data sources: A three-round Delphi study was undertaken to ask experts by profession or experience to rank PROs identified from a previous literature review. Fifty-four experts, including people living with advanced liver or kidney cancer (44.4%), family members and caregivers (9.3%), and health care professionals (46.8%), reached consensus on 49 PROs including 12 new items (eg, palpitations, hopefulness, or social isolation). Items with the highest rate of consensus included quality of life, pain, mental health, and capacity to do daily activities.

Conclusion: People living with advanced liver or kidney cancer experience complex health care needs. Some important outcomes were not actually captured in practice in this population and were suggested as part of this study. There are discrepancies between the views of health care professionals, patients, and family in what is important, highlighting the need of using measures to facilitate communication.

Implications for Nursing Practice: Identification of priority PROs reported here will be key to facilitate more focused patient assessments. The actual use of measures in cancer nursing practice to allow monitoring of PROs must be tested for feasibility and usability.

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Introduction

Renal cell carcinoma (RCC) is the most common type of kidney cancer¹ and is most frequently diagnosed in men.² Although RCC is commonly diagnosed in early stages, around 30% of cases are of advanced RCC.³ Hepatocellular carcinoma (HCC) is the most common type of liver cancer and sixth most common irrespective of sex.² Most HCC cases are diagnosed at an advanced stage with very high mortality.^{2,4} From an incidence perspective, cases of advanced RCC and advanced HCC are on the rise globally and are associated with poor prognosis.^{1,4,5}

People with advanced RCC/HCC may experience significant symptoms, such as cachexia, fatigue, pain, dyspnea, and venous thromboembolism.^{6,7} Some physical symptoms are cancer-specific; for example, people with advanced HCC may experience ascites, pruritus, or muscle cramps.⁶ However, many health care needs are similar in both advanced RCC and advanced HCC and are not solely physical, but also related to emotional, cognitive, or practical problems.^{7,8}

Targeted therapies (T) and immunotherapy (IO) have transformed the treatment, symptom experience, and overall survival landscape in cases of advanced RCC/HCC.^{9,10} Combinations of immunotherapy and targeted therapies, either as two immunotherapies (IO/IO) or targeted therapy with immunotherapy (IO/T), are now the standard of care for patients with advanced RCC/HCC. Regarding first-line treatment, a combination of cabozantinib plus nivolumab is

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recommended for management of advanced RCC, whereas combined atezolizumab with bevacizumab is recommended for advanced HCC.^{11,12}

IO/IO or IO/T combinations for the treatment of advanced RCC/HCC patients are generally well tolerated, but not without side effects.⁸ Although they may cause fewer emergencies, they are often associated with non-life-threatening side effects that can affect a patient's daily living, quality of life, and treatment continuation.^{13–15} Treatment combinations for advanced RCC/HCC help to control but may not cure these cancers; therefore, they are seen as long-term treatments. Consequently, mild but persistent symptoms experienced could also highly affect daily living. A study comparing the effects of different treatments for advanced RCC found that those patients taking atezolizumab combined with bevacizumab had milder symptoms and reported less impairment with daily life, although they still reported considerable difficulties related to living with cancer and its treatment.¹⁴ When asking patients about their experience and their perspective of cancer care, people with RCC identified emotional concerns as a source of frustration during treatment, as well as other unresolved problems.¹⁶ Under the prism of polypharmacy,¹⁷ it is important to consider how the use of two or more anticancer agents can affect the manifestation of side effects, taking also into consideration aspects of tolerability, quality of life, and overall adherence.¹⁸

Managing the needs of patients with advanced RCC/HCC requires a multidisciplinary approach and must include patients' and carers' opinions. The involvement of patients in their care can help to improve individual, as well as clinical, outcomes and overall care experiences.¹⁹ When involving patients, it is particularly important not to underestimate their reported worries and concerns. In advanced cancer cases, research has shown that health care professionals might consider patients' quality of life poorer than patients themselves, and they also tend to underestimate treatment side effects.²⁰ Also, the toxicities and late effects that are a priority for health care professionals might not be necessarily reflective of the issues that have the most detrimental effect on quality of life for patients.²¹ However, patients tend to report symptom frequency and severity earlier than health care professionals.²² High-quality cancer care requires health care professionals to actively listen to individuals, as well as their carers, when they directly self-report on symptoms, treatment burden, or performance.²³ These self-reported outcomes are called patient- (or person-) reported outcomes (PROs). Clinical trials do normally look at PROs via use of self-reported PRO measures (PROMs) that explore diverse patient domains, such as physical symptoms, global health-related quality of life, or toxicities.²¹ However, PROs are still not routinely collected in the clinical setting, and implementation of PROMs is still ongoing.^{24,25}

To date, there is little research to help health care professionals understand what outcomes are considered a priority for people with advanced HCC/RCC on targeted therapies.^{17,26} Knowing what is important to an individual can help promote person-centered approaches to treatment and disease management. The aim of this study was to identify PROs that people diagnosed with advanced RCC/HCC, their carers, and health care professionals consider to be "core" when providing care in the context of targeted therapies for advanced RCC/HCC.

Methods

Study Design

A modified, three-round, international online Delphi study was designed.²⁷ The Delphi technique allows opinion sharing and helps achieve consensus from a group of experts by giving independent ratings to each of the topics identified.²⁸ The Delphi technique gives experts the opportunity to express their individual opinions in the

first round, then review their answers in subsequent rounds while taking into account other experts' answers.²⁹ Experts can give an opinion about a topic and can make suggestions; in following rounds they can review the results, allowing them to revalidate their decisions.³⁰

This study is part of a larger project (https://cancernurse.eu/research/proms_project/). The project has received research ethics approval from the University of Glasgow, MVLS Ethics Committee (number 200200106).

Sample and Sample Size

Delphi participants can be considered experts because of their professional background or their personal experience.³¹ Participants must also be willing to engage in the Delphi process and share their views and experience.²⁷ Here, our experts were people with advanced RCC or advanced HCC, as well as family members or informal carers, and health care professionals involved in advanced RCC/HCC care. Delphi participants could take part from anywhere in the world, although they were required to be able to read and write in English.

Experts were identified internationally via several sources, including advertisements on professional and charitable organizations via Twitter, Facebook, and LinkedIn, as well as via direct invitations to professionals, researchers, and representatives, and a snowballing technique, where participants were asked to identify additional participants from their networks.

There is no suggested optimal sample size for a Delphi study, and it can vary from a small number to up to 50 participants. For a heterogeneous sample, it is suggested that a minimum representation of 36 participants per panel will allow for diversity of views, while also accounting for expected attrition.^{30,32,33}

Identification of Potential PROs

Before the Delphi phase, a rapid review of the literature was undertaken to identify common PROs reported in the context of advanced RCC and HCC.²⁴ This review identified a total of 66 potential PROs; these were synthesized into eight categories (physical symptoms, emotional issues, cognitive issues, practical issues, sexual and intimacy issues, relationship with others, faith, and general health) and then presented to the experts in the first round of the Delphi.

Before the launch of the Delphi, the first round was piloted by a project steering group that comprised clinical and research experts and lived experience representatives. The content was adapted and finalized in response to their feedback.

The Delphi Process

Questionnaires for the Delphi rounds were constructed and distributed via the secure platform Jisc (<https://www.jisc.ac.uk/>). In the first round, the online questionnaire comprised four sections. The first included a participant information sheet, privacy notice, and consent. The second collected participant information, including personal or professional area of expertise, country of residence, and ethnicity. In the third section, participants were invited to rate the importance of the 66 PROs divided into eight categories and rate the overall importance of each of the eight overarching categories. The first round also included free-text questions after each category for participants to propose additional PROs or to clarify their choices. The fourth section included contact details and a free-text field for any additional comments. In the first two rounds, participants were asked to rate the importance of each PRO item using a nine-point Likert scale (1–3 = not important, 4–6 = unsure, 7–9 = important). In our study, 70% agreement or above was considered to suggest

consensus.²⁹ When a PRO item reached 70% agreement, it was included; if an item either reached 70% as not important or less than 30% as important, the item was removed from subsequent rounds. All the additional PRO items were discussed by all authors and incorporated into the existing categories.

In round 2, participants were invited to re-rate the importance of all initial and new PRO items, as well as the categories that were found to reach 70% importance, and also those that did not reach consensus. Finally, in round 3, participants were asked to review those PRO items that had not yet reached consensus by indicating whether they agreed the item was important by rating the item as “important” or “not so important.” Each round remained open for five weeks.

After opening each round, reminders were sent to all participants every two weeks.

After finishing the rounds, we asked participants to check the results. We also asked health care professional experts to informally show these results to patients in their caseload (not participants in this study) to check whether these patients also felt represented by the results.

Data Analysis

Data were exported to a Microsoft Excel spreadsheet, anonymized by one author (CDRS), and analyzed by two authors (CDRS, GK). Analysis of the Likert scale was carried out using descriptive analysis and focusing on percentage agreements of importance.

Results

Accrual Rates and Expert Characteristics

The study took place between October 2021 and February 2022. In the first round, 54 experts participated in the Delphi study. Thirty-nine experts responded to round 2 (72%), and 35 experts completed round 3 (69%).

Demographic characteristics of the experts in round 1 are presented in Table 1. The sample of participants was almost equal between health care professionals (46.3%) and individuals with experience (44.4%), with family members/informal carers being the least represented group (9.3%).

Health care professionals

Twenty-five participants (46.3%) were health care professionals, mainly originating from European countries. Most were nurses (n = 17), followed by physicians (n = 6), one psychologist, and one pharmacist. Most health care professionals (40%) cared for both RCC and HCC patients, whereas 36% treated only RCC patients and 24% only those with HCC. Health care professional experts had a mean professional experience of 16.5 years (standard deviation: 10.5 years; range: 6–45 years).

Patients and family members

Twenty-four experts were people with a diagnosis of RCC or HCC (44.4%), and five were family members or informal caregivers (9.3%). Those diagnosed had a median age of 58 years (standard deviation: 10.09; range: 38–75 years old). Most had renal cancer (n = 20, 83.3%), and they and their families were mainly from the United Kingdom (93%).

Delphi Rounds

In the first round, 21 of the 66 proposed PROs reached consensus as important (percentage agreement \geq 70%), whereas the rest did not (Table 2). Six of eight domains, also reached consensus, ie, physical symptoms, emotional problems, cognitive problems, practical issues, relationship with others, and general health. Experts also provided 55 free-text comments. Eight were generic and not about PROs, so they were excluded; 17 comments were already reflected in the existing PRO items. From the remaining comments, 25 new PRO items were constructed and included in round 2: physical symptoms (n = 7), emotional issues (n = 7), practical issues (n = 6), sexuality (n = 1), and relationships with others (n = 4).

In the second round, experts were presented with all 91 PRO items (original 66 plus 25 new) divided into the eight categories. Of these, 29 PRO items (excluding 21 having already reached consensus) and six categories were deemed important. Four PRO items were deemed “not important” (feeling bloated, hair depigmentation, LGBT issues, and faith) and were eliminated from round 3.

In the third round, the remaining 58 PRO items were presented to the experts. Twenty-five PRO items reached consensus, 20 as important and 5 as not important (hair loss, muscle cramps, worrying what others think of me, support from the wider community, and

TABLE 1
Demographic Characteristics of Sample.

	Total n = 54		Patients/family n = 29				Health care professionals n = 25					
	n	%	Liver cancer		Renal cancer		Liver cancer		Renal cancer		Both	
Personal/professional background	n	%	n	%	n	%	n	%	n	%	n	%
A health professional with experience looking after people living with advanced renal or liver cancer	25	46.3%	N/A	N/A	N/A	N/A	6	24%	9	36%	10	40%
A person diagnosed with advanced renal or liver cancer	24	44.4%	4	16.7%	20	83.3%	N/A	N/A	N/A	N/A	N/A	N/A
A family member or carer of a person diagnosed with advanced renal or liver cancer	5	9.3%	1	20%	4	80%	N/A	N/A	N/A	N/A	N/A	N/A
Country of residence/practice	n	%	n	%								
United Kingdom	35	34.8%	27	93.1%			8		32%			
Spain	3	5.5%	0	—			3		12%			
Netherlands	2	3.7%	0	—			2		8%			
Italy	2	3.7%	0	—			2		8%			
Greece	2	3.7%	0	—			2		8%			
France	2	3.7%	0	—			2		8%			
Canada	2	3.7%	2	6.9%			0		—			
Belgium	1	1.8%	0	—			1		4%			
Denmark	1	1.8%	0	—			1		4%			
Georgia	1	1.8%	0	—			1		4%			
Palestine	1	1.8%	0	—			1		4%			
Portugal	1	1.8%	0	—			1		4%			
Switzerland	1	1.8%	0	—			1		4%			

TABLE 2
Delphi Results Rounds 1–3 Organized (in %) From More Important to Less Important in Their First Round.

Module/Topic	Round 1 (n = 25)			Round 2 (n = 25)			Round 3 (n = 28)	
	Important %	Unsure %	Not important %	Important %	Unsure %	Not important %	Important %	Not important %
Physical symptoms								
Physical symptoms (general)	90	8	2	100	0	0	–	–
Pain	87	6	8	97	3	0	–	–
Fatigue/lack of energy	75	19	6	82	16	3	–	–
Fevers	71	15	13	68	29	3	91	9
Shortness of breath	69	23	8	97	0	3	–	–
Vomiting	67	21	12	68	26	5	100	0
Weight loss	67	22	12	63	32	5	76	24
Sores in the mouth/throat	66	23	11	68	24	8	76	24
Rash or skin change	64	26	9	58	39	3	62	38
Diarrhea	64	28	8	76	21	3	–	–
Nausea	63	29	8	63	29	8	79	21
Difficulty swallowing	63	27	10	63	26	11	94	6
Leg/arm swelling	62	23	15	53	39	8	69	31
Headache	62	25	13	61	26	13	59	41
Urinary symptoms	61	22	18	47	45	8	79	21
Constipation	60	27	13	55	34	11	65	35
Sleep disturbances	57	31	12	55	39	5	59	41
Lack of appetite	57	28	15	53	37	11	68	32
Tingling or numbness in hands and/or feet	56	27	17	45	45	11	50	50
Coughing	56	29	15	45	45	11	79	21
Dizziness	56	33	12	61	28	11	65	35
Itching	55	32	13	54	43	3	53	47
Drowsiness	52	31	17	46	49	5	44	56
Dry mouth	48	33	19	38	46	16	48	52
Feeling bloated	43	32	25	29	55	16	–	–
Sweats	42	40	17	45	34	21	53	47
Change in the way food tastes	37	46	17	45	32	24	53	47
Hair loss	33	38	29	42	24	34	34	66
Muscle cramps	–	–	–	58	34	8	38	62
Vertigo	–	–	–	57	27	16	50	50
Burning hands or feet	–	–	–	55	37	8	71	29
Eyesight changes	–	–	–	55	39	5	62	38
Palpitations/heart racing	–	–	–	55	34	11	74	26
Bruising	–	–	–	35	46	19	44	56
Hair depigmentation	–	–	–	18	42	39	–	–
Emotional problems								
Emotional/psychological problems (general)	88	10	2	95	5	0	–	–
Mental health	77	15	8	92	5	3	–	–
Enjoyment of life	76	14	10	87	13	0	–	–
Stress	72	19	9	81	14	5	–	–
Depression	72	17	11	82	16	3	–	–
Anxiety	71	21	8	76	18	5	–	–
Optimism	71	12	18	62	32	5	62	38
Motivation	71	14	16	80	17	3	–	–
Fear of dying	68	17	15	74	21	5	–	–
Worry condition will get worse	67	24	9	76	18	5	–	–
Mood	65	19	15	73	24	3	–	–
Sadness	65	20	16	61	26	13	85	15
Feeling nervous	63	12	25	62	30	8	66	34
Anger	59	31	10	53	34	13	68	32
Irritability	53	33	14	65	24	11	59	41
Hopefulness	–	–	–	76	18	5	–	–
Loss of dignity	–	–	–	74	16	11	–	–
Fear	–	–	–	68	21	11	74	26
Loneliness	–	–	–	61	29	11	76	24
Guilt	–	–	–	55	21	24	42	58
Grief for the life before	–	–	–	53	39	8	41	59
Helplessness	–	–	–	53	39	8	74	26
Cognitive problems								
Cognitive problems (general)	73	20	7	95	5	0	–	–
Confusion	62	17	21	63	32	5	88	12
Difficulty remembering things	56	17	27	54	43	3	66	34
Trouble concentrating	54	21	25	49	49	3	65	35
Daily activity issues								
Practical things/daily activity issues (general)	91	7	2	100	0	0	–	–
Capacity to do the daily activities	85	9	6	89	11	0	–	–
Mobility	85	9	6	92	5	3	–	–
Energy levels	79	13	8	84	16	0	–	–
Self-care	79	15	6	76	21	3	–	–
Walking/exercise	77	17	6	84	14	3	–	–

(continued)

TABLE 2 (Continued)

Module/Topic	Round 1 (n = 25)				Round 2 (n = 25)			Round 3 (n = 28)	
	Important %	Unsure %	Not important %		Important %	Unsure %	Not important %	Important %	Not important %
End of life care	77	8	15	74	13	13	—	—	
Weakness	74	19	8	68	27	5	71	29	
Ability to take care of family/loved ones	66	23	11	68	21	11	79	21	
Work	54	31	15	50	34	16	52	48	
Finances and money issues	49	30	21	65	27	8	69	31	
Goals of your treatment	—	—	—	92	3	5	—	—	
Access to cancer screenings	—	—	—	84	11	5	—	—	
Diet	—	—	—	68	24	8	67	33	
Burden due to comorbidities	—	—	—	61	29	11	61	39	
Traveling/being able to attend appointments	—	—	—	58	39	3	71	29	
Accommodation	—	—	—	50	37	13	58	42	
Sexuality problems									
Sexuality/intimacy issues (general)	38	44	18	62	30	8	—	—	
Issues with sexual functioning	46	27	27	47	37	16	54	46	
Issues with sexuality (eg, thoughts related to sex, interest in sex, or ability to enjoy sex)	41	35	24	43	37	20	54	46	
Intimacy	40	38	23	46	38	16	53	47	
LGBTQ+ issues	26	25	49	26	32	42	—	—	
Risks to partner from body fluids while on treatment	—	—	—	46	19	35	44	56	
Relationship issues									
Relationship with others (general)	66	30	4	89	11	0	—	—	
Relationship with family/loved ones	78	9	13	74	20	6	—	—	
Changes in body image/appearance	64	19	17	71	24	5	—	—	
Relationship with others (not family)	53	32	15	63	32	5	76	24	
Support for partners/family members	—	—	—	82	13	5	—	—	
Social isolation/social connectedness	—	—	—	63	24	13	76	24	
Support from the wider community	—	—	—	47	42	11	24	76	
Worrying what others think of me	—	—	—	39	29	32	29	71	
Spirituality									
Spirituality/faith (general)	27	42	31	28	28	44	—	—	
Spirituality (sense or belief that there is something greater than myself)	31	28	41	34	34	32	29	71	
Faith (religious belief or following)	25	30	45	29	32	39	—	—	
General health									
General health (general)	96	4	0	95	5	0	—	—	
General health status	91	6	4	92	8	0	—	—	
Quality of life	91	6	4	97	3	0	—	—	
Satisfaction with your current quality of life	80	13	7	89	11	0	—	—	

spirituality); the remaining 33 did not reach consensus and were therefore also excluded.

In total, 49 PRO items reached consensus and achieved importance (Table 2), including 14 of 34 physical PRO items (41%), 15 of 21 (71.4%) emotional PRO items, 1 of 3 (33.3%) cognitive PRO items, 11 of 16 (68.7%) practical PRO items, 5 of 7 (71.4%) relationship PRO items, and all 3 (100%) general health PRO items. From the 25 new PRO items proposed by the experts, 12 reach consensus, including support for partners/family members, goals of treatment, hopefulness, loss of dignity, and palpitations. There were no significant differences between those with RCC versus HCC, or between health care professionals treating RCC versus HCC. Some discrepancies were noted between health care professionals and those diagnosed/family members. For instance, there were PRO items that health care professionals believed were important that did not reach consensus within the patient/family member expert group. These included lack of appetite (89% vs 68%), constipation (78% vs 65%), or intimacy (72% vs 53%). Conversely, palpitations were deemed important by patients but not by health care professionals (74% vs 56%).

With respect to PRO items agreed on as not important, three items reached consensus as not important for patients and also did not reach consensus for health care professionals: support from the wider community (76% vs 61%), spirituality (71% vs 61%), and worrying what others think of me (71% vs 67%) (Table 3). Inconsistencies between groups were discussed with the steering committee supporting the project that includes both experts by profession and experience that were not part of the Delphi study.

Summary results of the Delphi were returned to all experts and shared with people affected by RCC and HCC from around Europe who were not part of the Delphi for feedback. There were comments returned to us indicating that people affected by RCC and HCC felt represented by these results overall; they also believed some of the items were difficult to discuss with health care professionals (such as issues with sexual functioning), and this could be one reason for this item not reaching consensus (Table 4). We were also asked to inform them or involve them in future steps to incorporate this into the clinical practice.

Discussion

People living with advanced RCC/HCC experience complex needs associated with their cancer, the effects of the treatments, and the psychosocial issues associated with their diagnosis.^{6,7,17} This study was designed with the aim of bridging an important knowledge gap by identifying core PROs in the context of targeted therapies for advanced RCC or advanced HCC. Following a Delphi technique, our expert panel reached consensus on 49 “priority” PROs that were deemed similarly important by both HCC and RCC experts.

Many emotional, practical, and general health issues reached consensus immediately in the first round. There were already seven PROs on emotional issues (eg, mental health, enjoyment of life or stress), seven on practical issues (eg, capacity to do daily activities, mobility, and energy levels) and the three related to general health (general health status, quality of life, and satisfaction with your

TABLE 3
Discrepancies Between Health Care Professionals and Patients and Family Organized in % of Importance for Health Care Professionals

	Health care professional		Patient		Cutoff > 70%	% Difference
	Important %	Not important %	Important %	Not important %		
Lack of appetite	89	11	68	32	Discrepancy - important	21
Constipation	78	22	65	35	Discrepancy - important	13
Sleep disturbances	78	22	59	41	Discrepancy - important	19
Anger	78	22	68	32	Discrepancy - important	10
Finances and money issues	78	22	69	31	Discrepancy - important	9
Burden due to comorbidities	78	22	61	39	Discrepancy - important	17
Leg/arm swelling	72	28	69	31	Discrepancy - important	4
Feeling nervous	72	28	66	34	Discrepancy - important	7
Work	72	28	52	48	Discrepancy - important	21
Issues with sexual functioning	72	28	54	46	Discrepancy - important	18
Intimacy	72	28	53	47	Discrepancy - important	19
Diet	71	29	67	33	Discrepancy - important	4
Accommodation	71	29	58	42	Discrepancy - important	13
Palpitations/heart racing	56	44	74	26	Discrepancy - important	-18
Support from the wider community	39	61	24	76	Discrepancy - not important	-15
Spirituality (sense or belief that there is something greater than myself)	39	61	29	71	Discrepancy - not important	-10
Worrying what others think of me	33	67	29	71	Discrepancy - not important	-5

current quality of life) with percentages higher than 70% agreement. Previous qualitative studies have identified practical and emotional issues being a source of frustration and unmet need for these patient populations.^{17,34} Of note, our expert panel reached consensus on PROs not previously identified in the relevant literature, ie, two emotional issues (hopefulness, loss of dignity) and two practical issues (goals of your treatment, access to cancer screenings).

Conversely, there were items that had very small percentage of agreement from the beginning. For instance, all items related to faith, religion, and spirituality. Some studies have found a connection between religion and spirituality and patients' outcomes, suggesting that addressing such needs may lead to better experience of care.³⁵ Different populations, ethnicities, and cultures give faith different levels of importance during cancer treatment. The fact that most of our patient experts were white and British may have influenced our findings toward placing less importance to religion and spirituality compared with other populations and cultures in Europe known to have strong religion and spirituality beliefs.³⁶

Items regarding sexuality and intimacy did not reach consensus either; they were deemed important by more than one-half of the experts, however, still not reaching the 70% benchmark. Previous studies have alluded to the importance of sexual health care in these patient populations. In a study among people with advanced HCC,

problems with sexual interest was in the top five distressing symptoms.³⁷ This difference may be related to the comments received after the study when one person affected by cancer referred to finding difficulties speaking to their health care professionals about some of those issues: "Really not comfortable having this discussion with oncologist. Would make a stressful appt even worse for me, especially if husband present" (comment 3 in Table 4).

Our expert panel reached consensus on 12 new PROs to be considered in this disease context. PROs such as hopefulness, loss of dignity, burning hands or feet, or being able to attend appointments, for example, are either entirely new or part of existing PROMs but so far not considered in PRO research with people with advanced RCC/HCC, helping researchers to reconsider whether the actual PROMs used are the most appropriate tools to follow up these peoples' needs.²⁴

The use of PROs can help improve communication between patients and health care professionals.³⁸ The routine use of PROs has also proved useful in improving symptom control, reducing the incidence of oncological emergencies, and increasing patient satisfaction.^{25,38} Cancer nurses have a very important role in involving those diagnosed with these cancers in a multidisciplinary care context, and thereby improving the quality of care of people with RCC or HCC.^{8,39}

Health care professionals may appreciate the value of PROMs in facilitating conversation with patients, but many may not use them regularly in practice because of lack of knowledge, time pressures, and difficulty in interpreting findings.⁴⁰ In this study, we could identify PROs that had different levels of importance for health care professionals and patients/family members. They included physical concerns that were perceived as more important by health care professionals (including lack of appetite, constipation, leg/arm swelling, or sleep disturbances) than people affected by RCC/HCC, except for one, palpitations. There were also other nonphysical issues that were deemed more important by health care professionals than patients, such as anger, finances and money issues, or additional burden owing to comorbidities. These discrepancies make more visible the need of good communication and aids such as PROMs between health care professionals and those living with advanced HCC and RCC.

Strengths and Limitations

An important objective of this Delphi study was to obtain consensus from a diverse and representative panel of experts by experience and profession in advanced RCC/HCC. Although there were health care professionals involved from different countries, the

TABLE 4
Comments and Feedback.

1	<i>Rare cancers need to be better understood, this result look[s] important to me.</i>
2	<i>Health care professional working with RCC patients reported: Two of my patients reviewed the results and are happy with the final choices.</i>
3	<i>Regarding sexuality: Really not comfortable having this discussion with oncologist. Would make a stressful appt even worse for me, especially if husband present.</i>
4	<i>Spirituality OK if I ask...for referral but do not want my oncology team probing.</i>
5	<i>All research and study to improve our communal understanding of the various cancers is important in my opinion. I am in the middle or getting to the end of this journey and this will kill me one day, but I find this result useful and insightful for others.</i>
6	<i>Health care professional email: I spoke to two of our patients and they are PROs identified as important (first page in gray) they feel represented by these issues and consider them important as well and they think the second page is not important for them.</i>
7	<i>The overwhelming importance for me and my family is that I survive as long as I can even though quality of life is deteriorating. So many of [these] are not as important for me but they add to my burden.</i>

representation of those living with these cancers, as well as their carers, came primarily from English-speaking countries.

Language is a known barrier in research and in clinical practice because it can lead to inequalities of care and poorer health service.⁴¹ Differences in health care resources and systems of care mean that PROs that are deemed important by people in different countries may differ. For example, economic limitations will pose differences in access to medications, professionals, and specialist nurses that would consequently make a difference in the assessment and management of problems.⁴² Although we did not translate the questionnaire, it was a positive result to achieve responses from health care professionals from different countries, but this did not happen with those living with advanced HCC and RCC, or their families and carers, which poses a limitation of representation of this important group.

The similar number of participants representing health care professionals and those with personal experience did enrich the results and permit both views to be heard.⁴³ The involvement of people directly affected by these diseases was key to understanding their needs. Although we involved health care professionals treating people with RCC or HCC or both, cancer type representation was unequal, as most personal experience was from individuals diagnosed with RCC. While the number of patient experts with HCC was lower, there were no notable differences between the groups in terms of which PROs were deemed important or not, thus allowing us to generalize, with some caution, the results to both groups. More insights from those living with HCC are now needed.

The number of family members and carers involved in the Delphi study was significantly lower than the number of health care professionals and patients. Although there are many organizations and support groups for people affected by advanced RCC and HCC, there are not so many for carers. Cancer-specific organizations and social media were used in the recruitment of participants. The participation of fewer people affected by HCC could be because of these participants being less connected to advocacy organizations as well as their shorter survival compared with advanced RCC patients. They also tend to be diagnosed at an older age, which may affect their confidence levels when using internet and social media.⁴⁴ People with cancer and their carers also tend to not participate in the studies owing to lack of interest or motivation.^{43,45} Whether this was factor here requires further research.

Conclusion

This Delphi study aimed to obtain consensus on core PROs to evaluate in the context of the treatment of people with advanced RCC or advanced HCC. Our findings highlight the need to examine existing PROMs used with these cancer populations to identify which PROs are already being assessed, as well as the specific issues not yet captured that should now be considered. Our findings also provide information for the development of new PROMs or adaptation and validation of existing tools for use with these populations.

Statements and Declarations

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Ethics approval

This study has received research ethics approval from the University of Glasgow, MVLS Ethics Committee (number 200200106).

Consent to participate

Every participant gave written consent as approved by University of Glasgow, MVLS Ethics Committee.

Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Amanda Drury reports a relationship with European Oncology Nursing Society that includes board membership. The corresponding author serves on the editorial board of the journal we are submitting (GK).

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