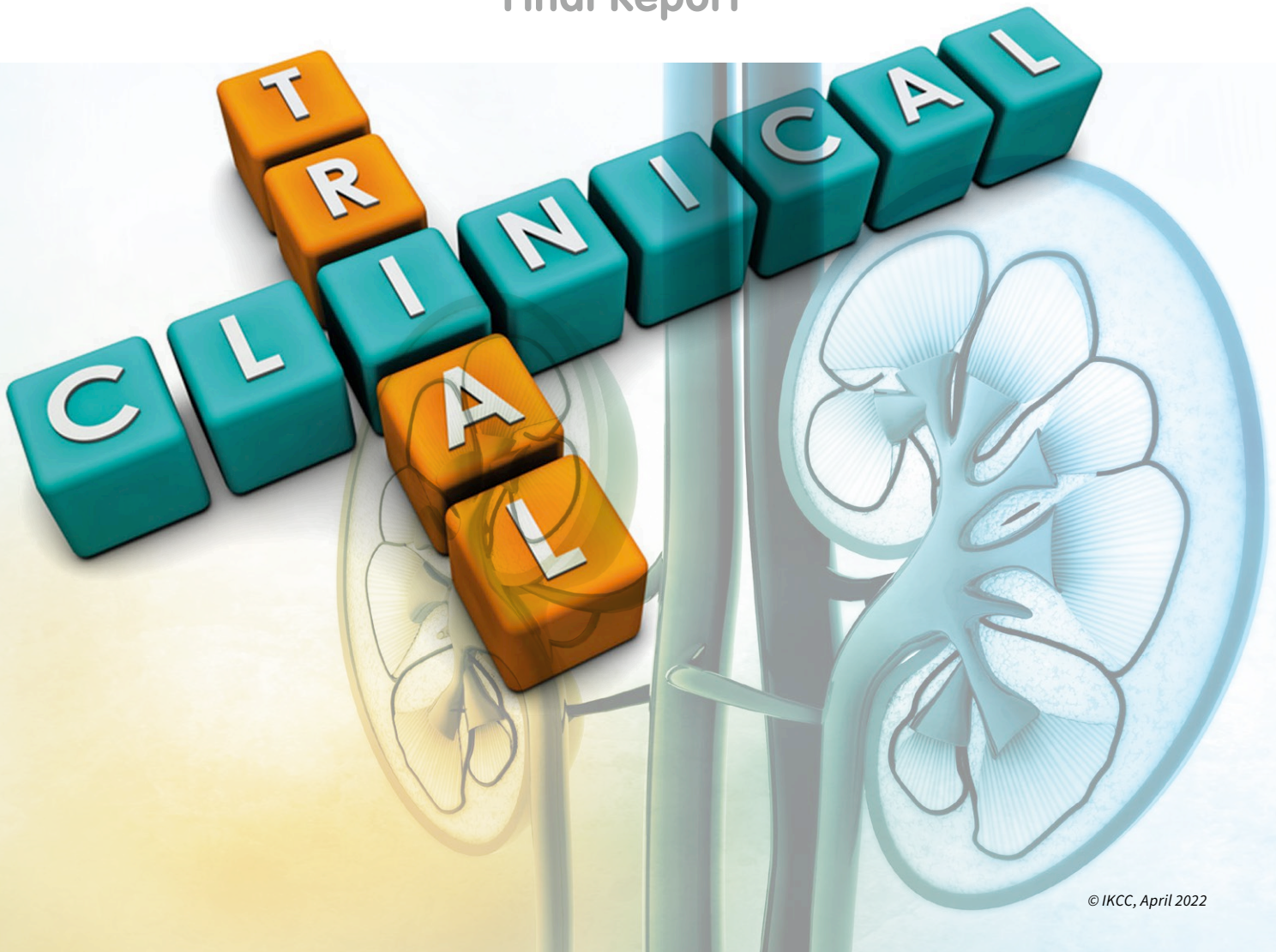


Retention in clinical trials: the kidney cancer patient perspective

Final Report



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<https://ikcc.org/infohubpost/clinical-trials/>

Project Summary

Introduction

Clinical trials are the cornerstone of advancing treatment for kidney cancer and they provide evidence about which treatments work. Every patient deserves access to the highest quality care and the opportunity to participate in research through clinical trials. Challenges with keeping patients enrolled in a trial may result in delays in completing the trial or issues with using the findings of the trial to make decisions about clinical care. The aim of this project was to understand the barriers kidney cancer patients face to remain on a clinical trial once they are enrolled and to review the medical literature to consider available interventions for protecting trial retention.

Methods

A qualitative study was designed and the Theoretical Domains Framework (TDF) was used to inform the interview guide. Semi-structured interviews were carried out with people affected by metastatic kidney cancer who had taken part in a clinical trial to investigate factors associated with clinical trial retention. A literature review was conducted alongside the qualitative study to identify available interventions for protecting trial retention that could be applied for kidney cancer trials.

Results

Four participants from across different geographical areas took part in the semi-structured interviews (50% of participants had completed a clinical trial and 50% had left a trial). We identified 8 domains within the TDF that were important to patient retention in clinical trials for kidney cancer, namely: knowledge, skills, social influences, environmental context and resources, beliefs about capabilities, reinforcements, beliefs about consequences and emotion. Environmental context and resources, specifically navigating travel to trial visits, was associated with a high financial and emotional burden in some geographical areas such as the US. Reimbursement for travel costs and taking a patient-centred approach when planning timing and frequency of trial visits may improve retention in trials. COVID-19 has highlighted potential means to further reduce the burden for trial participants by allowing some routine study tests to be conducted locally. Improving patient knowledge of benefits and harms of trial participation at recruitment stage, including signposting to supportive care to manage treatment side-effects, may further improve trial retention. Finally, there is a need to increase awareness of clinical trials for kidney cancer and proposed strategies include developing a kidney cancer trial navigator, using patient networks to increase awareness of clinical trials and improving length and clarity of participant information materials.

Discussion

This project has used a theory-informed approach to identify key barriers and consequent enabling factors to consider for improving retention in clinical trials for kidney cancer. Improving access to information and understanding of clinical trials via patient organisations and improved patient information and informed consent forms may help increase awareness and participation in trials. Travel can be a significant barrier to retention in trials and potential strategies to reduce the participant burden include reimbursement of travel costs and taking a patient-centred approach to scheduling trial visits. Patient organisations and support groups are an important social influence for trial participants and can offer social support to increase retention in clinical trials. Finally, sharing summaries of trial findings with participants may act as reinforcement and encourage future trial participation. Further research to evaluate the effect of involving the kidney cancer patient community in planning and running clinical trials is needed.

Introduction

Clinical trials are essential for advancing kidney cancer treatments and patient care. Clinical trial success rates for oncology are significantly lower compared to the success rate of trials overall.¹ Furthermore, there is a global trend of increasing duration of clinical trials, specifically phase II and phase III trials, along with increasing trial costs. Clinical trial duration remains higher for oncology, compared with other conditions.¹ An investigation of premature termination, or participant discontinuation, in phase II-III interventional adult clinical trials for genitourinary cancers was conducted between 2005 and 2011. The study found that 25% of genitourinary cancer trials risked premature termination, including a 10% risk of premature termination due to poor recruitment and retention of participants.²

Challenges with keeping patients enrolled in clinical trials can lead to significant waste of research resources and funding.³ While researchers, funders and governing bodies have clear targets for recruitment, there has traditionally been less focus on the importance of retention in clinical trials.⁴ Non-retention in clinical trials can be defined as participants withdrawing their consent or losing participants to follow-up, resulting in a loss of valuable outcome and safety data. It is estimated that on average 10-20% of participants leave clinical trials.^{5,6} Issues with retention and loss to follow-up may reduce the power of the study and the ability to assess the safety and effectiveness of the intervention. Furthermore, high discontinuation rates in clinical trials and the associated missing data can result in a validity threat if there is a discrepancy in missing data between trial arms. Such a discrepancy may indicate that participants are not lost randomly but instead signalling that participants with certain characteristics experience better or worse outcomes.^{7,8} A loss to follow-up of 5-20% may cause issues with bias and a loss of 20% or more can start to cause a serious threat to validity and limit the generalisability of study findings.^{9,10} Increasing the sample size during recruitment may help to mitigate issues with retention; however, this will increase the cost and length of clinical trials, which may in turn delay access to or increase the cost of the final therapeutic intervention.

Investment in strategies to improve recruitment and retention may help reduce the duration and cost of clinical trials and lead to improved access to novel treatments for patients. The majority of research investigating clinical trial participation have focused on recruitment rather than how to keep participants involved in trials. A Cochrane Systematic Review published in 2020 identified 69 studies investigating retention in randomised clinical trials (RCTs) with more than 100,000 participants across the studies. However, the majority of studies included in the systematic review focused on improving retention for postal questionnaires and few studies focused on improving retention for trial visits and follow-up visits, which have a higher associated participant burden compared to questionnaire completion. No studies for retention in kidney cancer trials were included in the systematic review of the literature.¹¹ Consequently, there is a lack of research investigating retention in clinical trials from the kidney cancer patient perspective. Investigating retention for kidney cancer trials is especially important seeing as awareness of clinical trials is already low. In the 2020 IKCC Global Patient Survey 46% of all survey respondents reported that no one had discussed cancer clinical trials with them and for survey respondents that had taken part in a clinical trial only 67% were satisfied with their experience.¹² The clear unmet need in kidney cancer patients, specifically, could point to the rarity of the disease which leads to feeling isolated, the fact that some may have co-morbidities related to their cancer treatment, e.g. reduced renal function, or unresolved shock and anxiety at the often asymptomatic diagnosis of kidney cancer, which is often found incidentally (up to 59%).¹³

Aims and objectives:

The project aims were:

- 1) To understand the specific barriers kidney cancer patients face to remain on a clinical trial once they are enrolled via a qualitative study.
- 2) To review the medical literature and to consider available interventions thought to protect trial retention.

Methods

Pilot study

Four patients with metastatic kidney cancer were invited via IKCC affiliate organisations to take part in a semi-structured interview to investigate their experience of taking part in a clinical trial for kidney cancer. The Theoretical Domains Framework (TDF) was used to design the interview guide. The framework has been designed by a collaboration of behavioural scientists and implementation scientists to provide a comprehensive and theory-informed approach to identifying the factors that determine behaviours. The framework consists of 14 domains of theoretical constructs and has been validated and used across a wide range of healthcare settings to understand what influences behaviour.¹⁴ For example, one domain within the TDF is Beliefs about Consequences and within this domain there are a number of associated theoretical constructs, including Beliefs, Outcome expectancies, Characteristics of outcome expectancies, Anticipated regret and Consequents. TDF provides a framework to consider the affective, cognitive, social and environmental influences on behaviour.¹⁵ Participation in clinical trials includes a number of behaviours such as attending trial visits or follow-up clinics. Interviews were transcribed and analysed using the TDF, with the assistance of NVivo 12 software.

Literature review

The ORRCA (Online Resources for Research in Clinical triAls, www.orrca.org.uk) database was used to identify retention strategies that could be applied in kidney cancer clinical trials. ORRCA is an online database of studies assessing recruitment and retention in clinical trials. The ORRCA database was developed to help improve the quality and ease of updating systematic reviews in the area of trial recruitment and retention and to improve the selection process of recruitment and retention strategies for researchers designing clinical trials. The ORRCA database includes peer-reviewed retention studies reporting on evaluation strategies, methods and study designs to improve retention within healthcare research and is updated regularly through searches conducted in Medline, CINAHL, PsycINFO, Scopus, Web of Science Core Collection and the Cochrane Library.⁴

Results

Participants

Four participants from across different geographical areas took part in this pilot project (50% of participants had completed a clinical trial and 50% had left a trial). Three participants had a diagnosis of kidney cancer and one participant was a family member of a patient with kidney cancer, who answered on behalf of the patient. Participants had taken part in a number of different kidney cancer trials ranging from phase I to phase IV, with the most common experience being participation in phase III trials for kidney cancer.

Barriers and enablers for retention

Eight domains within the TDF were identified as important to patient retention in clinical trials for kidney cancer, namely: knowledge, skills, social influences, environmental context and resources, beliefs about capabilities, reinforcements, beliefs about consequences and emotion. Definitions of the eight domains and their associated barriers and enablers for retention are listed in Table 1 (p.9).

Knowledge

Three avenues were cited as sources of awareness of clinical trials for kidney cancer patients; namely, via the patient's own physician, via kidney cancer patient organisations or via the participant's own research. Importantly, patient organisations and physicians were cited as trusted sources, which increased the likelihood of patients agreeing to participate in a clinical trial.

“I stumbled across the Kidney Cancer Support Network when I first got diagnosed and they helped me right in the beginning with how much to have scans cause it was a little bit vague over here. And then obviously I looked through their website and stumbled across all the clinical trials that at the time I didn’t need to know about that, but I knew it was there. And then when I got approached by [clinical trial site], when they said we think you could go onto the trial, I looked it up on the Kidney Cancer Support Network’s website and had a few online chats with [Head of Kidney Cancer Support Network] about it. And that’s how they helped. It’s just all the knowledge that they’ve got on their website is what everyone really needs to know.”

– Trial participant, UK

Furthermore, an understanding of what to expect from trial participation, specifically the potential risks, was cited as an important factor for retention. Poorly designed participant information materials and informed consent forms were cited as a barrier to patient understanding of the trial. Three out of four participants interviewed cited participant information and consent forms as being either too long or too difficult to understand.

“Most of my questions were about language I didn't understand and I consider myself a fairly reasonably educated literate person but there was language in those documents I have no idea what it meant, and it was just boiler plate, you know, from other studies and legal protections and things.”

– Trial participant, Canada

Furthermore, three out of four participants cited that their main understanding of the trial came from listening to what was communicated by the healthcare professional rather than the information they read in the participant information materials and informed consent form. Therefore, the quality of the dialogue between healthcare professionals involved in trial recruitment and patients is critical, including signposting participants to relevant supportive care when encountering side-effects during the trial. Participants cited both positive and negative experiences regarding access to supportive care as part of trial participation.

“You could have done with a bit more information about preparing for it because after you're on the trial, like I couldn't go to the dentist because it made my mouth bleed. I couldn't go...my feet and hands, you could have done with visit to a chiropodist and just somebody to check you out before going on it to have all this work done. Because once you're on it and on the drugs, it was, you couldn't really touch parts of your body like that because it's just so painful when just you bleed so much. So maybe a bit more of getting you prepared for the trial might have helped.”

– Trial participant, UK

“So they were very clear about the risks and they were very clear that they were not trying to talk me into the study at all. And that it was my decision. So I have two very different experiences.”

– Trial participant, Canada

Social influences

Social influences were mentioned by all four participants, specifically social support and social pressure. Trust was an important factor in decision-making regarding trial participation. Healthcare professionals were cited as a trusted source of information, with the capacity to persuade participants to take part in a trial and the ability to manage patient anxiety regarding treatment outcomes. Equally, loss of trust between healthcare professionals and patients was a barrier to retention.

“When his liver values went out of bounds there was a conversation that took place outside the door, which should have taken place in a conference room, with them arguing about whose fault it was that the liver values had been set that low. ...And we had heard that whole backstory in the hall and it didn't give us a, ‘we want to help you’ kind of feeling.”

– Family member of trial participant, US

Social support from family members was mentioned as an enabler to trial participation by all four participants. Conversely, social pressure by family and friends resulting from low awareness of the importance and benefits of trial participation, was mentioned as a potential barrier to retention.

“Because in your social context, a lot of your friends and family think you're absolutely nuts to be doing this. And some people would say to me, like, why are you letting them experiment on you?”

– Trial participant, Canada

Furthermore, healthcare professionals were cited as sources of social support, particularly the trial nurse or clinical nurse specialist. Nurses were cited as important sources of support due to their communication skills and practical knowledge for how to manage side-effects of treatments.

“I had a wonderful specialist nurse that you could ring up any time and you could talk to her and ask her any questions. And obviously she dealt with every other patient. The nurse is probably more of a focal point than the doctors. Because you could talk to her anytime and she knew you more intimately than the doctors did. So she knew more about your everyday problems. If you're seeing the doctor, they might see hundreds of people a week or a month, whereas you saw her more or less every week, you could talk to her every day.”

– Trial participant, UK

Skills

Patient organisations and support groups gave participants additional access to expertise to help find and enrol in trials but also to navigate the complexities of trials, including coping with travel requirements for trial visits.

“And I thought, how can I possibly do this? Go back and forth and back and forth. And the other patients helped me understand how I could get by with the logistical barriers. Once I got through the initial period, which you have to travel every week, that things would settle down and that this would become just part of my life to go to [city in the US] for a couple of days every month. And so the other patients really helped me get my head around how I could possibly do this.”

– Trial participant, Canada

Environmental context and resources

Navigating travel to trial visits, was associated with a high financial and emotional burden in some geographical areas such as the US. However, whilst patients living in rural areas of the UK also identified travel as a barrier this barrier was mitigated by trial staff offering flexible appointments to suit participant needs and reimbursement of travel costs. COVID-19 has highlighted potential means to further reduce the burden for trial participants by allowing some routine study tests to be conducted locally. No participants mentioned monetary rewards as an incentive to take part, except for when it was used as a means to cover travel costs. However, the cost of trial participation was cited as a potential barrier for other patients, especially since the time involved in trial participation and the side-effects of treatment could affect patients' ability to work. Improved trial design and reduced participant burden could therefore improve retention and make trials more accessible for participants across different socio-economic backgrounds.

“You know, the thing that could be done best to remove the travel barrier is reduce the number of trips required. There are a lot of real institutional barriers to those. You know, we found with COVID that it's possible to ameliorate some of those, like having your labs drawn locally, if you need labs every week. I mean, it, it would be a hard choice. I mean, even if it was, you know, the best drug ever invented, if it required a weekly trip to [cancer centre], which was two hours or [name of city], which was four hours. You know, each one of those is a day out of your life and a day of recovery. So, you know, if you could have the checklists and the blood draws done locally and reduce the number of trips.”

– Family member of trial participant, US

Beliefs about capabilities

Self-efficacy and self-motivation to stay involved in the trial were identified as an important factor for retention. However, belief about capabilities was mainly affected by distance of travel required and flexibility of appointments (see participant testimony above). Furthermore, the impact of treatment side-effects on quality of life was identified as a barrier to clinical trial retention for three out of four participants.

“I think there were times when I basically told my oncologist, I'm going down to half dose for the Christmas holidays or something like that. And I said like, it's non-negotiable for me. I need, you know, I need get a little bit of my life back.”

– Trial participant, Canada

Emotion

Fear and anxiety influenced the extent to which participants were able to process information about clinical trials and their ability to take part in decision making about trial participation. Here, family members attending trial visits together with the participant were cited as a source of support. Furthermore, two out of four participants expressed anxiety and stress about being excluded from trials due to changes in disease progression and no longer meeting inclusion criteria for the trial.

“One of the things that in terms of my mental health, on both studies, was this concept of restaging every eight weeks. It means that you are forever on a very short tether. And I likened it to the show, I hope you don't have this television show, the Survivor show, where people get booted off the island. And, so every eight weeks I faced being booted off the island. And so it was tremendous personal stress every eight weeks going through that.”

– Trial participant, Canada

Beliefs about consequences

The main beliefs about the outcomes of trial participation included a belief that participation would ultimately help others or contribute to furthering the science and treatment of kidney cancer (altruism) and a belief that participation might benefit the participant's own health via access to novel treatments or access to better surveillance and better healthcare (personal benefit). Personal benefit was cited as a major motivation to stay on a trial, particularly when there were few treatment options available. Equally, altruism contributed partially to trial retention.

“The only thing was the side effects, basically it stopped me working. I mean, the side effects for me in particular were horrendous. So I managed to last two and three quarters of a years out of three, but I couldn’t work at all and I was self-employed so obviously that affect my income, it affected my work. But you felt like if it wasn’t going to help me, it would help somebody else. That’s the way I thoughts about it.”

– Trial participant, UK

Whilst, treatment-related side effects did cause participants to discontinue trials in two instances, participants did also cite multiple examples of staying on trials despite major side-effects or adverse events.

“I was worried when I had the heart attack. I was really worried about that, because we didn’t know what it was. My gut feeling was that it was probably a mixture of both. But yeah, since then, I’ve not been worried about anything. I’ve resumed and it’s so far all going okay.”

– Trial participant, UK

Reinforcements

Reinforcements from healthcare professionals and trialists may help increase retention. Participants highlighted that summaries of trial findings were not routinely disseminated to participants, which partially devalued their participation. Equally, participants expressed that demonstrating the value of participation by offering a thank you or some small token of appreciation may help to encourage wider trial participation.

“There was never a nice letter from the study centre saying thank you for participating, here are the results in, you know, lay terms, and here’s a link to the paper that is free access to you because you were a patient in the trial. Yeah. So, no there was never anything like that. I understand some of that is starting to happen with some industry trials sometimes. But generally speaking, the patients are the last to know.”

– Trial participant, Canada

Monetary incentives were not considered appropriate by participants interviewed in this project, except for when they could be used to reimburse travel costs for studies that did not already provide routine reimbursement for travel.

Summary of barriers and enablers for retention

A summary of the identified barriers and enablers for retention in clinical trials for kidney cancer are presented below in Table 1, along with a definition of each TDF domain.

Theoretical Domain (TDF)	Barrier to retention	Enabler for retention
Knowledge An awareness of the existence of something	<ul style="list-style-type: none"> ● Long or complex participant information materials ● Not enough time to process participant information materials ● Low awareness of potential risks 	<ul style="list-style-type: none"> ● Understanding of participation requirements
Social influences Those interpersonal processes that can cause individuals to change their thoughts, feelings or behaviours	<ul style="list-style-type: none"> ● Loss of trust in healthcare professional ● Scepticism of clinical trial participation from family or friends 	<ul style="list-style-type: none"> ● Trust in healthcare professional ● Social support (family member; nurse; patient organisation or support group)
Skills An ability or proficiency acquired through practice		<ul style="list-style-type: none"> ● Sharing of experience within patient organisation or support group
Environmental context and resources Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence and adaptive behaviour	<ul style="list-style-type: none"> ● No travel reimbursement or complex process for travel reimbursement 	<ul style="list-style-type: none"> ● Improved trial design ● Reimbursement of travel costs ● Time (e.g. not in employment)
Beliefs about Capabilities Acceptance of the truth, reality or validity about an ability, talent or facility that a person can put to constructive use	<ul style="list-style-type: none"> ● Distance required to travel ● Severity of side-effects 	<ul style="list-style-type: none"> ● Routine study tests done locally ● Reduced number of study visits
Emotion A complex reaction pattern, involving behavioural and physiological elements, by which the individual attempts to deal with a personally significant matter or event	<ul style="list-style-type: none"> ● Fear and anxiety influencing decision-making 	<ul style="list-style-type: none"> ● Support via family member or patient support group
Beliefs about Consequences Acceptance of the truth, reality or validity about outcomes of a behaviour in a given situation	<ul style="list-style-type: none"> ● Loss of quality of life 	<ul style="list-style-type: none"> ● Altruism (Benefits for others; benefits to science) ● Benefits self (access to novel therapies or increased surveillance)
Reinforcements Increasing the probability of a response by arranging a dependent relationship or contingency, between the response and a given stimulus	<ul style="list-style-type: none"> ● Lack of acknowledgement 	<ul style="list-style-type: none"> ● Acknowledgement

Table 1. Barriers and enablers for retention from the perspective of kidney cancer patients.

Summary of literature review

The ORRCA database contains 1167 retention studies, including 136 (12%) studies of retention within cancer. Retention studies within the database are coded to the retention domain framework developed by Kearney and colleagues.⁴ A summary of relevant studies within the medical literature that may offer interventions for protecting trial retention is presented below.

Data collection and patient burden

The acceptability of the study protocol and the associated patient burden is an important factor influencing retention. Side-effects, including nausea, vomiting, cardiovascular side effects, alopecia and blood-related side effects are amongst the most common problems that result in patients leaving cancer clinical trials. Furthermore, decline in health related quality of life is linked to high dropout in longitudinal cancer studies.¹⁶ Involving the patient community or patient advocates in trial design can help to reduce patient burden and identify outcome measures that are important to the patient population but not routinely collected in RCTs.¹⁷ Frequency of trial visits and data collection have also been shown to influence retention in clinical trials. Reducing participant burden via synchronising study data collection with routine care appointments and routinely collected healthcare data can improve retention.¹⁸

Blinding and treatment preferences

Attitudes towards randomisation, particularly negative attitudes towards assignment to placebo or control group, may affect trial participation. Whilst RCTs provide the most reliable evidence for treatment efficacy trial participants often have a preference for a specific treatment. As such, participants may express a reluctance to join or remain on a trial when they are blinded or unaware of the treatment they are receiving.¹⁹ King and colleagues conducted a systematic review of patient and physician preferences in clinical trials and found that substantial numbers of patients across trials refused randomisation because of preferences.²⁰ Integrating qualitative studies within trials can help to identify issues around randomisation and retention.²¹ Open label trial design, where there is no placebo and participants are aware of which treatment they are receiving has also been shown to improve retention in clinical trials.¹⁹ Furthermore, open label trial design is closer to routine healthcare practice.¹⁹ Finally, selection bias in open label trials can be avoided by randomly allocating participants to a treatment group.

Supporting participation

Strategies to enhance clinical trial participation should consider the participants with the highest threshold for participation and design trials accordingly. Flexible scheduling and prioritising the convenience of participants when scheduling trial appointments has been shown to improve retention.²² Furthermore, providing support towards transportation costs for travelling to trial visits has been identified as a key retention strategy and actively promoting support for transportation costs and subsidised child care can help to improve participation in clinical trials.²³

Clinical trial navigators

Clinical trial navigators can help patients identify trials that are appropriate for their condition and circumstance and may improve recruitment and retention. For example, researchmatch.org is a US-based online platform funded by National Institutes of Health (NIH) that extracts information from ClinicalTrials.gov and presents the information in an easy to access manner to help match patients with researchers looking for trial participants.²⁴ Another example is the Fox Trial Finder from the Michael J. Fox Foundation for Parkinson's Research, which matches Parkinson's patients with trials based on their answers to a few basic questions about their condition.²⁵

Study information materials

Patient information materials are becoming increasingly complex. Challenges with informed consent include patients not reading study information due to its length and not understanding the material due to its complexity. For example, 1 in 3 older adults in England are reported to have difficulty reading and understanding basic health-related information, which is associated with higher mortality.²⁶ Furthermore, important predictors of dropout in clinical trials include lower education attainment, functional impairment, poorer cognitive performance and lower verbal intelligence.^{18,27} Patient involvement in design and review of study materials can help to ensure study materials are clear and appropriate for the target population. For example, web-based and video communication can be a helpful method of communicating participant information for a trial, particularly for teenagers and young adults.²⁸

Older adults generally have a lower level of education and health literacy compared to younger people²⁹ and older patients are significantly underrepresented in clinical trials.³⁰ Older patients may struggle to fully comprehend what is expected of them as part of trial participation and as a result, they are more likely to leave trials.³¹ A study investigating the experience of elderly patients with breast cancer and trial participation surveyed 156 physicians across 10 different cancer centres in the US. The study found that the main barriers to trial participation for older patients with breast cancer included comorbidities, difficulties understanding what is expected of them in a clinical trial and treatment toxicity.

The main strategies for improving trial participation as suggested by the physicians in the study included making personnel available in the clinic to explain and check understanding of trial participation expectations, increasing physician's knowledge of treatment toxicities in older adults, simplifying protocol design and reducing treatment toxicities.³¹

Relationship with clinical staff

Communication between trial participants and their doctor or trial nurse has been shown to influence retention. Patients may be more likely to remain in trials if they perceive communication by their doctor or nurse as positive, including a perception of open and honest communication and compassion, which may increase trust.⁷ Poor communication around the benefits and side-effects of study participation can contribute to patients leaving trials. Nurses have been recognised as an important link between principal investigators and participants in clinical trials.³² Follow-up telephone calls can help to increase retention in clinical trials and keep participants involved; however, they may require additional staff time to be built into the trial design.¹⁶

Community-centred support

Relationship building to establish trust between researchers and the participant community is recognised as an important strategy for retention.¹⁶ Recommendations by National Cancer Institute (NCI) and the American Society of Clinical Oncology (ASCO) identified a number of patient and community-centred recommendations for improving patient retention in cancer clinical trials:

- 1) Patient advocates should be involved when reviewing and implementing trials to ensure patient views are included in trial design;
- 2) Involve patient advocates and advocacy organisations in education about trials and promotion of trials;
- 3) Engage racial/ethnic minorities and other underrepresented groups in developing strategies to increase access to clinical trials.
- 4) Use principles of community-based participatory research in trial design.
- 5) Provide access to other patients who have participated in a clinical trial (peer mentors) and patient navigators for additional support.³³

Patient navigation have also been recommended by the NCI and ASCO as a potential strategy to improve retention and recruitment of patients in clinical trials. The Patient Navigator model includes hiring and training lay members of the public to assist with educating and supporting patients about clinical trials.³³ The Patient Navigator model has also been shown to improve retention of African Americans in cancer clinical trials.³⁴

Cultural considerations

Addressing cultural barriers to participation are essential within the conduct of clinical trials. Racial and ethnic minorities are less likely to participate in clinical trials and less than 10% of all patients enrolled in clinical trials are minorities.³⁵ Low participation of people from across all sociodemographic indicators can lead to issues with the generalisability of study findings and may contribute to health disparities.⁷ Importantly recruitment and retention methods in clinical trials need to consider the specific needs of the participant population. An example of a multi-pronged approach to recruitment and retention for a randomised non-pharmacological intervention is the pressure ulcer prevention study (PUPS) in people with spinal cord injury in the US. The study met recruitment and retention targets via increasing staff time and hiring bilingual staff to assist with recruitment as well as designing participant information materials that were tailored to minority ethnic participants and their cultures.²²

Another example of a successful strategy to improve retention and adherence of African American women in clinical trials is to apply the Community Health Advisor (CHA) model, where trial participants receive support via trained Community Health Advisors in addition to routine retention activities such as reminder calls by trial nurses. The Community Health Advisor model is grounded in community support and trust and the model complements previous findings showing that African American women seek social support and health advice from women they deem trustworthy and knowledgeable.³⁴ Furthermore, decentralising recruitment in trials was shown to improve retention of ethnic minorities in a cancer prevention trial.³⁶ The Community Based Participatory Research design makes use of community stakeholders to lead recruitment instead of appointed trial recruitment staff. Additional strategies to improve retention of racial and ethnic minorities include hiring minority staff and providing additional resource to enable study personnel to work flexible hours including evenings and weekends to facilitate flexible trial visits.³⁷

Monetary incentives

A recent Cochrane review by Gillies and colleagues in 2020 identified monetary incentives as an effective retention strategy compared to usual follow-up; however, the level of certainty rating for this recommendation was low and there has been a call for further studies evaluating monetary versus non-monetary incentives for retention in clinical trials.¹¹

Discussion

This is the first project to use a theory-informed approach to identify barriers and enablers for retention in clinical trials from the perspective of kidney cancer patients. Strategies identified via this project may help to address barriers to both recruitment and retention for participants in clinical trials for kidney cancer, whilst certain barriers are more specific to retention only. Clinicians routinely raising the topic of clinical trials with kidney cancer patients can help to improve awareness and encourage future participation in trials.²⁸ Improving understanding and managing expectations at the initial recruitment stage may influence successful participant recruitment but it may also affect retention of participants for the duration of the study. Improving patient knowledge of benefits and harms of trial participation at recruitment stage, including signposting to supportive care to manage treatment side-effects, may further improve trial retention. Timing of recruitment and consent is key for kidney cancer trials. Newly diagnosed or newly staged patients require time to process and weigh up the benefits and harms of clinical trial participation. Patient networks may act as an additional source of information and support alongside the care team and trial staff. Patient networks may also help improve knowledge and skills of trial participants by sharing advice for how to find clinical trials and how to navigate the logistics of clinical trials, such as travel.

Participants in this pilot study cited altruism and personal benefit as the main benefits of trial participation. These findings are similar to research findings on trial participation across different health conditions.³⁸ Family members and caregivers were cited as an important source of social support for participants during trial participation; however, participants also expressed social pressure experienced when their own social network did not understand the importance of taking part in the trial. Here, patient organisations and support groups offered a valuable source of social support and were able to provide both practical advice and emotional support. Scheduling trial visits for patients on the same day or matching patients with experience of trial participation with newly diagnosed patients has been recommended for clinical trials for rare diseases²⁸ and may also be applicable for kidney cancer trials. Assessing a patient's level of available social support for managing their condition and trial requirements, and signposting patients to patient networks where appropriate, is therefore an important aspect of recruitment and retention in trials. Finally, the experience of caregivers and family members and the role of patient organisations in relation to retention in clinical trials have not been well explored and should be investigated further.

Travel can be a major barrier to retention in clinical trials due to the associated time commitment, cost and impact on quality of life. Potential strategies to overcome this barrier include assessing patients' access to transport and any logistical barriers at the initial point of recruitment.²⁸ Further retention strategies include taking a patient-centred approach when planning the timing and frequency of trial visits and considering which tests can be conducted locally to reduce the travel commitment and participant burden. The COVID-19 pandemic has revealed that it is possible to amend trial designs to include more visits at a local care site or via remote follow-up. Furthermore, while follow-up visits should ideally be conducted at the same location throughout the study to provide a controlled study environment, it is important that trial managers consider strategies for offering follow-up visits and routine testing appointments at a location that is suitable to the participant.³⁹ Routine reimbursement of travel costs for trial participants may also improve retention. All participants in this pilot study identified travel as a barrier; however, the financial and emotional burden of travel was highest for the US, where travel reimbursement was complex and irregular.

Participants highlighted several means to raise awareness of clinical trials, for example via a kidney cancer trial navigator, using patient networks to increase awareness of clinical trials, improving length and clarity of participant information materials and via mass communication such as television and radio. Awareness of clinical trials was reported as low in the IKCC Global Patient survey in 2020¹² and strategies for improving awareness need to be explored further.

The findings of this pilot project suggest that there is a need to investigate how overall design can be improved for clinical trials, including both investigator-led and industry-led trials. Furthermore, the project findings resonate with the call to investigate the impact of patient and public involvement in trial design as presented in the Top 10 research questions for trial retention, developed via a James Lind Alliance Priority Setting Partnership exercise.⁴⁰ A starting point is to include routine participation of patients in the design of trials, focusing in particular on the accessibility of patient information and informed consent forms, participant burden including travel and flexibility of appointments as well as strategies for dissemination of trial findings to participants and patient organisations. A suggested model of strategies for improving retention in kidney cancer trials is presented in Figure 1.

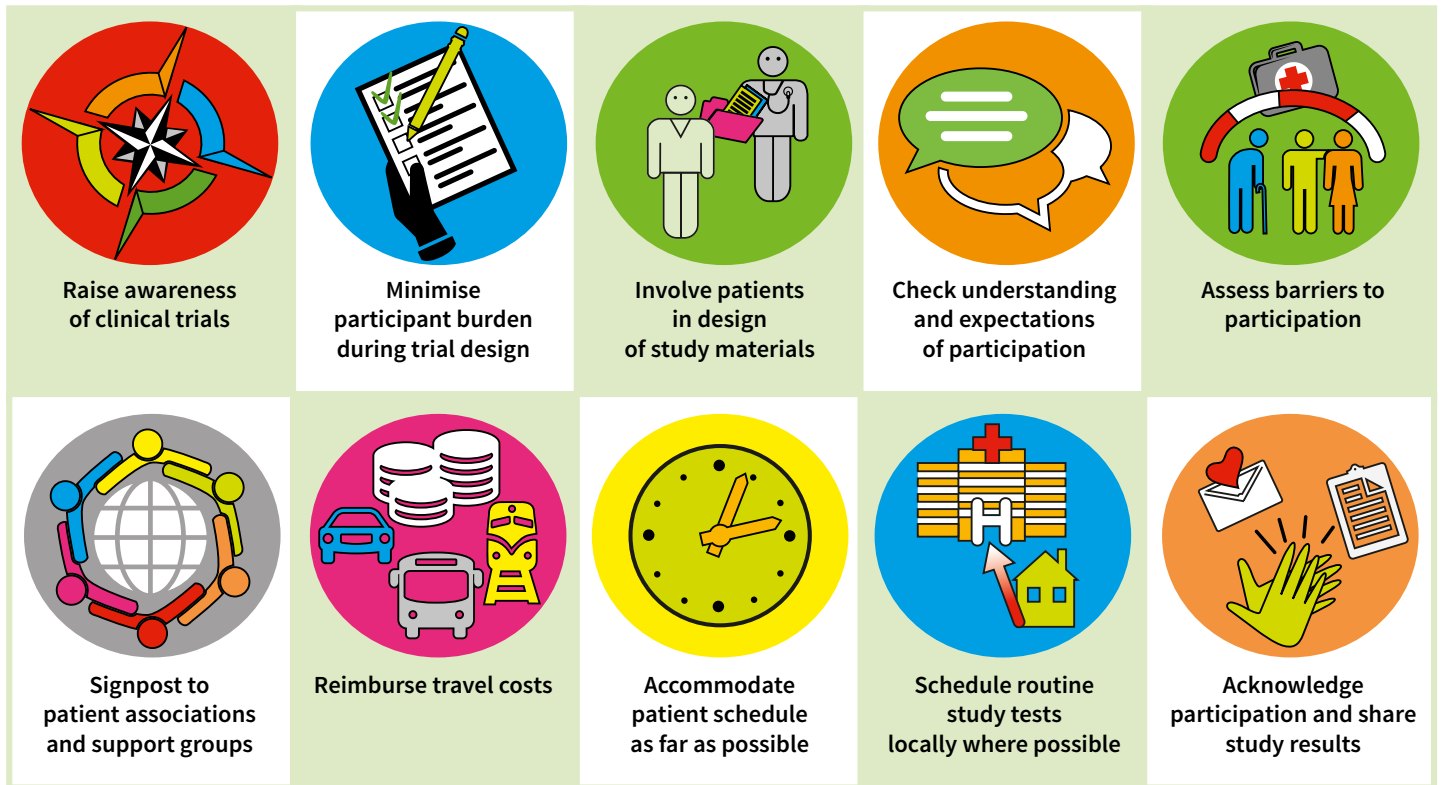
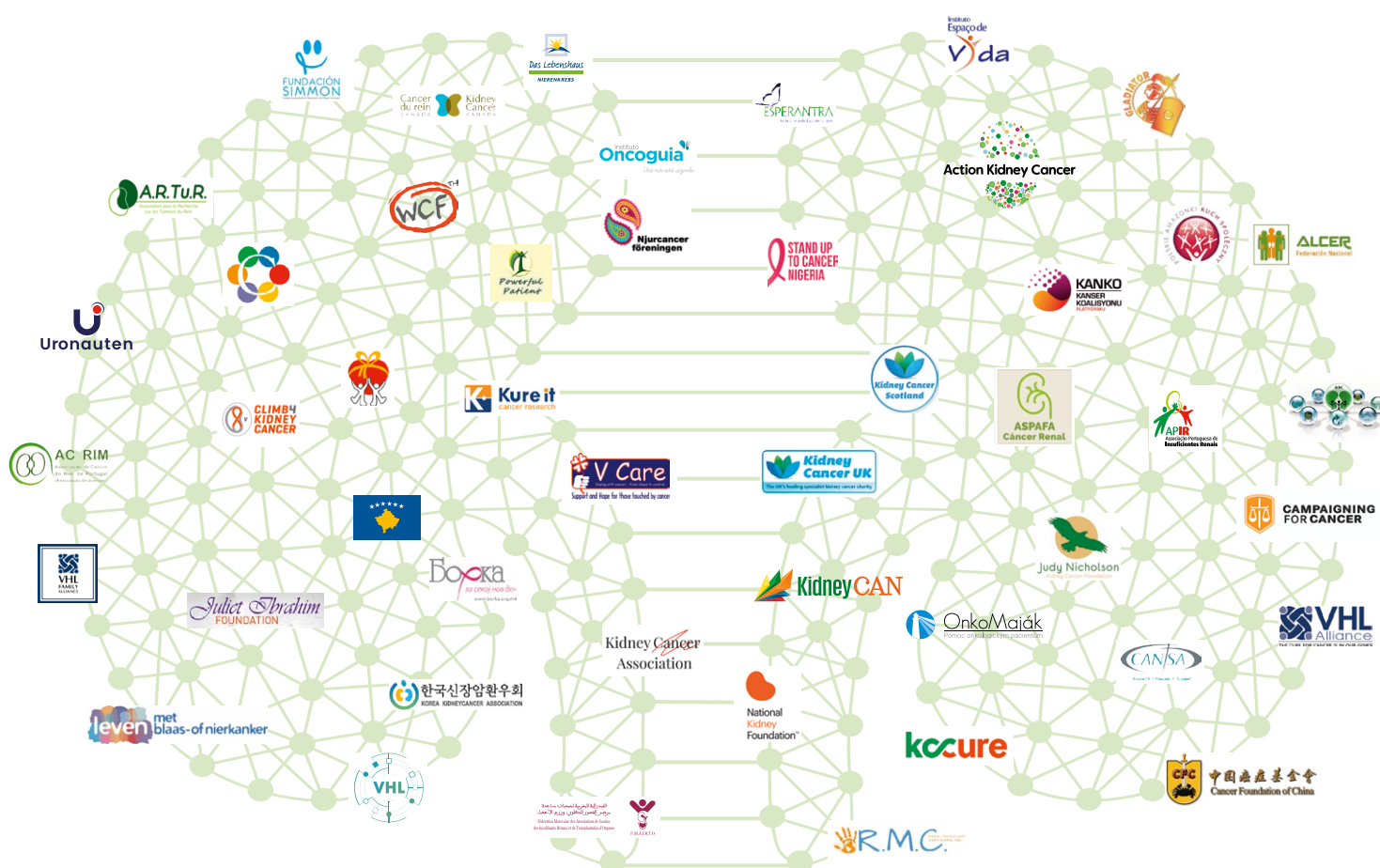


Figure 1. Model for integrating retention strategies in kidney cancer trials.

This was a hypothesis-generating pilot study, but beyond its small cohort, there are some limitations and potential biases to be considered. We recruited the participants through IKCC affiliate organisations, and in doing so, the data with regard to support from patient groups is biased, as all participants were allied with a patient support group. One common bias which may also be important here is survivor bias, in which only survivors of their cancer are included. We attempted to circumvent survivor bias by allowing close family members to speak on behalf of a kidney cancer patient. We recognise the need for larger, more robust studies to comprehensively address the identified barriers. For example, a larger study investigating the effect of involving the kidney cancer patient community in planning and running a trial is needed. The studies within a trial (SWAT) model, offered by the National Institute for Health Research (NIHR), may be an appropriate method for embedding a retention study investigating patient involvement in kidney cancer clinical trials within a larger host trial.⁴¹

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