Nephrol Dial Transplant (2020) 35: 755–764
doi: 10.1093/ndt/gfaa044
Advance Access publication 2 April 2020

ndt
Nephrology Dialysis Transplantation

SPECIAL REPORT

Recruitment and retention in clinical trials in chronic kidney disease: report from national workshops with patients, caregivers and health professionals

Patrizia Natale[1,2,3], Talia Gutman [1,2], Martin Howell [1,2], Kathryn Dansie[4], Carmel M. Hawley[5,6,7], Yeoungjee Cho[5,6,7], Andrea K. Viecelli[5,7], Jonathan C. Craig[1,2,8], Shilpanjali Jesudason[9,10,11], Jeremy R. Chapman[12], David W. Johnson[5,6,7], Lisa Murphy[10], Donna Reidlinger[5,6], Sally Crowe[13], Emily Duncanson[4], Shyamsundar Muthuramalingam[14], Nicole Scholes-Robertson[1,2], Amber Williamson[14,15], Stephen McDonald[4,9,11], Germaine Wong[1,2,12], Armando Teixeira-Pinto[1,2], Giovanni F.M. Strippoli[1,3,16] and Allison Tong[1,2]; on behalf of the Better Evidence and Translation in Chronic Kidney Disease (BEAT-CKD) Workshop Investigators*

[1]Sydney School of Public Health, University of Sydney, New South Wales, Sydney, Australia, [2]Centre for Kidney Research, Children's Hospital at Westmead, New South Wales, Westmead, Australia, [3]Department of Emergency and Organ Transplantation, University of Bari, Bari, Italy, [4]Australia and New Zealand Dialysis and Transplant Registry, SA Health and Medical Research Institute, Adelaide, South Australia, Australia, [5]Australasian Kidney Trials Network, University of Queensland, Brisbane, Queensland, Australia, [6]Translational Research Institute, Brisbane, Queensland, Australia, [7]Department of Nephrology, Princess Alexandra Hospital, Brisbane, Queensland, Australia, [8]College of Medicine and Public Health, Flinders University, Adelaide, South Australia, Australia, [9]Central and Northern Adelaide Renal and Transplantation Service, Royal Adelaide Hospital, Adelaide, South Australia, Australia, [10]Kidney Health Australia, Victoria, Melbourne, Australia, [11]Faculty of Health and Medical Sciences, University of Adelaide, Adelaide, South Australia, Australia, [12]Westmead Clinical School, Westmead Institute for Medical Research, New South Wales, Westmead, Australia, [13]Crowe Associates Ltd, Oxford, UK, [14]BEAT-CKD Consumer Advisory Board, Sydney, New South Wales, Australia, [15]Kidney Health Australia, Queensland Consumer Consultative Committee, Brisbane, Queensland, Australia and [16]Cochrane Kidney and Transplant, Centre for Kidney Research, Children's Hospital at Westmead, New South Wales, Westmead, Australia

Correspondence to: Allison Tong; E-mail: allison.tong@sydney.edu.au; Twitter handle: @allisontong1
*A complete list of the investigators is provided in the Acknowledgements section.

ABSTRACT

Background. Slow recruitment and poor retention jeopardize the reliability and statistical power of clinical trials, delaying access to effective interventions and increasing costs, as commonly observed in nephrology trials. Involving patients in trial design, recruitment and retention is infrequent but potentially transformational.

Methods. We conducted three workshops involving 105 patients/caregivers and 43 health professionals discussing patient recruitment and retention in clinical trials in chronic kidney disease.

Results. We identified four themes. 'Navigating the unknown'—patients described being unaware of the research question, confused by technical terms, sceptical about findings and feared the risk of harm. 'Wary of added burden'—patients voiced reluctance to attend additional appointments, were unsure of the commitment required or at times felt too unwell and without capacity to participate. 'Disillusioned and disconnected'—some patients felt they were taken for granted, particularly if they did not receive trial results. Participants believed there was no culture of trial participation in kidney disease and an overall lack of awareness about opportunities to participate. To improve recruitment and retention, participants addressed 'Building motivation and interest'.

Conclusions. Investigators should establish research consciousness from the time of diagnosis, consider optimal timing for approaching patients, provide comprehensive information in an accessible manner, emphasize current and future relevance to them and their illness, involve trusted clinicians in recruitment and minimize the burden of trial participation. Participation in clinical trials was seen as an opportunity for people to give back to the health system and for future people in their predicament.

Keywords: chronic kidney disease, clinical trials, patient recruitment, patient retention, research

INTRODUCTION

Substantial resources are invested in clinical trials to generate high-quality evidence about interventions designed to improve care and outcomes for patients. In nephrology, there are >14 000 reports of randomized trials [1], but problems with participant recruitment and retention can limit the prospects for successful completion and providing reliable results [2–6]. Of the 40 most recent records of completed randomized trials in patients with chronic kidney disease (CKD) registered at ClinicalTrials.gov (November 2019), only 18 (45%) trials recruited to target enrolment [7]. A recent review of publicly funded randomized trials in the UK, across different conditions, found that the target sample size was achieved in 56% of trials and the median retention rate was estimated to be 89% [8]. The inefficiencies of slow or inadequate recruitment and poor retention can result in patient harm due to delays in accessing effective treatments and increase costs [5, 9].

Barriers to recruitment and retention are broad ranging and complex. They include challenges relating to system or regulatory processes, trial design, lack of awareness and education about clinical trials and resource limitations. Patients may be concerned about the additional time and cost burden in having to travel and attend additional appointments, fearful of the interventions and the risk of side effects or mistrusting of medical research [10–14]. On the other hand, patients may be motivated to participate in trials to improve health outcomes for patients or because they trust the reputation of the institution and are galvanized to have access to the latest treatment [14]. A recent study involving patients receiving dialysis, clinic personnel and medical providers found that personal and professional priorities and limited understanding of research were barriers to participation in research, while buy-in, trust, convenience and incentives facilitated engagement in research [15].

Findings from systematic reviews suggest that tailoring recruitment, support of staff members in understanding consent forms, communication and feedback and financial incentives may improve patient participation and recruitment in trials, although the most effective strategies remain uncertain [16–19]. The Kidney Disease: Improving Global Outcomes consensus conference on the challenges of conducting clinical trials in nephrology suggested the need to provide constant and consistent education about the value of participation in research, improve information that connects and engages patients in potential trials, expand trial infrastructure, incentivize participation, simplify the consent process, integrate trial systems into electronic systems used in routine practice and cross-collaborate with other specialties [6].

There is also increasing recognition of the need to involve patients in recruiting participants in trials in CKD [11], although this remains infrequent [20]. An understanding of the needs and perspectives of patients, caregivers and health professionals in relation to participant recruitment and retention in trials in CKD is limited [21]. This report summarizes discussions from workshops with patients, caregivers and health professionals regarding recruitment and retention in trials in patients with CKD. This may inform strategies to improve participant recruitment and retention in trials in CKD.

WORKSHOPS

Context and overview

The workshops were conducted as part of the Better Evidence and Translation in CKD (BEAT-CKD) program. BEAT-CKD was established to generate and implement evidence to improve the health of patients with CKD [22] and is a collaboration among the Australian and New Zealand Dialysis and Transplant registry [23], Australasian Kidney Trials Network [24, 25], Caring for Australasians with Renal Impairment clinical practice guidelines [26] and Cochrane Kidney and Transplant [1]. We conducted three workshops with consumers and health professionals on involvement in research [27] and participation in clinical trials. This report summarizes the discussion on recruitment and retention in clinical trials.

Attendees and contributors

The BEAT-CKD Management Committee and Kidney Health Australia (the top consumer organization for CKD in Australia) contacted consumers by e-mail and letters who were registered on their mailing lists and networks and health professionals through collegial networks to attend the workshops. The workshops were also advertised through social media. Overall, 105 consumers, including 70 patients across all stages of CKD 1–5 (non-dialysis dependent, receiving dialysis or kidney transplant recipients), 28 caregivers (parents and family members), 7 who did not indicate their role and 43 health professionals (dietitians, nephrologists, nurses and researchers) attended the workshops.

Workshop program and materials

We held three workshops, one each in Adelaide, Brisbane and Sydney, from August to December 2017. Participants were allocated into breakout groups. In total, we conducted 17 group discussions across all three workshops. Each group had 6–10 patients, caregivers and health professionals and a facilitator who used a question guide with questions that asked about recruitment and retention in clinical trials (Supplementary data, Item S1). The groups reconvened for a plenary session in which a nominated member from each workshop group presented a summary of the discussion to a wider group and participants were invited to provide comments or request clarifications.

All workshops were audio-recorded and transcribed verbatim. P.N. coded the transcripts line by line and inductively identified concepts pertaining to participation in clinical trials. This ensured that the themes were derived from data from patients and caregivers. The transcriptions were imported into HyperRESEARCH software (Version 3.7, ResearchWare, Randolph, MA, USA) for qualitative data analysis. Similar concepts were grouped into themes and A.T. independently read the transcripts and revised preliminary themes. The themes were discussed with and reviewed by all authors to ensure that the analysis reflected the full range and breadth of data.

Post-workshop consultation

Participants were given a copy of the preliminary summary of the workshop discussion for feedback and comment and to confirm that the findings reflected their perspectives. Any additional comments were considered and integrated into this final report.

Summary of workshop discussions

The discussions were synthesized into four themes: navigating the unknown, wary of added burden, disillusioned and disconnected and building motivation and interest. The respective subthemes are described in the following section with reference to patients, caregivers or health professional group, where relevant. Selected illustrative quotations to support each theme are provided in Table 1. A summary of themes is shown in Figure 1. The suggestions for participation, recruitment and retention in trials from the workshop are summarized in Table 2.

Navigating the unknown

Unaware of the research question. Some patients who had participated in trials felt they were not sure of the aims of the study and the outcomes that were being assessed. Some were not concerned, as being in a trial did not seem to have a substantial impact in their lives, and it was 'not a big deal in the journey' (patient). Others felt that information about the purpose of the trial needed to be provided in a standardized way, and '[doctors could have] a little sheet to tick off all the boxes' (patient) to ensure that all participants are informed in a consistent manner.

Confused by technical terms. Patients felt that the use of medical terms in explaining a trial prevented them from understanding the benefits, risks and results. They could not read and interpret clinical 'hieroglyphics' (patient) when presented with information about the trial. Clinicians acknowledged that 'we haven't really thought about appropriate language for consumers' (health professional). Being unable to adequately comprehend the information discouraged consumers from participating in the trial. They emphasized the need to use accessible and simple language so consumers could understand what the trial was about. Some patients mentioned it was important to receive clear information on how personal information was confidential and who could access these data. In particular, patients wanted to know the benefits and impacts that trials would have to them as participants.

Scepticism about the findings. Consumers who had participated in trials commented that the results were rarely fed back to them. The time-limited clinical consultations did not allow consumers to discuss the progress and results of the trial with their clinician. Some felt that the results of the trial were relayed inconsistently and incompletely, which created some scepticism about the findings and uncertainty about participation. Some consumers tried to search for information about the trial online but felt they could not find reliable sources and accurate information. For these reasons, some consumers felt disengaged and disinterested about trial participation. Consumers indicated the need to be regularly updated on the results, for researchers 'to give feedback in between, and make sure that they close the feedback loop' (patient) in order to sustain patient trust, interest and motivation to be in the current trial or trials.

Fearing the risk of harms of unfamiliar medications. In trials that involved unfamiliar or new pharmacological agents, some patients feared the potential risks of being exposed to new medications or worried about receiving a placebo and missing out on an active drug. They were reluctant to accept the chance of being exposed to new medicines that they fear could jeopardize their health, particularly if the information and consent form were not adequately comprehensible in explaining such interventions. Having to take new medications would also add burden—'and taking another drug, a lot of patients don't want to take one more pill' (patient). Some indicated that they had a 'fear of the unknown' (patient) in relation to participating in trials—'When you say medical trial, people think, "I know what they do with bloody monkeys. I'm not going to be a monkey!"' (patient). Some suggested that clinicians need to explain and reassure patients about possible benefits and harms of new treatments that were being evaluated in the trial.

Wary of added burden

Reluctant to attend additional appointments. The burden of CKD was already difficult for patients to cope with, and attending extra clinical appointments required for a trial would be a barrier to participating in clinical trials. They suggested that appointments should be scheduled at convenient times so as to not disrupt work, family and other daily responsibilities and activities. They also mentioned that trial-related administrative tasks could be completed at a time and place convenient to them—'you don't want to sit [in clinic] for another hour filling out forms [for the trial]; you've chewed up enough of your day, you've lost enough of your life' (patient). Using online platforms, including website and mobile telephone applications, was suggested as an alternative to minimize the need for travel and attendance in person at clinics for follow-up.

Uncertainty about commitment. Patients wanted to be informed upfront about the commitment required of them to participate in a clinical trial so they could understand 'what the impact to our lives as a patient would be' (patient). Some mentioned that work and other commitments could limit their ability to attend to the more frequent follow-up visits. Time and costs for travel to follow-up visits were identified as potential barriers to participating in trials.

Illness limiting capacity to participate. Participants highlighted the need for clinicians/researchers to be sensitive to the patients' journeys when discussing participation in a trial. They suggested it could be 'weaned' into patients' education—'when people turn up and they've been told, "you're in end stage renal failure, you need to go on dialysis," that in itself is a battle'. You just go 'whoa'. Then for someone to say would you like to participate in research, you would go 'no, I'm just learning about it'. 'As time goes on, to be introduced to research when it's appropriate to what's happening to us would be more

Table 1. Selected illustrative quotations

Theme	Quotations
Navigating the unknown	
Unaware of the research question	I imagine that my husband has been involved in trials over his extensive career of kidney failure. They don't stir any memories in my head, because he probably has just been part of something and never really known what it was for or what the outcomes were, so they're not a big event, but I'm sure he would've had to have been involved in something. But not a big deal in the journey. (Female, caregiver)
	You've got to explain what the trial involves and what the outcomes you expect to achieve. (Male, patient)
Confused by technical terms	This comes down then to the individual's understanding of the information being put in front of them. It could just be all hieroglyphics for all they could know, and what benefit is that? You've confused them or scared them or whatever. If they don't know what they're reading, that could itself be problematic. (Male, patient)
	Not the timing, the way in which they talk to you about a trial. If they are too clinical, and I have no idea what they're asking me to agree to I'll just say no. (Female, patient)
Scepticism about the findings	Sometimes those trials go on for a block of time, so if in that process you were to find out some of the outcomes of that trial, you probably have more awareness of research, or if there's something else I'd probably like to be part of it, because we did this and this little bit happened. (Female, patient)
	I've seen plenty of research in the papers, people wanted. I've looked at that and wondered what the outcomes that they get from a newspaper or print media, finding I don't know. (Female, patient)
Fearing the risk of harms of unfamiliar medications	And taking another drug, a lot of patients don't want to take one more pill. (Female, patient)
	You've got to take away the fear of what we have in our minds, because we know what to do with rats and mice and monkeys. When you say medical trial, people think, I know what they do with bloody monkeys. I'm not going to be a monkey. You've got to start off saying to the people what the trial's about, and it's not about, they're going to cut you open or give you something, you know what I mean? You've got to take the fear out of what you're trying to, what you're going to trial. Seriously, you've got to take the fear out. That's what people think. Medical trial, kidneys, no, not me. (Male, patient)
Wary of added burden	
Reluctant to attend additional appointments	When you have a transplant and you're well and you go back to your life of three children, own business, a busy life—if someone says, you've got to come to Brisbane a bit more often, that would definitely be a barrier in that situation, that would definitely be a barrier for us. When would we fit that in? (Female, patient)
	Try and link the appointments, so we try to link our patients' appointments [for the trial] in with their clinic appointments. (Female, patient)
	Also, you don't have to do it right now because if you're on dialysis, you want to do it at home. You don't want to sit there for another hour filling out forms or anything like that. You've chewed up enough of your day, you've lost enough of your life. (Female, patient)
Uncertainty about commitment	It's the only one, that's the only one that would prevent me. I work full time, so time constraints would be the only. (Male, patient)
	Maybe in the communication it could be about what it would mean in terms of the time that it would take out of our to be involved? What the impact to our lives as a patient would be. (Female, patient)
Illness limiting capacity to participate	And the lack of concentration, I've had that happen. What were we talking about? We're joking, but you're right. How do people participate when, that's the million dollar question. (Female, patient)
	If they're telling me on a day that I'm really unwell and I feel like I'm going to vomit on my dialysis chair, I'm not going to say yes either. It's really about that engagement at that level. Maybe there needs to be, not just a verbal communication. (Female, patient)
	They've got to have some sort of knowledge of when they hit you up for it. Not when you're at your worst. (Female, patient)
Disillusioned and disconnected	
Being taken for granted	Quite often they need to go for five to seven years to get the statistical power that is needed to generate it. The patients do feel, I think, quite lost in that five to seven years. (Female, patient)
	Very important. It's nice to know where you're actually standing, whether you're going up or you're going down or you're sitting stable. Mentally I think it's very, very important. (Male, patient)
	The other thing with research, I suppose the messaging, is that I think that we need to be communicating early, but then also give feedback in between, and make sure that they close the feedback loop. I can't tell you how many trials throughout my kidney journey that I've actually been involved in, and they've taken a lot of information from me, but I've never heard back about what the outcomes are. I know there's outcomes, but where are they? I think that for me as a consumer makes me disengage. Because we're around for a long time, you want to make sure that you keep us. (Female, patient)
No culture of trial participation in kidney disease	The amount of media coverage to heart and cancer research would be a hundred times what you hear about kidney research, because you virtually don't get any kidney research. (Male, patient)
	A long time ago when she was first diagnosed, one of the doctors said to us we will need a politician's child to get this, because then we'll get money for it. Like we sort of, you know, shut it. But I know exactly what he means and what he meant now was that you need that advocate that has a profile. (Female, caregiver)
	All the celebrities that we know that have been linked to kidney disease, actually we know about it when they die, but that's probably because of their own battle with kidney disease themselves, and they're not wanting to share themselves and share their vulnerability. (Female, patient)

Continued

Table 1. Continued

Theme	Quotations
Opportunities are unknown	The nurses would also have more of an idea of which patients would be more suitable to wanting to be involved, to participate, and other patients that really do have too much on, or they wouldn't be a good participant. The nurses are a very good source. Also maybe allied health, they'd get involved. (Female, health professional)
	Everyone is asking directly says well, this is the start of your treatment for your kidney problems, do you want to participate in one of these research or want to know about it, of course it says either yes or no, and none of us are asked . . . from the specialist I found out about it through your site the guy who did my transplant, he came, he happened to see me in his waiting room, he said you're a kidney patient, do you want to participate in this? I said yeah, no problems. (Male, patient)
Building motivation and interest	
Trusting the doctor's advice	I don't think my husband would get involved with a trial unless his doctor asked him and promoted it to him. (Female, caregiver)
	The kidney specialist can play a bigger role than they do about talking to the patient about research and getting yourself involved and everything. (Male, patient)
	When we've been consenting patients for different studies, sometimes it depends on who's actually asking them to consent, and if they know that person. I think that sometimes a lot of personal trust, and if it's a person not familiar to them people would be wary and rightly so. (Female, health professional)
Establishing research consciousness from the time of diagnosis	It comes back, way back to the very beginning, and it's about patients having an understanding that there is research there and the benefits of research. It's probably not really in your face, you know? (Female, health professional)
	We say to our patients, if someone didn't try—there was a research project done with aspirin, how would we know that it's one of the best drugs there is for many different conditions and now one of the cheapest, you know? Everyone will have half an aspirin, or so many people use aspirin for different things, but we did need those people at the beginning to work it out that it's good for this, and now it's good for this and this and this. We find you need to speak to people so they understand why it's happening. If they can understand why it's happening and the process, they're more likely to be involved. (Female, health professional)
	We need to explain what's in it for the patient, what's the opportunity that it might present for the patient, what's the potential benefit for the future, and why is it important for patients to get involved. If we make the messaging all speared towards why the consumer's part of this is so important, we'll get much better uptake. It's spinning it around and not talking about the clinical stuff. It's talking about the patient reasons of why it's important. (Female, health professional)
	If we could do research into how the communication methods would be most effective in that early stage, that's where the journey has to start. If you let us go too far, we've become too disengaged with our health, and we become a non-active participant. (Female, health professional)
An opportunity to give back	I was so keen to help other patients. (Female, patient)
	At the end of the trial we were asked the same questions as we were asked on whether we could improve on it, and I couldn't come up with anything that I recall that I said could be improved. I was really pleased with the effort that the people put into it. I got a lot of knowledge out of the trial that I didn't know beforehand, so it was really good for me. I got a lot of information from it. (Male, patient)
	And also, participants who have been involved in research talking to potential new participants. (Female, patient)

beneficial' (patient). They also remarked—'they've got to have some sort of knowledge of when they hit you up for it. Not when you're at your worst' (patient). They said it was difficult for patients who were too shocked or unwell to understand the research question, make decisions and concentrate and process information about the trial. One patient commented, 'If they're telling me [about the trial] on a day that I'm really unwell and I feel like I'm going to vomit on my dialysis chair, I'm not going to say yes either'.

Disillusioned and disconnected

Being taken for granted. During the trial, some patients lost motivation because they felt they were not receiving updates or results about the trial—'I signed the form [for the trial] two and a half years ago, and only recently have I heard a forum that we can hear about what's happening' (patient). Similarly, another patient mentioned, 'I can't tell you how many trials throughout my kidney journey that I've actually been involved in, and they've taken a lot of information from me, but I've never heard back about what the outcomes are. I know there are outcomes, but where are they? As a consumer this makes me disengage'. Some patients felt they were 'lost' because of the lack of information about results and suggested that general information on the trial and findings would stimulate patients' enthusiasm—'as a consumer you just want to know some generalized information about this has been good, or we worked this out' (patient). Patients said they should be updated during the study to give them an opportunity to raise concerns and feedback that could be taken into consideration in the future. On an individual level, patients said, 'it's nice to know where you're actually standing, whether you're going up or you're going down or you're sitting stable'.

No culture of trial participation in kidney disease. Participants noted that CKD was not a prominent disease in the public domain and received less attention compared with cardiovascular disease or cancer because of the lack of media attention—'All the celebrities that have been linked to kidney disease, actually we know about it when they die' (patient). Participants urged the need for more efforts to increase attention to kidney disease in the general community to strengthen the culture of trial participation. Consumers perceived that participation in trials in CKD was limited due

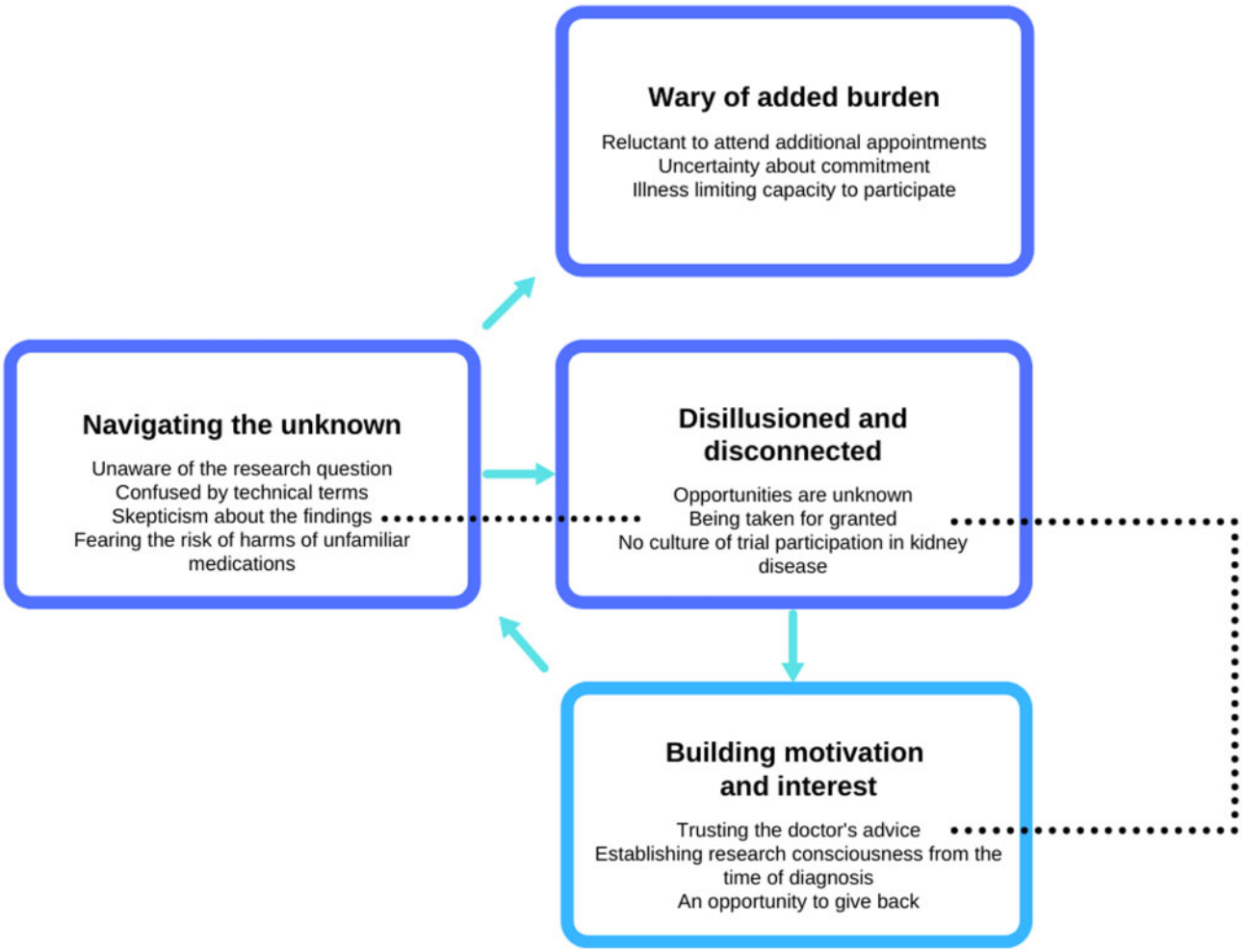

FIGURE 1: Thematic schema. Thematic schema depicts the main themes addressed by attendees in the three workshops on recruitment and retention in clinical trials. Navigating the unknown causes both 'wary of added burden' and 'disillusioned and disconnected' due to the inability to sustain meaningful relationship. Without consistent communication, motivation and interest decrease because patients are not completely aware and involved in research. In addition, scepticism about the findings leads to disillusionment in being taken for granted and trust with medical staff disappears. Considering these themes, we can find some strategies to enhance a patient-centered culture.

to limited government funding allocated to kidney disease and existing CKD trials are not communicated effectively to enhance general population awareness of kidney disease.

Opportunities are unknown. Participants noted that clinicians, including physicians and nurses, may not be aware about clinical trials and thus do not invite consumers to participate in trials. Some patients felt isolated because they did not receive information about trials. They suggested that clinicians 'who have a lot of contact with patients,' in particular 'nurses who would also have more of an idea of which patients would be more suitable and would want to participate in the trial' (health professional), should be informed about trials that are recruiting patients and be proactive in identifying and recruiting participants—'we have found that we really need to get our medical staff involved in the clinical trials and approaching patients' (health professional). Some perceived that those who did home therapies may not be as aware of trial opportunities. Patients commented that there were no communities to support active patient participation in trials.

Building motivation and interest

Trusting the doctor's advice. Participants agreed that having an established relationship with their clinicians is important since 'I don't think [that my husband] would listen to anyone else, [except his nephrologist]'. Similarly, a researcher stated that 'When we've been consenting patients for different studies, sometimes it depends on who's actually asking them to consent, and if they know that person. If it's a person not familiar to them, people would be wary and rightly so' (health professional). Patients felt more inclined to take part in trials if they could see that clinicians supported the trial. Health professionals noted that patients 'probably would only do a clinical trial if their doctor suggested it'.

Establishing research consciousness from the time of diagnosis. Some participants mentioned that opportunities for participating in trials were not communicated early in the trajectory of CKD, 'it comes back, way back to the very beginning, and it's about patients having an understanding that there is research there and the benefits of research' (health

Table 2. Suggestions for improving participant recruitment and retention in trials in CKD[a]

Domain	Considerations and suggestions
Enhance awareness of CKD research	Improve the visibility of CKD research in all relevant settings including primary care and clinics (e.g. newsletters/ brochures, pamphlets, posters, website, videos and social media)
	Advocate for coverage of CKD (including research in CKD) in the media
	Establish a network or database for consumers to receive information about trials (creating a community or registered in group and forums)
Strengthen the research culture in clinical settings	Provide information about trials to clinicians at the recruiting site
Provide trial-specific information	Clarify the aims and outcomes
	Use plain language or explain medical and technical terminology
	Convey the implications of trial participation on lifestyle and time commitment
	Provide a point of contact for questions about the trials
	Provide information in a comprehensive and consistent manner
Harness trust	Involve trusted clinicians (general practitioners, nephrologists, nurses) in providing information about the value of trials and recruitment of consumers
	Promote effective and clear communication
Consider timing of engagement	Provide information early (e.g. at diagnosis) to stimulate interest
	Avoid recruitment at times when patients may feel overwhelmed (e.g. during episodes of illness, complications)
Address concerns	Discuss potential burden, risks and side effects of treatment (particularly those that may be new or less familiar)
	Facilitate peer promotion of trials 'patients educate patients'
Communicate results	Provide iterative updates of individual results, if appropriate (e.g. forum groups)
	Provide trial results during and at the completion of the trial
	Involve patients in writing patient version summaries of clinical trial results
	Give opportunity for consumers to ask questions and provide feedback on the process and results
	Focus on benefits that are relevant to consumers (e.g. improvement in lifestyle)
Minimize burden of participation	Schedule appointments with their clinical appointments to minimize disruption to other commitments (work, study, family)
	Enhance flexibility in preferred days and times
	Allow for remote participation (e.g. teleconference, telehealth)
	Offer convenient modes of follow up (e.g. online or electronic platforms, telephone)
	Reimburse consumers for out-of-pocket costs incurred with participating in the trial

[a]As suggested by workshop attendees.

professional). They suggested that to increase awareness about research in primary care settings, for example, primary healthcare professionals could be involved in identifying and recruiting patients. They also suggested communicating about trials at the beginning of the patient's journey to encourage patients more proactive about their health.

An opportunity to give back. For some patients, participating in trials was seen as an opportunity to contribute and connect with the patient community—'without participation you don't get the feedback, without feedback you really don't know what's going on' (patient). They mentioned that the concept of peer trial recruitment could enhance uptake. Patients could educate other patients about trial opportunities, discuss and provide 'patient-written' information and encourage peers to participate.

DISCUSSION

Overall, patients were interested in trials and were motivated to participate if they trusted the clinicians involved in recruitment and because they wanted to give back to the community. However, patients, caregivers and health professionals identified several challenges relating to recruitment and retention in clinical trials in CKD. Patients who had participated in trials were often unaware and uncertain about the research question, including the intervention and outcomes, and felt confused by medical terminology used in the information given about the trials. They were wary of the implications that participating in trials would have on their health, finances, time and energy, as these were already physically, mentally and emotionally consumed by CKD and the burden of treatment. Some patients who had participated in trials felt disillusioned and dissatisfied about not receiving trial results.

Some of these challenges, including lack of awareness, inadequate communication, burden of trial commitment and lack of transparency or trust in healthcare providers, have been previously identified in other medical specialties [12, 14, 15, 28]. There may be some specific challenges in CKD related to the burden and timing of recruitment. Patients with CKD have a high symptom and treatment burden that interferes with day-to-day activities [29, 30], and they may be particularly concerned about the impact of trial participation on their daily activities and commitments. They are also at risk of serious comorbidities and complications, including cardiovascular disease and infection [31, 32]. Fatigue and cognitive impairment are also common in people with CKD [31, 33, 34] and may limit their capacity to make decisions about participating in trials.

Our workshops identified a number of suggestions for improving recruitment and retention in trials in the areas of enhancing awareness of research in CKD, strengthening the research culture in clinical settings, providing trial-specific information in a format that can be understood by consumers,

harnessing trust, considering the timing of engagement, addressing concerns, communicating results and minimizing the burden of participation. These are outlined in Table 2.

We acknowledge that it was not feasible to include patients and caregivers from all ethnic minority and social subgroups, and possibly those who may have low health literacy, and we did not include non-English-speaking patients/caregivers. Further efforts are likely to be needed to engage diverse and vulnerable populations to develop strategies for improving access to participation in randomized controlled trials.

Of note, there has been an increasing focus on ensuring that the results of trials are communicated back to participants. The World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects states that research participants 'should be given the option of being informed about the general results and outcomes of the study' [35]. Reporting research findings to trial participants is an ethical imperative because participants have had to accept the burden and risks of participating in trials and have a right to know about the research outcomes [36–38]. Despite this, a survey completed by >3000 trialists found that less than half had disseminated the results to participants, and only half had provided these findings in plain language [39]. Providing results can stimulate enthusiasm in research, encourage feedback and dialog, strengthen the relationship between consumers and physicians and facilitate patient involvement in disseminating and publishing the results [38, 39]. As emphasized in our workshop, failure to communicate results to participants can cause them to feel devalued and confused, which in turn can lead to loss of motivation and engagement. We also identified that such guidance may not go far enough.

There is a need to develop models for implementation to address trial recruitment and retention [40]. Closing the feedback loop, addressing health literacy concerns to enhance communication and the opportunity to invest in peer trial recruitment would be ideal solutions to implement these strategies in recruitment and retention in clinical trials. In a recent priority-setting partnership on research questions in the area of trial retention, the top 10 research priorities addressed aspects related to patient motivation to complete a trial, use of routine clinical care and existing data to improve retention, minimizing burden on staff and participants, supporting the completion of tasks (e.g. follow-up visits), using technology for follow-up, communication of trial results and involving consumers in planning and running trials to improve retention [41]. Involving consumers in this process may inform approaches that address their priorities, concerns and needs. Some evidence suggests that patient involvement in recruitment increases the odds of a patient enrolling in the trial compared with having no patient involvement [40].

To address the challenges and barriers to recruitment identified in the workshop, investigators should establish research consciousness from the time of diagnosis, consider optimal timing for approaching patients, provide comprehensive information in an accessible manner, emphasize current and future relevance to them and their illness, involve trusted clinicians in recruitment and minimize the burden of trial participation. Participation in clinical trials was seen as an opportunity for people to give back to the health system and for future people in their predicament.

SUPPLEMENTARY DATA

Supplementary data are available at ndt online.

ACKNOWLEDGEMENTS

We thank all consumers and health professionals who volunteered their time and expertise to contribute to the workshops. We acknowledge, with permission, all the attendees listed below who participated in the workshop. Workshop participants (consumers and health professionals), Sydney: Jane Beech-Allen, Mukesh Chandra, Helen Coolican, Ian Cornell, Judith Cornell, Clive Cornish, Vanessa Cullen, David Ellis, Jullianne Ellis, Esparanzo Evans, Jason Fisher, Paul Gilligan, Sandra Hesford, Tevor Hesford, Therese Hoogesteger, Colin Jones, Bruce Lin, Phillip McCready, Sherry Mead, Harry Michael, Rhonda Michael, Phillip Noble, Susan Noble, Michael Pennacchio, Peter Ramshaw, Lisa Richardson, Meral Senol, Tugba Senol and Tim Simpson. Workshop facilitators and co-facilitators (not listed in the main authorship): Yeongjee Cho, Margie Conley, Phil Clayton, Josephine Forbes, Angela Henson, Nikky Isbel, Laura James, Angela Ju, Pamela Lopez-Vargas, David Mudge, Lisa Shanahan, Matthew Sypek, Anita van Zwieten and Andrea Viecelli. Workshop participants (consumers and health professionals), Adelaide: Sydney Aidinis, Ainslie Bolton, Alla Bondaruk, Lydia Bondaruk, Paolo Cardelli, Michael Clark, John Dennis, Lois Ellery, Neville Fazulla, Rosalind Fulwood, Michael Geesing, John Griffith, Lynda Hall, Rob Hall, Bronwyn Hockley, Patricia Ireland, Marina Karidis, Richard Le Leu, Marie Ludlow, Lindsay Lugg, George Majarian, Fabian Marsden, Tom Mayer, Tom Mayer Jr, Amritha Muthuramalingam, Debbie Newton, Garrie Newton, Tamara Paget, David Roberts, Joy Roberts, Bronte Sterk, Barbara Stopp, Maureen Taylor, Peter Taylor, Polly Taylor, Ann Tejada, Sandra Turner, Diana Voss, Amber Watt, Patricia Waxman and Trevor Wynne. Workshop participants (consumers and health professionals), Brisbane: Carlyn Ames, Neville Arkinstall, Gwen Arkinstall, Jenny Best, Jill Biedermann, Andrew Biedermann, Colin Brown, Anne Cameron, Phillip Carswell, Martin Chambers, Loraine Chambers, Frances Cowper, Jenevieve Dooley, Tony Dunning, Sue-Ann Dunning, Kerry Dwyer, Donna Felschow, Bernard Goan, Kate Greenup, Laurie Hindom, Linda Hindom, Wendy Hoy, Gaye Jennings, Sofia Kudlak, Mark Luchterhand, Amy Luchterhand, Irene Mewburn, Russell Morgan, Anthony Nester, Veronica Oliver, Carl Pedersen, Chris Sandford, Lloyd Smith, Andrea Viecelli, Julie Walker, Richard White, Rhonda Widdows, Ian Widdows and Amber Williamson.

FUNDING

This work was supported by the National Health and Medical Research Council (NHRMC) Better Evidence and Translation

in Chronic Kidney Disease (BEAT-CKD) Program Grant (APP1092957). A.T. was supported by an NHMRC Fellowship (APP1106716). T.G. was supported by a scholarship through the NHMRC BEAT-CKD (APP1092957). Y.C. was supported by an NHMRC Fellowship (APP1126256). D.W.J. was supported by an NHMRC Fellowship (APP1117534). A.K.V. was supported by a Jacquot Research Establishment Fellowship and a Princess Alexandra Research Foundation Grant.

AUTHORS' CONTRIBUTIONS

T.G., M.H., K.D., C.M.H., J.C.C., S.J., D.R., E.D. and A.T. were involved in the research idea and study design. T.G., M.H., K.D., C.M.H., Y.C., A.K.V., S.J., D.W.J., D.R., E.D., S.M. and A.T. were responsible for data acquisition. P.N., T.G., M.H., K.D., C.M.H., Y.C., A.K.V., J.C.C., S.J., D.W.J., D.R., E.D. and A.T. were involved in data analysis/interpretation. A.T., J.C.C., S.J., S.M. and C.M.H. were involved in supervision or mentorship. Each author contributed to the important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST STATEMENT

None declared. The results presented in this article have not been published previously in whole or part, except in abstract format.

REFERENCES

1. Cochrane Kidney and Transplant, Australia. 2018. https://kidneyandtransplant.cochrane.org (26 November 2019, date last accessed)
2. Kearney A, Daykin A, Shaw ARG *et al.* Identifying research priorities for effective retention strategies in clinical trials. *Trials* 2017; 18: 406
3. Boivin A, L'Espérance A, Gauvin F-P *et al.* Patient and public engagement in research and health system decision making: a systematic review of evaluation tools. *Health Expect* 2018; 21: 1075–1084
4. Bower P, Brueton V, Gamble C *et al.* Interventions to improve recruitment and retention in clinical trials: a survey and workshop to assess current practice and future priorities. *Trials* 2014; 15: 399
5. Al-Shahi Salman R, Beller E, Kagan J *et al.* Increasing value and reducing waste in biomedical research regulation and management. *Lancet* 2014; 383: 176–185
6. Baigent C, Herrington WG, Coresh J *et al.* Challenges in conducting clinical trials in nephrology: conclusions from a Kidney Disease-Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney Int* 2017; 92: 297–305
7. ClinicalTrials.gov. 2019. https://clinicaltrials.gov (25 November 2019, date last accessed)
8. Walters SJ, Bonacho Dos Anjos Henriques-Cadby I, Bortolami O *et al.* Recruitment and retention of participants in randomised controlled trials: a review of trials funded and published by the United Kingdom Health Technology Assessment Programme. *BMJ Open* 2017; 7: e015276
9. Huang GD, Bull J, Johnston McKee K *et al.* Clinical trials recruitment planning: a proposed framework from the Clinical Trials Transformation Initiative. *Contemp Clin Trials* 2018; 66: 74–79
10. Selewski DT, Herreshoff E, Gipson DS. Optimizing enrollment of patients into nephrology research studies. *Clin J Am Soc Nephrol* 2016; 11: 512–517
11. Cukor D, Cohen L, Cope EL *et al.* Patient and other stakeholder engagement in patient-centered outcomes research institute funded studies of patients with kidney diseases. *Clin J Am Soc Nephrol* 2016; 11: 1703–1712
12. Boden-Albala B, Carman H, Southwick L *et al.* Examining barriers and practices to recruitment and retention in stroke clinical trials. *Stroke* 2015; 46: 2232–2237
13. Kadam RA, Borde SU, Madas SA *et al.* Challenges in recruitment and retention of clinical trial subjects. *Perspect Clin Res* 2016; 7: 137–143
14. DasMahapatra P, Raja P, Gilbert J *et al.* Clinical trials from the patient perspective: survey in an online patient community. *BMC Health Serv Res* 2017; 17: 166
15. Flythe JE, Narendra JH, Dorough A *et al.* Perspectives on research participation and facilitation among dialysis patients, clinic personnel, and medical providers: a focus group study. *Am J Kidney Dis* 2018; 72: 93–103
16. Shippee ND, Domecq Garces JP, Prutsky Lopez GJ *et al.* Patient and service user engagement in research: a systematic review and synthesized framework. *Health Expect* 2015; 18: 1151–1166
17. Boote J, Baird W, Beecroft C. Public involvement at the design stage of primary health research: a narrative review of case examples. *Health Policy* 2010; 95: 10–23
18. White MA, Verhoef MJ. Toward a patient-centered approach: incorporating principles of participatory action research into clinical studies. *Integr Cancer Ther* 2005; 4: 21–24
19. Treweek S, Pitkethly M, Cook J *et al.* Strategies to improve recruitment to randomised trials. *Cochrane Database Syst Rev* 2018; 2: MR000013
20. Molnar AO, Barua M, Konvalinka A *et al.* Patient engagement in kidney research: opportunities and challenges ahead. *Can J Kidney Health Dis* 2017; 4: 205435811774058
21. Healy P, Galvin S, Williamson PR *et al.* Identifying trial recruitment uncertainties using a James Lind Alliance Priority Setting Partnership—the PRioRiTy (Prioritising Recruitment in Randomised Trials) study. *Trials* 2018; 19: 147
22. Better Evidence and Translation—Chronic Kidney Disease (BEAT-CKD). www.beatckd.org (29 October 2019, date last accessed)
23. Australia and New Zealand Dialysis and Transplant Registry (ANZDATA). http://www.anzdata.org.au (29 October 2019, date last accessed)
24. Australasian Kidney Trials Network (AKTN). https://aktn.org.au (29 October 2019, date last accessed)
25. Morrish AT, Hawley CM, Johnson DW *et al.* Establishing a clinical trials network in nephrology: experience of the Australasian kidney trials network. *Kidney Int* 2014; 85: 23–30
26. Kidney Health Australia—Caring for Australasians with Renal Impairment (KHA-CARI). http://www.cari.org.au (29 October 2019, date last accessed)
27. Gutman T, Tong A, Howell M *et al.* Principles and strategies for involving patients in research in chronic kidney disease: report from national workshops. *Nephrol Dial Transplant* 2019; pii: gfz076. doi: 10.1093/ndt/gfz076
28. Chhatre S, Jefferson A, Cook R *et al.* Patient-centered recruitment and retention for a randomized controlled study. *Trials* 2018; 19: 205
29. Scherer JS, Combs SA, Brennan F. Sleep disorders, restless legs syndrome, and uremic pruritus: diagnosis and treatment of common symptoms in dialysis patients. *Am J Kidney Dis* 2017; 69: 117–128
30. Brown SA, Tyrer FC, Clarke AL *et al.* Symptom burden in patients with chronic kidney disease not requiring renal replacement therapy. *Clin Kidney J* 2017; 10: 788–796
31. Jha V, Garcia-Garcia G, Iseki K *et al.* Chronic kidney disease: global dimension and perspectives. *Lancet* 2013; 382: 260–272
32. Cheikh Hassan HI, Tang M, Djurdjev O *et al.* Infection in advanced chronic kidney disease leads to increased risk of cardiovascular events, end-stage kidney disease and mortality. *Kidney Int* 2016; 90: 897–904
33. Kallenberg MH, Kleinveld HA, Dekker FW *et al.* Functional and cognitive impairment, frailty, and adverse health outcomes in older patients reaching ESRD—a systematic review. *Clin J Am Soc Nephrol* 2016; 11: 1624–1639
34. Foster R, Walker S, Brar R *et al.* Cognitive impairment in advanced chronic kidney disease: the Canadian frailty observation and interventions trial. *Am J Nephrol* 2016; 44: 473–480
35. World Medical Association. Declaration of Helsinki, 2013. www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-humansubjects (26 November 2019, date last accessed)

36. Long CR, Purvis RS, Flood-Grady E *et al.* Health researchers' experiences, perceptions and barriers related to sharing study results with participants. *Health Res Policy Sys* 2019; 17: 25
37. Lévesque E, Joly Y, Simard Y. Return of research results: general principles and international perspectives. *J Law Med Ethics* 2011; 39: 583–592
38. Taylor J. Reporting research findings to participants is an ethical imperative. *BMJ* 2019; 367: l6324
39. Schroter S, Price A, Malički M *et al.* Frequency and format of clinical trial results dissemination to patients: a survey of authors of trials indexed in PubMed. *BMJ Open* 2019; 9: e032701
40. Crocker JC, Ricci-Cabello I, Parker A *et al.* Impact of patient and public involvement on enrolment and retention in clinical trials: systematic review and meta-analysis. *BMJ* 2018; 363: k4738
41. Brunsdon D, Biesty L, Brocklehurst P *et al.* What are the most important unanswered research questions in trial retention? A James Lind Alliance Priority Setting Partnership: the PRioRiTy II (Prioritising Retention in Randomised Trials) study. *Trials* 2019; 20: 593

Received: 13.1.2020; Editorial decision: 10.2.2020