

The Challenges of Recruitment to a Randomised Trial Registry – What Information Matters to the Patient?

Ellen Murphy

Glasgow Clinical Research Facility <https://orcid.org/0000-0001-7874-4331>

Niamh O Shea

HRB Clinical Research Facility, University College Cork

Aoife O'Keeffe

HRB Clinical Research Facility, University College Cork

Eva Long

Department of Nephrology, Cork University Hospital

Joseph Eustace

HRB Clinical Research Facility, University College Cork

Frances Shiely (✉ f.shiely@ucc.ie)

HRB Clinical Research Facility and School of Public Health, University College Cork

<https://orcid.org/0000-0003-0969-8321>

Research

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Abstract

Background

Randomised controlled trials (RCTs) are the gold standard for demonstrating efficacy of new therapies. Despite this, nephrology trials, especially of patients with end stage renal disease (ESRD) are much fewer in number than other specialties. Recruitment difficulties are cited as a particular challenge. Using registries to conduct RCTs is a reasonably new practice but is appealing as it combines the benefits of observational studies and clinical trials. There is limited literature on patient motivators, barriers, and consent to these registries. The purpose of our study is to establish this.

Methods

We conducted a cross-sectional questionnaire-based study. A questionnaire consisting of closed and open-ended questions was collected at a dialysis centre in Southwest Ireland representing a catchment patient population of approximately 430,000. Quantitative data were coded and analysed in SPSS (v16). Descriptive statistics were produced, and open-ended questions were analysed by thematic analysis.

Results

87 patients completed the questionnaire. Motivators for participation included personal and altruistic benefits. Barriers/concerns include time requirements, risks (incl. data safety) and side effects along with impacts on current treatment. Though a total of 29.8% of patients 'strongly agree/agree' to having concerns regarding their data storage in a registry, 79.3% of patients were 'very likely/likely' to consent to participate in the registry. It was important to patients to have their GP (general practitioner) involved in the decision to participate, despite little day-to-day contact with their GP for renal dialysis management.

Conclusion

Improving patients understanding of clinical trials, emphasising personal and altruistic benefits, and addressing patient's concerns regarding time and risks of involvement, may improve their likelihood to participate in a registry for RCTs and more broadly speaking, RCTs.

Background

Randomised controlled trials (RCTs) are the gold standard for demonstrating efficacy of new therapies (1). Despite this, nephrology trials, especially of patients with end stage renal disease (ESRD) are much fewer in number than other specialties (2). Among the reasons cited for this are recruitment difficulties and lack of funding (3, 4). Using registries to conduct RCTs is a reasonably new practice (5, 6), attracting attention from trialists and trial methodologists (6–8) as patient data within registries provides an ideal platform for the conduct of RCTs due to the availability of case records, participant randomisation and follow-up data (5, 6, 9, 10). Registry based randomised controlled trials (rRCTs) combine the benefits of clinical trials and observational studies (11–13). rRCTs are appealing due to their low cost, significant

reduction in trial workload (5, 14, 15), improved generalisability of study findings, ease and rapidity of enrolment, potential for complete/long term follow-up (5, 6, 14–18) as well as the ability to infer causality (17). Literature on patient consent to rRCTs (19–21) is limited, even more so for kidney RCTs. The inadequate data that exists focuses mainly on oncology (20, 22, 23). There is a need thus to identify strategies that are effective at increasing participation in rRCTs (24). The PRioRiT_y study identified 20 unanswered questions around trial recruitment (25). Priority 2 was “What information should trialists communicate to members of the public who are being invited to take part in a randomised trial in order to improve recruitment to the trial” (25). The objective of our study is to contribute to this evidence base and establish what information matters to patients when making an enrolment decision to participate in a registry for conducting RCTs. This will enable relevant personnel to provide important, focused information to patients, giving patients the confidence to enrol, mitigating poor recruitment, a major reason RCTs fail (21, 26)

Methods

Research Design and Methodology

A questionnaire with both closed and open-ended questions was distributed to renal dialysis patients at a major dialysis centre in Southwest Ireland. Patients were approached and consented to take part in the study during their normal dialysis schedule (3-times per week). Data were collected in the morning, afternoon, and some night shifts, over a 6-week period, in order to capture a representative sample of the population. This is particularly relevant as younger patients with day-time jobs were more likely to be part of the night shift. 140 patients receive dialysis in this centre but not all were approached to participate. Patients that were actively unwell and those with severe cognitive impairment, as assessed by dialysis staff, were not approached to participate. Patients who were sleeping were not disturbed. 87 patients completed the questionnaire. We estimate fewer than 15 people refused though we did not record this. The questionnaire was self-reported, but the researcher was with the patient to assist in explaining terminology or fill in the questionnaire for those not physically able to do so. This reduced the likelihood of response bias. Any missing data is non-systematic and missing completely at random.

After completion of part one of the questionnaire (see Additional file 1), key terms related to clinical trials and registries (health care registry, kidney research registry, clinical trial, randomisation, informed consent), were explained to the patient by the researcher. Part two of the questionnaire was then completed.

Statistical Analysis

Data were coded and analysed in SPSS (v16). Descriptive statistics were produced. Missing data were coded as 999 and excluded from analysis. Chi-squared tests were used to detect between group differences with alpha set at the 5% level. A one-way ANOVA was conducted to establish age related differences in knowledge of key terms. Open ended questions were analysed by thematic analysis. The STROBE cross sectional reporting guidelines were used in producing this manuscript (27).

Results

Patient Characteristics

69% of patients were male. The median age was 67 years. All were receiving renal dialysis in a hospital setting.

Quantitative Findings

Patient understanding of trial and registry related terminology

Patients were asked about their understanding of key phrases related to clinical trials and rRCTs (Table 1). The term registry, whether a 'healthcare registry' or a 'kidney research registry', was not well understood. 37.9% and 34.4% of patients reported a 'fair/poor' understanding of 'healthcare registry' and 'kidney research registry' respectively, with only 27% having 'excellent/very good' understanding of each term. Over a third (36.8%) of patients had 'excellent' or 'very good' understanding of clinical trials. 'Randomisation' was poorly understood with 57.5% of patients reporting only 'fair/poor' understanding. Patients showed greatest understanding of 'informed consent' with more than 80% having a 'excellent/very good/good' understanding of its meaning. A one-way ANOVA of age versus each of the terms found age was not a factor in understanding the terms, i.e., there was no statistically significant differences at the 5% significance level. When broken down by median age category (below 67yrs, and 67yrs and above), the chi-squared test yielded no statistically significant difference in understanding levels for any of these phrases.

Table 1 Patients' understanding of key rRCT phrases

Research phrase	Percentage (%)				
	Poor	Fair	Good	Very Good	Excellent
'Healthcare Registry' (n=87)	18.4%	19.5%	34.5%	20.7%	6.9%
'Kidney Research Registry' (n=87)	14.9%	19.5%	37.9%	23.0%	4.6%
'Clinical Trial' (n=87)	16.1%	14.9%	32.2%	27.6%	9.2%
'Randomisation' (n=87)	34.5%	23%	23%	14.9%	4.6%
'Informed Consent' (n=87)	6.9%	10.3%	36.8%	31.0%	14.9%

Patient's openness to receiving information on a kidney randomised trial registry, from whom, and how.

91.7% and 89.5% respectively either 'strongly agree' or 'agree' that they would be happy to receive or discuss information about potential participation in a kidney randomised trial registry (kRTR) during dialysis/during a regular clinic visit. <3% 'disagree' and 7% were ambivalent (neither agree nor disagree). In terms of researchers contacting patients via telephone, during out of working hours, to discuss registry participation, only 76% 'strongly agree/agree' with this method of contact with 13% showing ambivalence. 86% 'strongly agree/agree' to receiving information by post with an option to discuss it at the next dialysis/clinic visit.

54.1% prefer receiving oral information with the option to consent after the discussion about potential inclusion in a kRTR during dialysis treatment. 28.2% would prefer to receive information by post (consent at next visit to dialysis unit). The least popular methods to receive information were by email (9.4%) and by telephone (8.2%) with options to consent at the next dialysis session. Figure 1 represents the preferences with whom patients would like to receive and discuss information on the kRTR. Consultants represent the largest group.

Patient data storage concerns

3.4% 'strongly agree' and 26.4% of patients 'agree' to having concerns about their medical data being stored in a registry. As a result, 2.3% 'strongly agree' and 21.8% of patients 'agree' to not wanting their data uploaded and stored in a registry as they consider their information private. Despite that, only 4.6% were 'not likely' to consent and 5.7% of patients said they would be 'very unlikely' (Table 2).

Table 2: Patients views on receiving information about the Kidney Randomised trial (RCT) registry.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
I would have concerns about my medical data being stored in a registry (n=87)	10 (11.5%)	39 (44.8%)	12 (13.8%)	23 (26.4%)	3 (3.4%)
My medical information is private and I do not want it uploaded to a kidney RCT registry (n=87)	11 (12.6%)	40 (46%)	15 (17.2%)	19 (21.8%)	2 (2.3%)
	Very Unlikely	Not Likely	Neutral	Likely	Very Likely
How likely would you be to consent to your medical information being uploaded and stored in a kidney RCT registry (n=87)	5 (5.7%)	4 (4.6%)	9 (10.3%)	49 (56.3%)	20 (23%)

Patients read a paragraph that explained randomisation, the consent process, and the benefits of signing up to a kRTR (see Additional file 1). 37.9% of patients were 'very likely', 42.5% were 'likely' to participate, 13.8% were 'neutral', 3.4% were 'not likely' and 2.3% 'very unlikely' to join the kRTR.

58.8% of patients thought their dialysis doctors should be involved in conducting clinical trials while 41.2% felt their doctors should focus on patient treatment and let somebody else conduct the trials. When signing up to participate in a kidney randomised trial registry 67.8% of patients would discuss it with somebody. The majority would discuss it with their spouse/partner (35%), their GP (15%), their child (13.3%), parent (6.7%) or friend (1.7%). 28.3% selected 'other' and the top preference was their consultant. 51.2% of patients felt it would be 'very important/important' for their GP to be involved in their decision to partake in a kRTR while 48.8% felt it was 'moderately important/of little importance'. Regarding patients' views on getting involved in other aspects of study processes, such as study design or conduct. 62.4% reported it was 'very important/important', while 11.8% said 'moderately important' and 25.9% of patients said it was 'of little importance'. Finally, 94.7% felt it was 'very important/important', to participate in medical research by means of a clinical trial to improve healthcare treatments for others.

Qualitative Findings - Thematic Analysis

80% (n = 70) of patients were 'very likely/likely', to give their consent to participate in a kRTR. Of those, 87% provided at least one reason as to why they were likely to agree. Reasons were not ranked.

Theme: Motivators for participation in a kidney randomised trial registry

Self-benefit

This emerged as a strong theme (n = 32). Patients would participate in a kRTR "to help myself", "beneficial for myself", "personal benefit", "own self-interest/benefit", "to improve my health, "to improve my own situation", and for "better health".

Within the theme of self-benefit patients cited reasons orientated around learning: "to learn more about my condition", "to understand my condition", "like to know more about it" (n=1), "to learn better/improve quality of life" (n=4), "for further knowledge" and for "education". Patients were also motivated to participate for benefits related to their own care process: "if it would help to get off dialysis", "reduce dialysis hours", "so treatments can be given to me correctly", "knowing you are being looked after by experts in that field", "to help my own care" and "open to better treatments because I have bad kidneys", "to improve kidney care", "to improve healthcare".

Help Research, Science and Medical Advancement

This was an equally strong theme (n = 31). Patients said they would be likely to agree to participate in the kRTR for "research purposes", because it would be "good for research", "beneficial for research", "to help research", "bettering research" or making "medical discoveries". Others said it was because "I love research", "I believe in research", it is "good for" and "helps science" and it would be "advancing

medicine". Others felt "more research is necessary" and that it is "essential every effort is made to improve the situation for people with kidney issues" or help "find a cure for kidney problems" and to "find answers to why they are sick". Patients also felt it was an "important study", they would participate because it was "for a good cause...if it is an advantage to the study" and because it is "valuable research", it might "find new improved treatments", and it would be "basically positive to clinical trials (to improve procedures)".

Help Others

Helping others was another dominant theme (n = 19), "to help others", "to help someone else" "to help others on dialysis", "helping others" "to improve someone else's situation", "to improve others health", "for others benefit", "benefit to other patients not in the trial" or "ultimately be beneficial to all". Linked to this was the help/benefit of future generations of patients, e.g., "it will help those who come after me", "to help people in the future", "so others can benefit in future studies" and "very important for the future". Three patients were willing to "help" in general and other patients were "eager to make a contribution", "excited to participate in something new", to "better things" and another believed that their participation would "save time for staff and patients". One patient believed participation "would help" as "more information is always good".

Why not do it?

Other patients (n=5) agreed to participate because they believed "there's no harm in it", they had "no reason not too" or they would "be interested" or because if they were "asked to participate".

Theme: Inhibitors to participating in a kidney randomised trial registry

Responses here are few (n=2) as most patients were likely to participate. Amongst the three reasons they were asked to cite for non-participation were "have no interest, have "no complications so leave it", "distance" and "inconvenient".

Three key pieces of information of most concern to patients when recruiting to a kidney randomised trial registry.

75.9% (n=66) responded, of those 50% provided at least 1 answer. Reasons were not ranked.

Risk (incl. data protection) and side effects

Risks and side effects were also important (30%; n=20). Ten patients wanted to know more "about the side effects" and "what level of danger there would be" and others wanted more information (n=8), for example "what is involved in a clinical trial", "if trials went wrong what would happen". One patient was concerned about being "a Guiney pig in the drug trials". Concerns about the safety of patient medical information was also cited frequently: "who would be entitled to view the information" "how safe is my information" "what would they do with my information" and "who has access/who will see the data".

Other data and registry related concerns included “if the trial was open to review” and “has this method (of trial recruitment) been used in other areas of research and if so what are the results?”. Ten patients had “no concerns”, e.g. “doesn’t worry me” and “no questions I have total confidence in my consultant”.

Time and commitment

A key piece of information was time and commitment. This was listed by 27.2% (n=18): “how much time would it take”, “how long would it take”, “is there a time requirement”, and commitment - “time and place of meeting”, “where would you have to go”, “when would it be” and “when would it start and finish”.

Personal benefit

Personal benefit was also a key piece of information required (22.7%; n=15): “what is the benefit for me”, and would it be “beneficial to my kidneys”. Three patients wanted to know “if it will help other patients”, “what benefit would it be for my consultant”, “how would it help” and two patients wanted to make sure it would help research if they participated “make sure it is helping research” and “would participation help”).

Effect on current treatment

Effect on current treatment was another piece of information required (15%; n=10): “would my normal treatment be constrained”, patients wanted to know if it would interfere with “my medication”, “my dialysis” or the “times of my dialysis treatment” and “does it reduce dialysis time”.

Discussion

This is the first study we are aware of that explores patient’s preferences regarding consent to a registry designed to conduct RCTs. Patients are willing to take steps to participate in clinical trials by consenting to be part of a registry. Addressing the barriers of time and transportation and highlighting the benefits of participation, both personal and altruistic may improve patient’s willingness to partake. Our findings have relevance for those establishing rRCTs and disease-specific registries but can also be extrapolated to consent issues in RCTs and mitigating the risk of ‘losing’ patients before trials begin. This study also contributes to the evidence base for priority 2, what information patients trialists should communicate to those being recruited, in the James Lind Alliance Priority Setting Partnership, PRioRiTy Study, on trial recruitment (25).

Our findings show more than 80% of patients have an ‘excellent/very good/good’ understanding of ‘informed consent’. This is critical to ensuring that patients’ decision making is autonomous. This finding contradicts other studies that show poor understanding of consent for medical procedures (28–30). The finding is also higher than results from a prior meta-analysis which showed the proportion of patients who understood various components of informed consent ranged from 52.1–75.8% (31), though the level of understanding in the meta-analysis is not stated, making direct comparison unreliable. Patients had poor understanding of registries but there is limited data to compare it to. However, it informs future

researchers establishing registries of the importance of explaining them. Patients' understanding of 'randomisation' was particularly poor. This is not new (32–37). For example, in one trial only 23% of patients were able to explain what randomisation meant (35), similarly only 19.5% of our patients had a 'excellent/very good' understanding of 'randomisation'. We feel this lack of understanding is a reason why most patients are willing to discuss (89.5% strongly agree/agree) and receive (91.7%) information about the kRTR and associated clinical trials. We have gained a valuable insight here on what to focus on, for education interventions and designing informed consent forms for recruiting patients to a registry for subsequent RCT use.

One third of patients are concerned about the storage of their medical data. There has been an immense amount of progress in this area, e.g., GDPR (General Data Protection Regulation) (38) and the new EU (European Union) clinical trials directive which commenced in 2014 (39). It is reassuring that despite these concerns, 80% of patients would still be 'very likely/likely' to provide consent to participate in a kRTR. Only five patients stated they would be 'not likely/very unlikely' to consent to participate. Some patients did not respond to the question asking them about their concerns about participating in a kidney registry, this aspect of the study would benefit from a qualitative investigation, to delve into the nuances of these findings.

Our findings confirm that patients are often altruistic, which is in line with literature based on clinical trial participation (32, 40–42). Two of our four emerging themes dealt with helping others or helping Science, reasons also listed by Swedish haemodialysis patients (43). However, personal benefit was also a key motivator. Patients want to improve their health and the quality of care they receive. This theme has been highlighted in studies on clinical trial participation (32, 44, 45). The theme of personal benefit was also dominant in terms of reasons why patients would participate and as a key piece of information that is of value to them e.g. 'how participation in a registry would affect a patient's current treatment' is extremely relevant. This is easily addressed on enrolment to a registry. The key point here is knowing this is important to patients. These findings are significant to assist those recruiting to a registry as it allows the patient information leaflets to be more focused on the self and altruistic benefits of participation as well as impacts on current treatment, resulting in truly informed consent.

Literature indicates individuals are prone to ask for advice on clinical trial participation from their GP or other physicians before consenting to partake (45). Healthcare providers attitude towards clinical trials are important to patients when making the consent decision (40, 46), our findings were consistent with this, 51.2% of our patients stated they felt it was 'very important/important' for their GP to be involved in their decision to participate in a kRTR, despite dialysis patients attend their GP infrequently because most of their care is through the hospital clinics/dialysis units. This is likely the reason our finding is slightly lower compared to other literature, e.g., in one study 77% of patients stated they wanted to make the decision to participate in a clinical trial with their doctor and only 14% wanted to make it independently (35). Trusting the physician is clearly very important to patients a finding concomitant to the literature (45, 47) further evidenced by the fact a third of our patients would like to receive information on the registry from their consultant. Targeting healthcare professionals to ensure they have adequate

knowledge and information about clinical trial registries and how to relay this to potential participants may be a worthwhile intervention to improve recruitment to clinical trial registries.

Identifying key pieces of information patients want when getting involved in a rRCT is essential to successful recruitment. Mitigating any factors that will deter people is important. Time and travel requirements were common concerns in this study. Many patients in the dialysis unit avail of HSE (Health Service Executive, (government funded)) provided transport to attend their dialysis sessions. They travel in small groups therefore, arranging transport to participate in any potential research is an issue. However, we anticipate this finding would not be unique to a dialysis cohort and would be applicable to all rRCTs for patients requiring ongoing regular treatment, e.g., oncology trials. Trialists need to make time and travel requirements very clear and potentially need to be inventive in the design phase of the study, e.g., multiple data collection on the same day, when considering the trial processes to mitigate this, and to improve recruitment especially of those in rural areas with poor transport links. Additionally, this must be budgeted for.

Barriers and concerns in this study are mirrored in other literature based on clinical trial participation. Concerns about medical risks, harms, and side effects (42, 46, 48, 49), time requirement and travel commitment concerns (20, 46, 48, 50–52), data safety concerns (49, 53) are all noted previously. Lack of understanding of randomisation (32, 33, 54) as well as the research for which they are consenting to (33) is previously and was also evident in this study. This is a relatively easy topic to address and our study suggests that if done well, recruitment should be positive. The question of how to do this well should be investigated separately through further SWATs (Studies Within A Trial).

Strengths And Limitations

The sample size is relatively modest (n = 87) consisting of elderly adults (median age 67yrs) with underlying health conditions, potentially affecting the external validity and generalisability of the findings. However, the unit's demographics are broadly representative of the dialysis population nationally, (J Eustace, personal communication) therefore may inform efforts to create a dialysis trial registry that will facilitate rRCTs. Although the sample size is modest it captured 60% of the available patients. Data was collected in the morning, evening, and some night shifts. This was a strength as younger patients with day-time jobs are more likely to be part of the night shift, ensuring the sample was broadly representative.

Selection bias is a possibility as participation was voluntary, those participated in the study may have a greater interest in research and be more willing to partake in further research/clinical trials compared to those who declined to participate. Some very sick patients filled out the questionnaire with assistance, ensuring representation across disease levels. However, assistance may have increased engagement in the research among patients and unintentionally caused response bias. Patients could have provided answers they felt the researchers desired.

Conclusion

This study contributes to trial methodological research by answering a modified PRioRiTy study (25) question, no.2, “what information should trialists communicate to members of the public who are being invited to take part in a randomised trial registry in order to improve recruitment to the registry”. It contributes to evidence-based decision making for recruitment strategies to trial registries and more broadly speaking, RCTs. Patients are willing to take steps to participate in clinical trials by consenting to be part of a registry. Tackling the barriers of time and transportation and highlighting the benefits of participation, both personal and altruistic may improve patient’s willingness to partake. Trialists can improve/tailor their participant information leaflets when aiming to recruit participants. The information that is provided to participants needs to be specific and relevant to their needs and the needs of other participants, and most importantly guided by participants like those who participated in this study. If participants do not understand trial processes, or are not adequately informed, it may hinder the quality and integrity of the study (20, 55).

Abbreviations

RCT(s)

randomised controlled trial(s)

ESRD

end stage renal disease

GP

general practitioner

rRCT(s)

registry based randomised controlled trial(s)

KRTR

kidney randomised trial registry

GDPR

General Data Protection Regulation

EU

European Union

HSE

Health Service Executive

SWATs

Studies Within a Trial

Declarations

Ethics approval and consent to participate

Ethical approval and consent to conduct this study was granted by the Clinical Research Ethics Committee of the Cork Teaching Hospitals in 2019.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

EM designed the questionnaire, collected the data, drafted the manuscript, and approved the final version. FS conceived the study, designed the questionnaire, and contributed to the writing of the manuscript. She contributed to all drafts. JE conceived the study and facilitated the data collection. He reviewed the final version. AOK designed the questionnaire and collected the data. She reviewed the final version. EL facilitated data collection and gave clinical interpretation. She reviewed the final version. All authors are accountable for this work.

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Figures

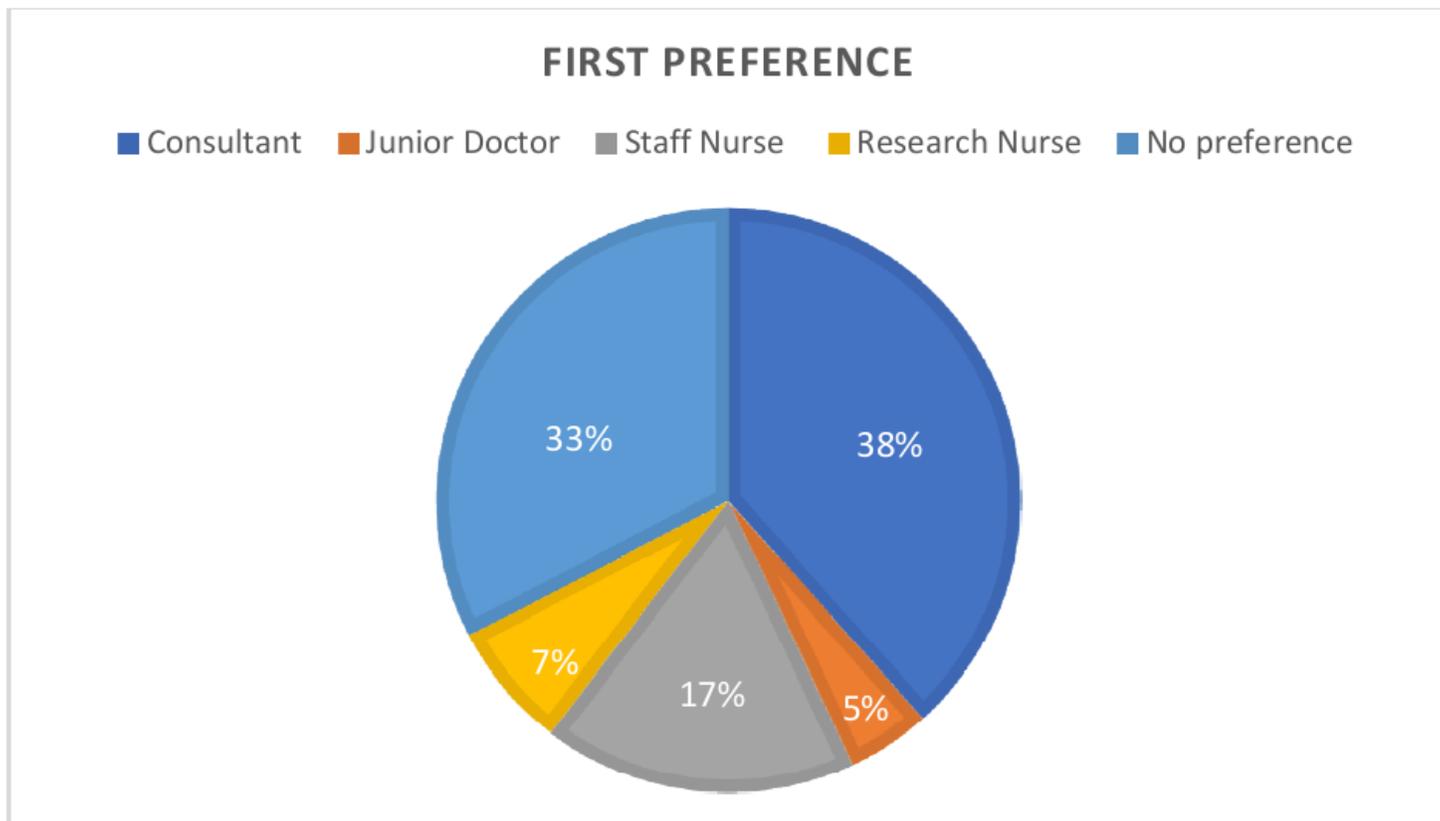


Figure 1

Patient preferences for receiving information from about the kidney randomised trial registry. Consultants represent the largest group at 38% of patients' first preference to receive/discuss information from about the kidney randomised trial registry.

Supplementary Files

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- [AdditionalFile1Patientquestionnaire.pdf](#)
- [STROBEcrosssectionalchecklist.docx](#)