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Nephrologists' Views on a Workflow for Returning Genetic Results to Research Participants

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Introduction: Returning research-based genetic results (gRoR) to participants in nephrology research can improve care; however, the practice raises implementational questions and no established guidelines for this process currently exist. Nephrologists' views on this issue can inform the process but are understudied.

Methods: We developed a conceptual workflow for gRoR from literature and experience, covering aspects such as which results to return, how, and by whom. We surveyed US nephrologists to gauge their views on the workflow and anticipated barriers and collected participants' demographics, including professional backgrounds.

Results: A total of 201 adult and pediatric nephrologists completed the survey. Most of them agreed that all diagnostic kidney-related results (93%), secondary findings (80%), and kidney-related risk variants (83%) should be returned. No significant differences were found between adult and pediatric nephrologists' responses, except that 48% of adult nephrologists versus 26% of pediatric nephrologists supported returning polygenic risk scores (PRS) ($P < 0.01$). Seventy-nine percent wanted to know about research results before clinical confirmation. Most of them (63%) believed a genetic counselor should return clinically confirmed results. Key barriers included the cost of clinical validation (77%) and the unavailability of genetic counseling services (63%). Facilitators included educational resources on genetic kidney diseases (91%), a referral list of experts (89%), and clear clinical care guidelines (89%). We discuss findings' implications and provide "points to consider."

Conclusion: There is significant interest in gRoR among nephrologists; however, logistical and economic concerns need addressing. Identified facilitators can help large nephrology studies planning to return genetic results to participants.

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The expansion of genomic research provides insights into the pathobiology of kidney diseases and more precise diagnoses for some participants.[1-3] It raises the hope that gRoR to participants will improve patient care.[4] This growing expectation is also supported by recommendations of geneticists' professional organizations and an extensive body of literature on the ethical obligation to gRoR.[4-7] Notwithstanding the strong embrace of gRoR, implementation has lagged. In nephrology, implementation is likely hampered by the absence of guidelines on the process for gRoR,[8-10] resulting in duplicated and *ad hoc* efforts of studies to design a feasible and ethical workflow for themselves. Addressing these challenges will be critical to promote equity in kidney genomic care.

The process for gRoR from nephrology research faces several structural challenges, including the cost of developing and implementing granular gRoR protocols.[11,12] The logistical complexity of recontacting

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research participants to inform them about the availability of research-based genetic results while withholding the results from them until their clinical confirmation, as well as the process to clinically validate results and return them to providers, add financial and organizational burden.[4,13-15] This burden is compounded in settings where staffing shortages limit the integration of genetic testing into clinical care.[8] Developing a feasible gRoR process and identifying key issues to consider when adapting it to specific studies could alleviate some of this burden.

Other likely challenges for the wide implementation of gRoR involve genetic-specific issues, such as which results in return. In nephrology research, these may include 5 different types of findings as follows: (i) diagnostic variants, (ii) risk factors, (iii) variants of uncertain significance (VUS), (iv) polygenic risk scores (PRS), providing aggregate effect of many common variants across the genome, and (v) secondary findings. "Secondary findings" refers to results that are unrelated to the primary purpose of testing, with the American College of Medical Genetics and Genomics currently recommending an opportunistic screening for 73 genes, all associated with clinical conditions for which established interventions can improve prognosis (also called "actionable genes").[16] Nephrologists' views on which results to return, the utility of genetic results for clinical care, their role and involvement in the gRoR process, and confidence in delivering results and managing the subsequent patient care are crucial for the success of translational efforts[5,8,17] but are understudied.

To date, studies of nephrologists have largely focused on the return of the *APOL1* G1 and G2 risk variants;[5,18] however, their views on other types of results such as VUS or PRS may be different. Research participants have consistently expressed interest in receiving all genetic results in nephrology research studies[19,20] and in other areas of medicine.[21-25] However, previous studies reported that participants had only a limited understanding of the results[21,22] and often did not share them with their primary care physician, even when the results were actionable.[26] From the clinicians' perspective, return of all results could lay a significant burden on nephrologists who are then expected to engage with those results and explain them to their patients. Clinicians who may not be involved in the research study have been shown to only limitedly engage with unsolicited results.[27] In addition, clinicians' (including nephrologists') limited training in genetics and lack of confidence in discussing such findings with patients can impede gRoR implementation and its promise for improved patient care.[8,13,28-31] Understanding nephrologists' views and challenges related to gRoR can improve genomic care but only limited attention has been given to nephrologists' views.

Other questions when developing a gRoR protocol concern the process and implications of the clinical validation of results. In the US, research-based results can only be used in clinical decision making after genetic analysis was performed in certified laboratories under the Clinical Laboratory Improvement Amendments (CLIA) or validated in such a laboratory (CLIA validation).[32] However, the CLIA validation process is costly and may not be affordable to research studies and research participants. For example, a study on cancer reported that most patients did not clinically confirm their research-based genetic results, citing lack of insurance coverage as one of the reasons.[33] Whether nephrology research studies should only return clinically validated results and their responsibility for covering the costs of genetic counseling and CLIA validation have not been systematically studied. The potential limitations in clinicians' genomic knowledge (as discussed above) further necessitate consideration of the role of genetic counselors in the gRoR process, along with questions about related costs.

These questions have direct relevance for nephrology because kidney-related studies, such as the Cure Glomerulonephropathy Network (CureGN), the Chronic Kidney Disease in Children Study (CKiD), the Chronic Renal Insufficiency Cohort Study (CRIC), Neptune, and the *APOL1* Long-term Kidney Transplantation Outcomes Network (APOLLO), are increasingly considering or implementing gRoR.[34-42] In the absence of clear guidelines or workflow for gRoR, each study makes its own decisions about whether to return results, which types of results to return, and the process for returning them, including to whom (e.g., research participants or also clinicians) and whether CLIA-validated results are incorporated in the medical records. Such discrepant approaches may increase confusion among participants and nephrologists, especially when providers are not directly involved in those studies.

In this study, we report on findings from a national survey of nephrologists that explored their views on, and anticipated barriers for, the implementation of a conceptual model for gRoR. Based on the survey responses, we developed "points-to-consider" that can inform large consortiums of nephrology studies planning to return genetic results to research participants. In addition, we conducted 4 webinars with key stakeholders (parents, adult participants, adult and pediatric nephrologists) to share our findings and inform the final points to consider.

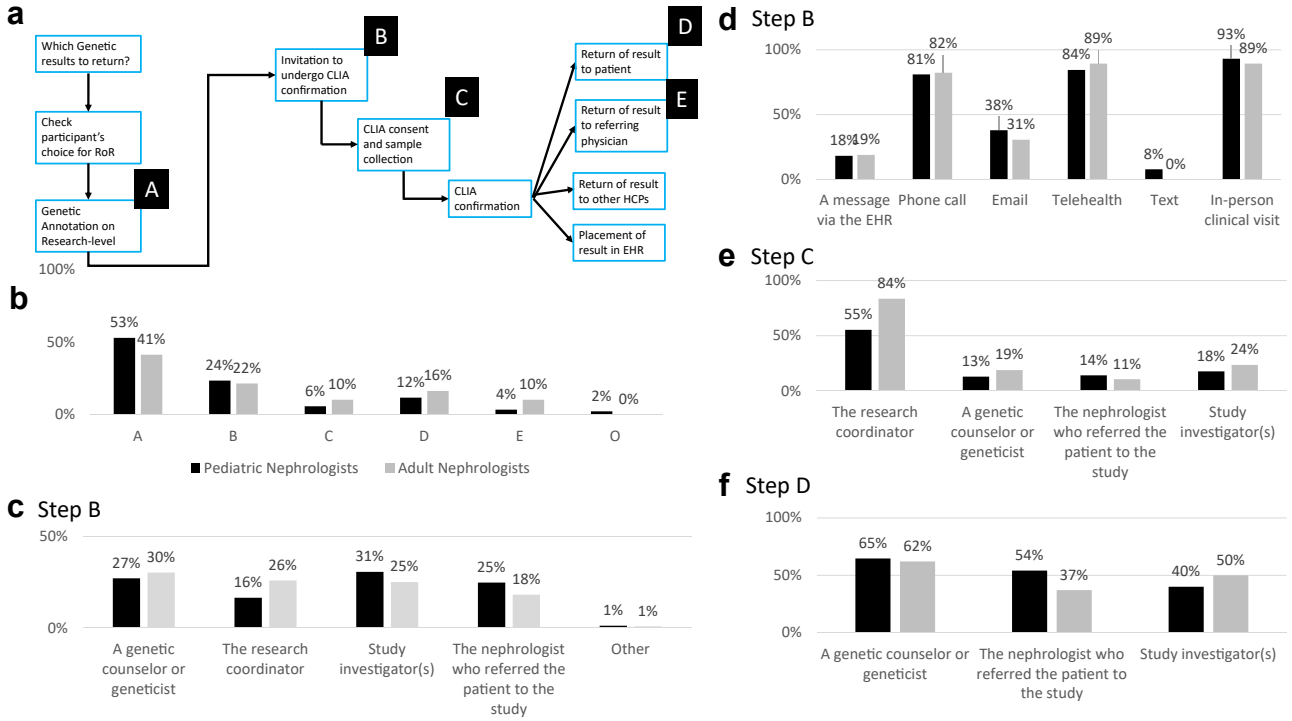

Figure 1. Nephrologists' views on the proposed workflow for return of research-based results from genetic research. (a) Proposed workflow and 5 time points at which nephrologists could be informed (A–E). (b) Adult and pediatric nephrologists' views on at what point should the referring nephrologist be informed of genetic findings. (A) As soon as the research team identifies a potential genetic result to be returned; (B) when contacting the participant and offering the option of clinical validation (without informing them about the result); (C) when consenting the participant for the clinical validation of the research-based result; (D) during the return of the clinically validated genetic result; (E) after the result has been returned to the participant; (O) the referring nephrologist does not need to be involved. (c) Nephrologists' perspective on who should recontact participants to inform them of genetic findings and invite them to undergo CLIA validation (step B on the workflow). (d) Nephrologists' perspectives on the appropriateness of each method to inform participants about research based genetic findings that need to be CLIA validation (step B on the workflow). (e) Nephrologists' perspectives on who should obtain CLIA consent from participants (step C on the workflow). (f) Nephrologists' perspectives on who should return results once clinically confirmed (step D on the workflow). CLIA, Clinical Laboratory Improvement Amendments; EHR, electronic health record; HCP, health care provider; RoR, return of results.

METHODS

Study Design and Survey Items

Study design included 2 steps. First, we developed a conceptual model for gRoR based on the existing literature[6,43] and practical experience[13] (Figure 1a). The model encompasses substantive and procedural aspects for gRoR from nephrology research: which results to return, how to return results (including CLIA validation and related costs), by whom results should be returned, and clinicians' possible involvement in the process. In our model, participants with genetic results are contacted and offered the option to undergo CLIA confirmation. If the participant agrees, consent is obtained, and a new sample is collected. After results are CLIA-confirmed, participants are recontacted by the study to review results. Results are also sent to the referring physician and placed in the electronic medical record.

Second, we conducted a national, internet-based survey to explore nephrologists' views about the proposed workflow for gRoR. The survey was developed by an interdisciplinary team, and in collaboration with CureGN. It was based on the existing literature and our experience in gRoR in nephrology studies.[13] The survey described our model and included this transition paragraph to explain the need for CLIA validation: "returning research-based genetic results to participants usually requires clinical validation of these results in certified laboratories (CLIA confirmation). Research participants need to consent for clinical validation before they can receive results. Genetic counseling services may be offered before and after the return of results." Overall, the survey comprised 41 items, including self-reported demographic questions (gender, race, and ethnicity, as required for National Institutes of Health reporting), questions about their practice, and questions that explored which research-based genetic results should be returned (with examples or short explanations for terms such as secondary findings, genetic risks factors, VUS, and PRS), the gRoR process, and potential barriers and facilitators for gRoR such as costs and availability of

genetic counseling services (Supplementary Appendix). Response choices consisted of mostly dichotomized (yes/no) or predefined options. The institutional review board at Columbia University Irving Medical Center approved the study.

Study Procedures

Recruitment was done by circulating invitation to participate in the study through several national nephrology organizations, the Cure Glomerulonephropathy network, the National Kidney Foundation, the Alport Syndrome Association, and the American Society of Pediatric Nephrologists. The survey questions were preceded by a brief eligibility screen, that is, adult and/or pediatric nephrologist practicing in the United States. Participants provided online consent. Participants were offered a $25 gift card for survey completion.

Statistical Analysis

Data were collected using REDCap.[44] All statistical analyses were performed with R software.[45,46] Demographic characteristics were reported as counts and percentages. Differences between adult and pediatric nephrologists were compared using chi-square (χ^2) tests for categorical variables. In addition, we assessed the impact of participants' genetic knowledge on responses to the questions below. As previously reported,[31] a third of the participants had limited basic genetic knowledge; nevertheless, we did not observe statistically significant differences between nephrologists with low basic genetic knowledge and others in any of the questions below, and it is therefore not reported further. Because of the wide-ranging dissemination technique and the absence of data about the total sample population, a response rate could not be calculated.

RESULTS

Study Population

Overall, 201 nephrologists completed the survey, including 116 adult nephrologists and 85 pediatric nephrologists (Table 1). Of these, 58% were men, 40% women, and 1% identified as nonbinary (1% preferred not to answer). Most identified as White (52%), followed by Asian American (31%); fewer identified as Hispanic/Latino (4%) and Black (2%). Most participants (65%) were university affiliated; 45% were MDs with an additional graduate degree; 42% were involved in genetic research though 48% were for less than 5% of their time.

Table 1. Survey participants' characteristics

Characteristics	Adult		Pediatric		Total
	n	Proportion (%)	*n*	Proportion (%)	
Total	116	58	85	42	201
Gender					
Males	80	69	37	44	117
Females	36	31	44	52	80
Nonbinary	0	0	2	2	2
Prefer not to answer	0	0	2	2	2
Race and ethnicity					
Asian/Asian American, not Hispanic/Latino	40	34	24	28	64
Black, not Hispanic/Latino	1	1	4	5	5
Hispanic/Latino	7	6	2	2	9
Native American or Alaskan Native, not Hispanic/Latino	0	0	1	1	1
Native Hawaiian or other Pacific Islander, not Hispanic/Latino	1	1	0	0	1
Unknown or preferred not to answer, not Hispanic/Latino	9	8	2	2	11
White, not Hispanic/Latino	58	50	49	56	107
Multiracial[a], not Hispanic/Latino	0	0	3	4	3
Degree					
MD (medical doctor)	68	59	42	49	110
MD and other degree (PhD, MS, MPH, other)	35	30	30	35	65
DO (doctor of osteopathic medicine)	7	6	1	1	8
DO and other degree (PhD, MS, MPH, other)	1	1	4	5	5
MBBS (Bachelor of Medicine, Bachelor of Surgery)	5	4	6	7	11
MBBS and other degree (PhD, MS, MPH, other)	0	0	2	2	2
Clinical setting					
University-affiliated hospital	71	61	64	75	135
Other hospitals	5	4	5	6	10
Solo or small practice with hospital affiliation	21	18	11	13	32
No hospital affiliation	15	13	4	5	19
Other	4	3	1	1	5
Experience referring to genetic evaluaion					
None	16	14	2	2	16
Referred 1–4 patients	50	43	8	9	58
Referred 5–9 patients	15	13	14	16	29
Referred 10–19 patients	20	17	9	11	29
Referred 20 patients or more	15	13	52	61	67
Experience returning genetic results					
None	23	20	4	5	27
Limited (1–9 patients)	68	59	22	26	90
Medium (10–25 patients)	14	12	30	35	44
High (>25 patients)	11	9	29	34	40

[a]Multiracial encompasses individuals who selected this response option or self-selected more than 1 racial category.

Types of Results

When asked about which results should be returned to participants, 93% of nephrologists supported returning diagnostic kidney-related results, 83% supported returning risk variants (i.e., *APOL1*), 80% supported returning other actionable secondary

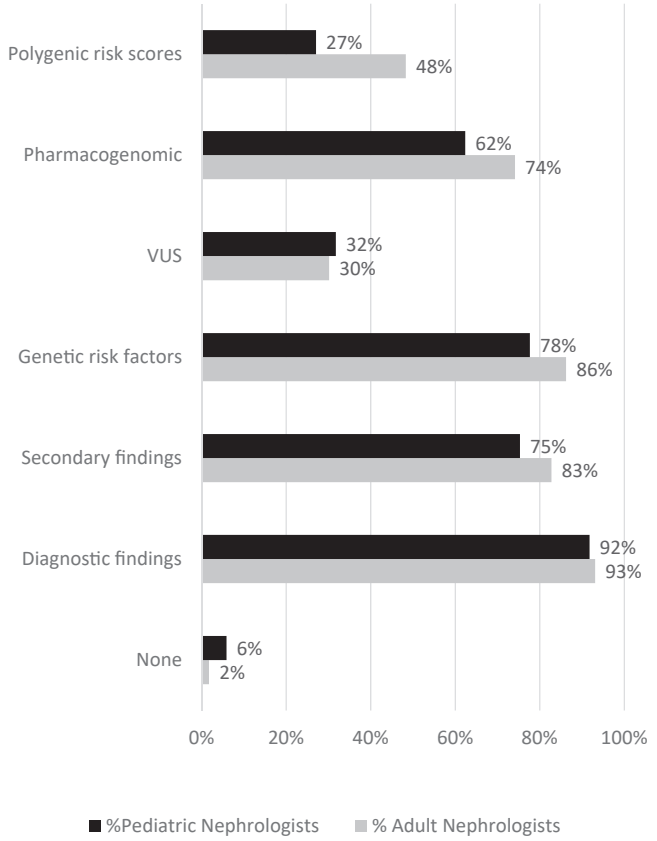

Figure 2. Adult and pediatric nephrologists' views on which research-based genetic results to return to research participants. Participants were asked "what types of results should be returned to participants following clinical validation?" The answers were: (i) no research-based results should be returned, (ii) results that are associated with the kidney disease (diagnostic finding), (iii) results unrelated to the kidney disease which can inform clinical care (e.g., *BRCA1/2*), (iv) genetic risk factors (e.g., *APOL1*), (v) VUS: (i.e., unclear association with kidney disease), (vi) results that may impact drug management (pharmacogenomic profile), (vii) results based on polygenic risk scores (calculation of the aggregate effect of common variants on disease risk). Figure indicates the proportion of adult and pediatric nephrologists selecting each type of result. VUS, variants of uncertain significance.

findings (e.g., *BRCA*1/2), 69% supported returning pharmacogenomic results (results that may impact drug management), 39% supported returning PRS (aggregate effect of common variants on disease risk) and 31% supported returning VUS (Figure 2). No significant differences were found between the responses of adult and pediatric nephrologists, except that 48% of adult nephrologists compared to 26% of pediatric nephrologists thought that PRS should be returned ($P < 0.01$).

Process for RoR

In response to the question about when they would like to be informed that their patient may have a returnable result, most adult nephrologists (83%) and pediatric nephrologists (73%) answered that they would like to be informed before the research-based result is CLIA-confirmed (Figure 1b). Responding to the question about who should inform research participants about the presence of research-based genetic findings that need to be CLIA-validated (without sharing the specific result), 29% of nephrologists endorsed "a genetic counselor or geneticist", followed by study investigator(s) (27%), research coordinator (22%), and the nephrologist who referred the patient to the study (21%); 1% opted for "other" and indicated that nephrologists should recontact with the help of the study investigator or a genetic counselor (nephrologists had to select a single choice, Figure 1c). Regarding the question about how it would be most appropriate to inform research participants about available findings, 92% endorsed in-person clinical visit, 87% endorsed telehealth, and 82% endorsed phone call (could select multiple answers, Figure 1d). Only 35% of the nephrologists opted for e-mail, 18% for a message through the electronic health record, and 4% endorsed through text. Regarding the question about who should obtain participants' consent for the CLIA validation, 59% selected research coordinator, 17% selected study investigator(s), 13% selected a genetic counselor or geneticist and 10% selected the nephrologist who referred the patient to the study (single response, Figure 1e). Finally, when asked who should return CLIA-validated results to participants, 63% selected a genetic counselor or geneticist, 46% selected study investigator(s) and 44% selected the nephrologist who referred the patient to the study (multiple answers choice, Figure 1f). There were no significant differences between the responses of adult and pediatric nephrologists, except that 37% of adult nephrologists and 54% of pediatric nephrologists thought that the referring nephrologist should return the CLIA-validated result (P-value < 0.05).

Barriers and Facilitators

Although 70% of nephrologists believed that genetic results should be returned to participants even if the study does not cover the cost of CLIA validation, most reported lack of coverage by the study (77%) and health insurances (87%) as barriers (Figure 3). In addition, 42% thought that gRoR is too time-consuming, and 63% reported that genetic counseling services are not readily available in their clinics. When asked about facilitators for gRoR, nephrologists indicated that having educational resources on genetic kidney disease (91%), a list of experts to whom the nephrologist can refer their patients (89%), and clear guidelines for clinical care after positive results are CLIA-confirmed (89%) are "very important." (Figure 4).

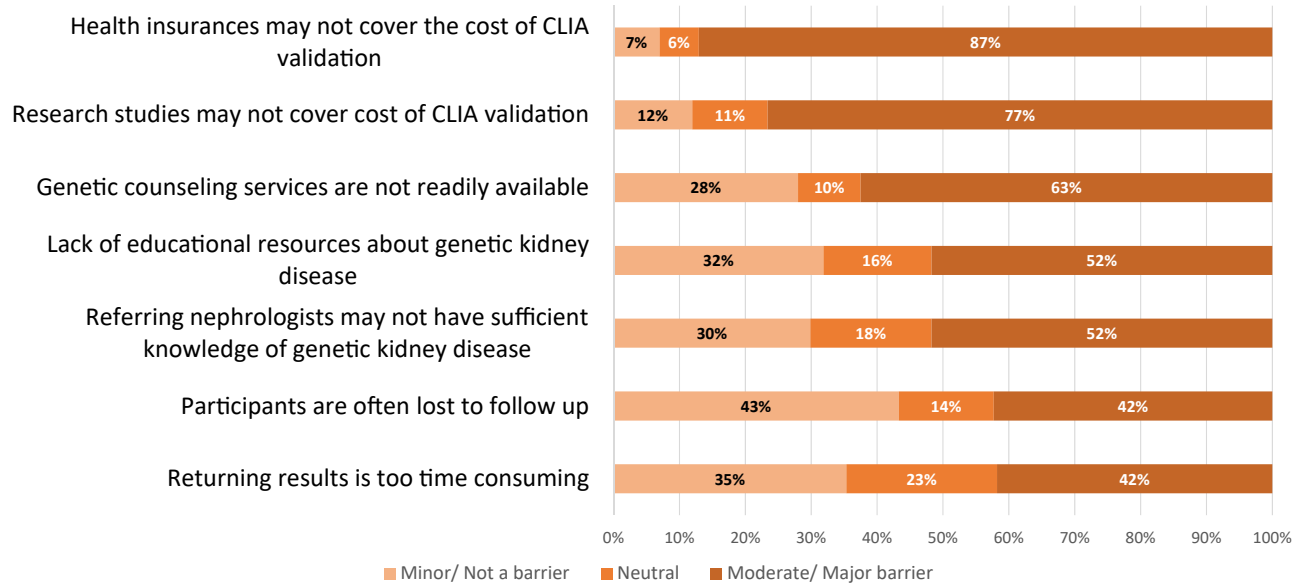

Figure 3. Barriers to the return of research-based genetic results. Participants were asked "how much of a barrier do you anticipate each of the following to be in returning research-based genetic results to participants?" The proportion of nephrologists answering: "minor or not a barrier" (light pink), "neutral" (orange) and "moderate or major barrier" (brown) is depicted.

DISCUSSION

This study provides a first insight into nephrologists' views about gRoR from nephrology research and about a proposed gRoR workflow. Overall, the study suggests strong support in returning clinically relevant results to research participants and highlights the need to consider 5 key issues in the gRoR process: types of genetic results to return, who should return results, to whom to return research-based results, distinction between clinical and research-based genetic results, and costs of gRoR (see points-to-consider, Table 2).

Most nephrologists (both adult and pediatric subspecialty) thought that diagnostic kidney-related findings, secondary findings, and risk variants (e.g., *APOL1*) should be returned to both adult and pediatric participants, which is consistent with previous studies indicating that physicians prioritize results with clinical utility.[22,47-50] However, the possible return of genetic results for adult-onset conditions to children (as

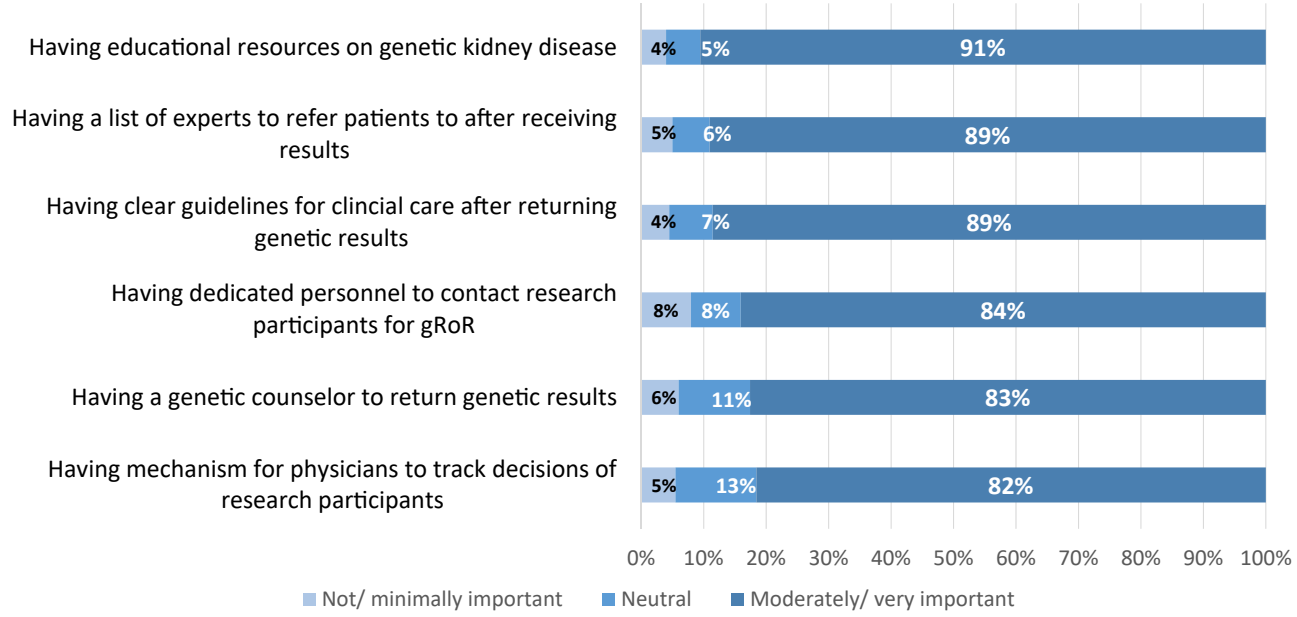

Figure 4. Facilitators to the return of research-based genetic results. Participants were asked "how important is each of the following in facilitating return of research-based genetic results to participants?" The proportion of nephrologists answering: "not or minimally important" (light blue), "neutral" (blue) and "moderate or major barrier" (dark blue) is depicted.

Table 2. Points to consider and proposed best practices for returning research-based genetic results (gRoR)

Point to consider	Proposed best practice
Which genetic results to return? Each study can decide whether to return genetic results, and if so, which results to return.	The informed consent should specify which results might be returned to the participant. The informed consent should specify if the research study does not know which results will be returned. A decision not to return secondary findings requires assurance that both participants and clinicians understand the scope of the study and its limitations.
Who should notify the patient regarding the need for CLIA confirmation? Research results can only be returned after CLIA-validated, which can delay gRoR.	Given that respondents were split regarding who should contact the patient, efficacy should be prioritized to ensure the process moves as quickly as possible.
Who should return the genetic results? Participants may have questions regarding their results; results should therefore be returned by someone equipped to answer them.	A research team member who is knowledgeable about hereditary kidney disease should return CLIA confirmed results. A genetic counselor is best equipped with the tools and knowledge to return results across types.
To whom to return genetic results? Participants may not want all their clinicians to know about genetic findings	Patients should be asked about and given the option to choose which physicians are notified about CLIA confirmed results.
What to do with research-based genetic results? Research-based results cannot be acted upon prior to CLIA confirmation.	Discuss with research participants the process and distinctions between clinical care and research settings. Discuss with the referring nephrologists their potential role in the return of research-based genetic results.
What about costs? Cost for gRoR can be a barrier for implementing genomic care in nephrology. There is a need to identify steps to mitigate the challenge.	Include the cost of the gRoR process in the grant application. This should include costs related to recontacting research participants, CLIA-validation, genetic counseling, and immediately recommended follow-up care. If the cost of gRoR is not covered, discuss the options with research participants clearly and early on. Engaged with community advisory board throughout the study.

CLIA, Clinical Laboratory Improvement Amendments.

are most conditions associated with secondary findings) has been controversial given that children would not benefit from this knowledge before they reach adulthood and it would prevent them from making an informed decision about it.[51] In the United States, returning such results to children can also impact their ability to obtain life insurance, which is not protected by the Genetic Information Nondiscrimination Act.[52] Despite the limited experience of nephrologists in discussing *APOL1* with patients, most nephrologists responded that risk factors such as *APOL1* should be returned, which is in line with previous studies.[9,18,53,54] This finding is significant: knowledge of specific *APOL1* variants can provide more accurate risk assessment and studies to evaluate possible therapies are ongoing.[55–57] In addition, 1 study found that disclosure of high-risk *APOL1* variants to patients and their clinicians was associated with improvement in blood pressure from baseline and more lifestyle changes compared to patients with low risk *APOL1* variants.[58] In contrast, most nephrologists in our study were not supportive of the return of VUS and PRS, especially pediatric nephrologists. This finding is consistent with findings from other areas of genomic medicine.[50,59] As research regarding PRS in nephrology is ongoing and its clinical utility is rapidly evolving,[60,61] it will be critical to ensure that nephrologists are educated about the potential benefits of PRS before such information is incorporated into clinical care. These findings highlight the importance of *a priori* discussion with research participants about gRoR and types of results that may be returned. Such communication would ensure that stakeholders' expectations are aligned with one another, and ideally be done during the informed consent process.

Despite the survey's explanation of requirements regarding CLIA validation prior to returning results, most nephrologists indicated that they preferred to know about results before the CLIA validation. This finding is concerning because it may indicate a lack of knowledge regarding the role and importance of CLIA validation or the legal prohibition of using research-based genetic results in clinical decision making before CLIA validation (the standard in the USA). Although study protocols that do not include a CLIA confirmation process may return results to participants with clear communication that the results should not be used for clinical decision making,[6] such scenarios could place the treating nephrologist in a delicate situation if their patient cannot afford or opts out of the CLIA validation process. Overall, the responses suggest a need for education about the distinction between clinical care and research settings as well as early discussion with the referring nephrologists about their potential role in the gRoR process.

Although nephrologists wanted to know about the results before their patients, few thought that the nephrologist should inform their patients about the option of CLIA validation, and they were evenly split about who should recontact and inform participants about the availability of results. Similar to findings from a study that examined participant preference for recontact,[62] nephrologists believed that participants should be notified of the option of CLIA validation orally, even though other options of letters, e-mails, or electronic health record–based messaging could reduce study costs and allow high-throughput gRoR.[13] Nevertheless, in previous studies, recontacting

participants to inform them about the available results has been noted to significantly slow the timeline of gRoR.[4] Such delays are often due to time limitation of personnel and lost-to-follow-ups; in large research networks, they could be due to the gap in time between recruitment and the genetic analyses and indirect communication with participants. Taken together, we suggest that efficacy be prioritized that is, early designation of the research team member who will recontact the participant (unless the referring nephrologist is amenable to do it), creating a process for direct communication with research participants (as needed), recontacting participants as soon as possible, and orally discussing with them the option of CLIA validation.

Although most nephrologists agreed that a genetic counselor or geneticist should return CLIA-validated results, most nephrologists also reported limited genetic counseling services as a barrier to gRoR. As other studies have suggested, genetic counselors are particularly skilled for gRoR: their ability to fill in the genetic knowledge gap is complimented by their advanced psychosocial training.[8,21,22,62,63] Genetic counselors may further improve the return rate, the timeline, the quality of the information provided, and familial communication of the results.[15,63,64] Conversely, the limited workforce of genetic counselor is particularly worrying because the nephrologists in our study were mostly from university-affiliated institutions, where genetic services are more available when compared to the acute lack of genetic counseling services in other settings.[41,65] Even among medical centers with a nephrology genetics clinic, waiting periods for genetic counseling can be up to 6 months.[41] Technology such as chatbots and virtual assistants can play an important role in helping genetics providers face the growing demand for their services and is currently being used in some health systems.[66,67]

Moving forward, it would be invaluable if nephrologists developed confidence in discussing genetic diagnoses with their patients. Although nephrologists' knowledge of genetics had no impact on views regarding all the questions above, nephrologists in our study reported that insufficient knowledge of genetic kidney diseases and a lack of educational resources would create barriers to gRoR.[31] Previous studies have similarly found that nephrologists felt unprepared to discuss genetic results with patients and that they were highly interested in obtaining more genetics education.[8,13,17,41] Changes to the nephrology learning curriculum and required continuous education in genetic kidney diseases may improve nephrologists' confidence returning results.[8,31]

As expected, nephrologists viewed the cost of CLIA validation and genetic counseling as a key barrier for gRoR. This finding is in line with previous research and practical experience: these costs can range from hundreds to thousands of dollars per participant and be prohibitive for research studies and participants.[14,15,50,68] In the absence of fundings to cover these costs, we suggest that studies do not withhold the results but clearly specify the option of out-of-pocket cost in the informed consent. However, we concur with previous recommendations that investigators should aim to build these costs into the study budget when applying for grants[68] and encourage funding agencies to provide such resources to promote equitable gRoR to all participants, regardless of their socioeconomic status.[5,12]

Finally, nephrologists in our study identified several potential facilitators to the gRoR process that could inform future endeavors: developing guidelines to facilitate clinical care management, creating a list of experts to whom nephrologists can refer their patients, having a mechanism for physicians to track participants' decisions to receive results and dedicated personnel for recontact would facilitate the gRoR process. Future research can further assess and refine the methods and approaches to mitigate the barriers.

Limitations

First, the survey described a specific protocol of gRoR, which included the requirement of CLIA validation for returning results to inform clinical decision making; however, we did not study participants' understanding of the role of CLIA validation which might have impacted their responses. Relatedly, our study did not consider other scenarios for, or aspects of, gRoR, including challenging cases of consent, such as adolescents (ages 13–17 years old) and adults with questionable capacity to consent. Such cases raise unique ethical, legal, and social issues that require nuanced considerations and are beyond the scope of this work.[69] For example, the genetic testing of adolescents raises questions about assent or parental consent given that adolescents may have competency to consent as adults but, legally, the authority is in the hands of their parents.[70,71] Similarly, the survey did not explore the views of nephrologists regarding return of non-CLIA validated results or the handling of such results, as well as the return of CLIA-validated results to the participants without being placed in the medical record. These issues should be explored in future studies. Second, our findings may have ascertainment bias given that most nephrologists worked in university-affiliated clinical settings, many of whom reported at least some degree of active genetic research, and only a few self-reported having African American ancestry, which

could be relevant given the high prevalence of *APOL1* in the patient population. Nonetheless, our sample is demographically comparable to the nephrologists' population. In addition, though nephrologists who are involved in genetic testing and those who work in university settings where genetic studies are conducted were more likely to respond to the survey, they are also more likely to refer their patients to genetic studies. While future studies can focus attention on nephrologists in other clinical settings, our findings of key stakeholders in the discussion on gRoR in nephrology research can inform future research in this area.

CONCLUSION

In the absence of formalized frameworks for implementing gRoR in nephrology research, separate research groups are required to invest time and resources to plan and design gRoR workflows. Such *ad hoc* and undirected processes for gRoR in nephrology negatively influence the analysis of the impact of genetic findings from research on patients' clinical management and health outcomes.[72] Our study provides a first account of how nephrologists view a proposed gRoR workflow, including how and who should return results, the role of clinicians in this process, and consideration of both barriers (e.g., costs) and facilitators. These findings can inform the development of measures to facilitate the coordinated translational efforts in precision nephrology and improve patient care and health outcomes.

DISCLOSURE

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Appendix. Copy of survey questions.

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