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Assessment of the Needs of Nephrology Divisions to Implement Return of Clinically Significant Research Genetic Results: A Survey of Nephrotic Syndrome Study Network (NEPTUNE) Investigators

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Genetic testing · Nephrotic syndrome · Precision medicine · Return of research results · Nephrology

Abstract
Introduction: There is an increasing need to return genetic testing results to patients with kidney disease who were first genotyped on a research basis. Operationalizing this process in nephrology clinics is challenged by a limited number of genetic providers with whom to partner and a general lack of support services for all clinicians. ***Methods:*** We administered a survey in March 2022 to assess the current ability and ongoing needs of nephrology divisions to return clinically significant research genetic results to patients and to implement clinical genetic testing. This survey was distributed to institutions within the Nephrotic Syndrome Study Network (NEPTUNE) as part of the planning process for return of research genetic results to participants with pathogenic variants in Mendelian nephrotic syndrome genes. ***Results:*** Twenty-seven of 28 sites (96%) completed the survey. 59% (n = 16) of sites said they could handle return of research genetic results independently, with the rest expressing hesitation about the volume and complexity of patients and the limited resources and access to genetics services. 81% (n = 22) of these institutions did have a genetics clinic and 26% (n = 7) have a nephrology genetics clinic. However, 70% (n = 10) of these clinics have a waiting time over 1 month. 89% of divisions (n = 24) were conducting genetic testing and 96% of those (n = 23) used a kidney multi-gene panel. In 46% of divisions (n = 11), nephrologists were handling logistics of obtaining genetic

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testing samples themselves. ***Conclusion:*** We identified specific areas of support needed for return of clinically significant genetic results from research studies. While the surveyed nephrologists were conducting genetic testing, there were limitations in the support services available. This survey will help guide other research studies that wish to return genetic results to participants and also highlight the need for increasing support to effectively operationalize genetic testing in nephrology clinics.

Introduction

The clinical implications and benefits of genetic testing for patients are well established – facilitating diagnosis, informing management and prognosis, guiding recommendations to screen for comorbidities, and prompting cascade family screening [1]. In nephrology particularly, the role and impact of genetic testing in clinical practice have become more prevalent across diverse conditions, including cystic kidney diseases, glomerular diseases, and chronic kidney disease of unknown etiology [2–5]. For example, exome sequencing identified a monogenic cause in 20–48% of patients with cystic kidney disease and 61% with tubular kidney disease, and anywhere from 9.3 to 39% of patients with undifferentiated chronic kidney disease, dependent on the population targeted [3, 4]. The types of genetic testing available clinically are growing, particularly with the rise of commercial kidney genetic panels. Given the growing relevance of genetic testing, it is expected that its clinical use will continue to increase, particularly by clinicians who are not geneticists, including nephrologists. Thus, there will also be increased need for resources to support its implementation.

From a research perspective, there is also a push from national organizations including the American Society of Human Genetics, the National Heart, Lung, and Blood Institute, and the National Academy of Sciences to return clinically significant genetic results from research studies back to patients because of the clinical benefits [1, 6–8]. These same organizations recommend that ideally a genetic counselor participate in disclosure of results, but also acknowledge that a provider with the appropriate expertise may not be readily available [1, 8]. In addition, because these genetic results are found in the research setting, there are operational challenges to consider if the test needs to be repeated to meet the standards of the Clinical Laboratory Improvement Amendment (CLIA) [9].

The need for return of research genetic results, as well as its challenges, have been similarly addressed globally. A panel of European experts in genetics and public health recently outlined the steps required for effective return of results, including determining which results to return and making a plan for how to disclose results [10]. They also acknowledge the challenges of accessing the extensive resources required for return of results and finding genetics-trained providers [10]. These findings are supported by a survey of psychiatrists worldwide about return of results, in which only 14% felt there are adequate guidelines for return of results and 59% felt their own knowledge about how to manage return of results was poor [11].

Incorporating return of research genetic results and increased clinical genetic testing is challenged by the limited number of clinical geneticists and genetic counselors across the USA [12, 13]. The 2019 Current Practices in Medical Genetics survey by the American Board of Medical Genetics and Genomics noted inadequate growth in the workforce to meet expanding needs, many geneticist jobs unfilled for over 3 years, and one-third of new nonemergency patients waiting over 3 months for an appointment [13]. In addition to the limited number of providers, they are also limited in distribution, with 73% of geneticists and 43% of genetic counselors practicing in academic medical centers, mostly in major metropolitan areas, and 42% of genetic counselors practicing only in adult cancer genetics [12, 13]. Around the world, the genetic counseling profession is growing, but there is variability in the formality of training and credentialing among different countries [14, 15]. Workplace shortages are noted worldwide – in 2019, there were estimated to be just 50 genetic counselors in Africa and 350 genetic counselors in Asia [15].

Fulfilling the expectations of patients, providers, and national organizations to return genetic testing results in a clinically valid manner will only be possible if physicians and allied health professionals have the confidence and the resources to do so. Return of results programs have taken varied approaches thus far. For other multicenter studies that incorporated research return of genetic results, each site completed the process independently with little centralized guidance [16, 17]. In nephrology, there is one pilot study of return of genetic results to adult patients at a single center [18]. Altogether, it is not yet known if nephrologists will have the knowledge and resources to return research genetic results, particularly from multicenter studies in which they may not be directly enrolling the patients or initially

analyzing the research results. Identifying the support they will require from the study is necessary in order to make this possible.

Given the genetics workforce limitations and the increasing uptake of genetic testing, it is important for nephrologists to be able to conduct some genetic testing independently [19]. However, among Australian physicians across all specialties, one-third of respondents had ordered genetic testing in the past year, but only one-quarter felt prepared to use genetic tests in their practice [20]. In Europe, because of the need for non-genetic providers to have the knowledge to perform genetic testing, the Genetic Education for Nongenetic Health Professionals project was undertaken in 11 countries, and reported wide variability in genetic education [21]. The European Society of Human Genetics put forth core competencies in genetics for all health professionals in order to improve use of genetics in healthcare [22]. These core competencies include identifying patients who would benefit from testing, communicating effectively with those patients, and tailoring management based on genetic results [22]. These studies highlight how more genetic training for all providers is still required. More specifically, among US adult nephrologists, while 72% were conducting genetic testing regularly, 79% indicated limited or no education in genetics [23]. An additional US survey of adult and pediatric nephrologists focused on genetic education in 2021 found 40% of nephrologists felt they had insufficient training in genetic testing [24]. Other barriers to genetic testing experienced by nephrologists include lack of access to testing, resources for learning, and support for the logistics of obtaining samples and processing insurance [19, 25–27].

Apart from these surveys, there is limited information on nephrologist education on genetic testing, the types of tests they use, and their knowledge of how to implement testing. The Kidney Disease Improving Global Outcomes Controversies Conference on Genetics in Chronic Kidney Disease included ordering and returning genetic results as desirable core competencies for nephrologists [28]. This formal statement illustrates that it is incumbent for nephrologists to have training on the educational and operational aspects of genetic testing – deciding which tests to order, handling testing logistics, interpreting results, and applying results clinically – as well as the resources to support this.

Here, we describe a survey of North American nephrologists, who are members of the Nephrotic Syndrome Study Network (NEPTUNE), ascertaining their ability to return clinically significant research genetic results to participants. NEPTUNE is a multicenter, nationwide, prospective observational cohort of children and adults with proteinuric kidney disease [29]. While the focus of our study was the resources needed for NEPTUNE's return of results program, our results are relevant for other research studies thinking about return of results and provide insight into general use of clinical genetic testing for kidney disease.

Methods

Survey Design and Content

The goal of this two-part, 32-question survey (online suppl. Fig. 1; for all online suppl. material, see https://doi.org/10.1159/000533501) was to assess the ability of each NEPTUNE site to return research genetic results to participants enrolled at their institution. Each site principal investigator (PI) was responsible for coordinating the return of results in their division and was asked to respond to the survey on behalf of all providers in their nephrology division.

The survey was developed by the NEPTUNE return of results working group, which comprised nephrologists, a genetic counselor, and an expert in the ethical, legal, and social implications (ELSI) of genetic testing. NEPTUNE created this working group with the goal of developing and implementing a plan to return clinically significant research genetic results to participants. This working group first reviewed the literature of surveys of both nephrologists and other physicians about use of genetic testing and barriers to genetic testing before developing our survey [20, 23, 25]. Because all questions in our survey were novel, they went through multiple rounds of review within this group to ensure clarity, relevance, and face validity for the target audience.

The first part (part A) contained questions about the availability of genetic services at each institution, the resources available for help with genetic testing, and how providers in each division approach genetic testing. The survey contained multiple-choice questions, some of which allowed respondents to choose multiple answers. Respondents were asked to rank their comfort level with different types of genetic testing using a 5-point Likert scale (1 = "very uncomfortable" to 5 = "very comfortable"). The goal of these questions was to confirm and expand on previous surveys about current use of genetic testing and availability of genetic providers, in part by including questions about specific types of genetic tests ordered, genetics clinics, and genetic providers.

Part B focused on return of genetic results for NEPTUNE patients. Respondents were asked how return of results could potentially be handled by their division and what types of support they would need. This included obtaining insurance coverage of genetic testing, the need to repeat clinical testing to meet CLIA standards, and ability to provide counseling to patients about their results. Questions were both multiple-choice format and open response. The goal of this part of the survey was to determine how return of results could be implemented at each institution. Because this survey did not involve any patient information and was only directed toward opinions and resources of physicians, it was granted exemption through the Boston Children's Hospital Institutional Review Board.

Table 1. Representative quotations from open response answers about NEPTUNE site concerns and needs to implement return of results

Need for genetic education
"We are a large group with both young and old faculty members with diverse interests. They all have different comfort levels. . .In discussion with our internal resource faculty we can generally handle 90% of the genetic results ourselves. With regards to pregnancy and other non-kidney issues we generally would have a genetic referral for medico-legal considerations."
"I would prefer that it is handled by the Genetic Counselor through the kidney genetics clinic. . .but it COULD be handled "directly" (depending on the complexity of the results)"
"Education for us in terms of best way to communicate the results"
"may need to have a structure in place to offer further counseling (likely beyond scope of general nephrologist) to answer patient questions"
"Would likely need additional training to report back to ensure entirety of consequences can be explained to patient or partner with genetics counselor"
Need for NEPTUNE support
"I would feel comfortable to meet with a NEPTUNE counsellor/Genetics MD to guide discussions and help with interpretation of results. Then convey results myself, with backup of referral to a local genetics clinic for additional counselling."
"Educate the medical staff. Make available expert genetics support."
"suggest a unified approach at sites and perhaps central support or referral for education."
Concerns about time and logistical support
"depends on the testing result, primary MD and availability of clinic time"
"Not sure what volume or protocol this would take, would happen through PI and coordinator"
"Staff resources are limited"
"I think a genetic counselor or geneticist would be ideal, however need to allocate funds to pay for services."
n = 12 respondents were represented.

Distribution

The survey was hosted on REDCap and was distributed via email to the site PI at each of 28 active NEPTUNE participant institutions in March 2022 (online suppl. Table 1). Only the PI at each site was asked to complete the survey on behalf of providers in their division. Survey respondents were asked to identify their institution, so it was ensured that each site was accounted for once; responses were then de-identified and analyzed in aggregate. Up to four rounds of personal reminders were sent via email as required, so that as many sites as possible were included.

Data Analysis

Descriptive statistical analyses were performed to summarize responses including demographics and multiple-choice questions about use of genetic testing and resources available. The questions with Likert scales of comfort levels were analyzed by quantifying the responses in each of the five categories. The responses of pediatric and adult sites were compared as a sub-analysis. Open-ended questions regarding the ability of institutions to implement return of results were evaluated for common themes.

Results

Ability to Perform Return of Research Genetic Results

Twenty-seven of 28 centers responded to the survey. All were from academic medical centers across North America and 21 were from adult hospitals (online suppl. Table 1). The site PI's were asked if they felt their division could handle return of research genetic results and what support resources they would require. 59% (n = 16) said their division could handle this process independently, 11% (n = 3) said they could not, and 30% (n = 8) responded "unsure." When asked to specify in an open-ended response, sites responded that it would depend on the number of patients, the complexity of the result, the amount of time required, and the comfort level of the individual physician providing care (Table 1). In responses to general comments about implementing return of results for NEPTUNE, we identified common themes of (1) challenges to implementation, (2) resources needed, (3) ability to partner with genetics, and (4) handling logistics of insurance coverage. More specifically, six sites requested support from NEPTUNE's core center, with two specifically requesting education; three sites said it would depend on the volume and complexity because of limited resources; and five sites said they would need access to genetics or genetic counselors to help (Table 1).

Interestingly, there was not a clear pattern of which sites could handle return of results. There was no obvious pattern with factors such as which sites had a nephrology genetics clinic, were already offering testing, or had more

Table 2. Respondents were asked if their institution had genetics clinics available (n = 22) and if so, what types of clinics

(a) Percentage of institutions who have each type of genetics clinic	
Type of genetics clinic	Institutions with that type of clinic, % (n)
Pediatric	63.6 (14)
Adult	50.0 (11)
Nephrology	31.8 (7)
General (adult and pediatric)	13.6 (3)
Prenatal	31.8 (7)
Cancer	27.3 (6)
Cardiac	13.6 (3)
Neuro	9.2 (2)
(b) Number of unique types of genetic clinics at each individual institution	
Number of unique genetic clinics by institution	Institutions, % (n)
1	40.9 (9)
2	22.7 (5)
3	9.1 (2)
4	13.6 (3)
5	9.1 (2)
6	4.5 (1)

logistical support. Of the sites that did not offer genetic testing clinically (11%, n = 3), one reported they could independently implement return of results and the other two responded "unsure."

When asked about partnering with genetics at their institution for return of results, 67% (n = 18) said it would be possible, but others responded that it would be challenging because of the low availability of genetic providers, limited time of all providers, and handling insurance coverage for two providers to see a patient. Most sites (78%, n = 21) had social work, financial assistance, psychology, or psychiatry available if needed to help with unintended consequences of genetic testing, such as psychological stressors or costs.

Availability of Genetics Services

Physicians were asked about the ability to access genetic services and experts at their institution, the availability of genetic counseling, and resources to support genetic testing. Of the 27 sites responding, 81% (n = 22) had a genetics clinic within their institution with 59% (n = 13) of those having more than one genetics clinic and 14% (n = 3) having more than five (Table 2). Three (13%) of these institutions only had a genetic counselor available with no geneticists and two (9%) had geneticists without any genetic counselors among all their genetics clinics. The most common types of genetic clinics present were pediatric genetics (64%, n = 14), adult genetics (50%, n = 11), and prenatal genetics (32%, n = 7) (Table 2).

Of note, 26% (n = 7) of the institutions surveyed had a specific nephrology genetics clinic. Of these nephrology genetics clinics, three (43%) had a genetic counselor and physician with genetic expertise, two (28%) had a genetic counselor and geneticist, one (14%) had a genetic counselor, geneticist, and additional physician with genetics expertise, and one (15%) had a geneticist and physician with genetics expertise. Institutions with a nephrology genetics clinic tended to have other additional genetics clinics: pediatrics (71%, n = 5), adult (57%, n = 4), and prenatal (43%, n = 3).

About half of all the nephrology divisions (52%, n = 14) referred patients to a genetics clinic for testing. Of note, over 70% (n = 10) had a waiting period longer than 1 month and 14% (n = 2) had a waiting period greater than 6 months. One site noted that for pregnancy planning, they referred to another institution where the wait time was greater than 8 months.

Current Use of Genetic Testing

Respondents were next asked for their assessment of how genetic testing is currently being used by providers in their nephrology division. Of the 27 divisions responding, 89% (n = 24) offered genetic testing, although this does not necessarily indicate that every physician in each division was conducting testing themselves. Most commonly, a kidney multi-gene panel was being performed (96%, n = 23). Eleven divisions (46%) were performing targeted variant testing and 11 divisions (46%) were performing single-gene testing; six divisions (25%) were conducting both. Seven sites (29%) were conducting whole-exome sequencing (WES) and only two (8%) were conducting whole-genome sequencing (WGS) (shown in Fig. 1). Fourteen sites (58%) were performing more than one type of testing; the rest (42%) were performing a kidney multi-gene panel as their only type of testing.

For those divisions in which the physicians were ordering genetic testing, 21% (n = 5) reported that physicians handled insurance authorization themselves without assistance (Fig. 2a). 75% (n = 18) had clinic support staff and nursing staff to assist; only one division reported help from the laboratory performing the testing. The average of the type of insurance coverage for patients across all sites were similarly distributed among private

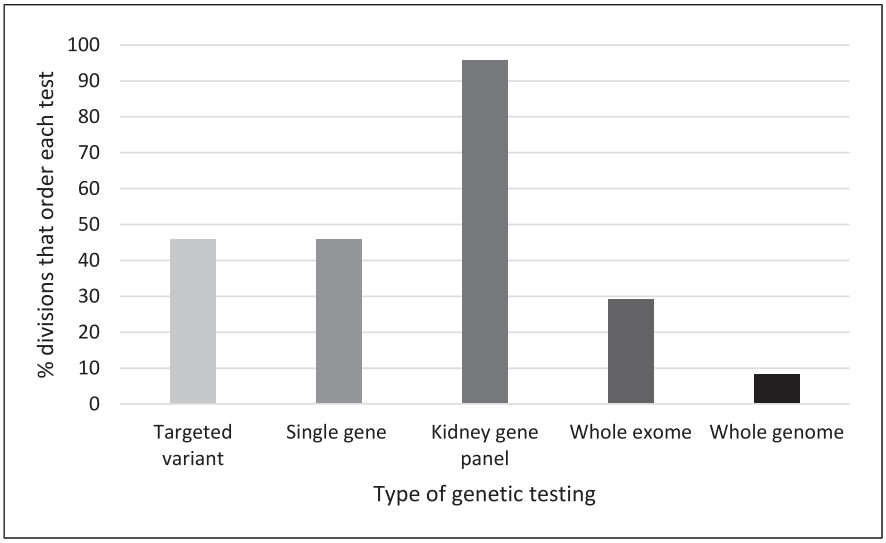

Fig. 1. Percentage of divisions (n = 24) performing each type of genetic testing, as responded by NEPTUNE site PIs.

(34.6%), Medicare (34.1%), and Medicaid (26.3%) with a smaller number of patients paying out of pocket (8.6%) (excluding two Canadian sites and one US federal government-funded site). When asked to comment on insurance coverage in an open-ended manner, respondents expressed challenges, writing that the process is highly variable and cumbersome, very dependent on insurance type, and that private insurance often does not cover testing. 46% (n = 11) of divisions reported that providers handled the logistics of obtaining samples themselves (Fig. 2b). Four institutions (16%) reported help from the laboratory performing the testing, with the rest having assistance from clinic support staff and nursing staff.

In most divisions, the providers who ordered genetic testing were interpreting the results of the testing themselves (71%, n = 17). The most common resource used to help interpret the result was the report from the laboratory (96%, n = 23), with one of these sites only using the report and no other resources. The other most common resources used were a literature search (71%, n = 17), and a conversation with a genetic counselor or geneticist at their institution (67%, n = 16); 92% (n = 22) were using more than one resource for interpretation (Fig. 3).

In general, respondents felt that providers were more comfortable ordering and interpreting targeted variant testing, single-gene testing, and kidney multi-gene panels and less comfortable ordering and interpreting WES or WGS (Fig. 4a, b). However, there was clear variability and very few respondents felt that providers were very comfortable with any type of testing.

In comparing pediatric and adult sites, overall, pediatricians were more comfortable with genetic testing. All six pediatric sites were performing some type of genetic testing with five (83%) indicating "comfortable" or "very comfortable" with the logistics of performing genetic testing. In contrast, only half of the adult divisions responded similarly. The only providers conducting WGS were at pediatric sites, although there was little comfort in interpreting WGS across all institutions.

Discussion

This study explores return of research results for a multicenter nephrology study of both adults and children and is one of few studies specifically focused on nephrologists and genetic testing. We identified current feasibility and existing needs of NEPTUNE sites to implement a protocol for return of clinically significant research genetic testing results to participants. In addition, we ascertained how nephrologists used genetic testing in their current practice and what needs existed to improve use of such testing. The results of our study uncovered challenges specific to return of genetic results as well as more generally for clinical genetic testing, particularly the need for more genetic education for providers.

In our survey, it was encouraging that over half of sites said they could handle return of results independently and that over half preferred that it not be done outside of their division. Surprisingly, there was no clear pattern of which sites could handle return of results independently.

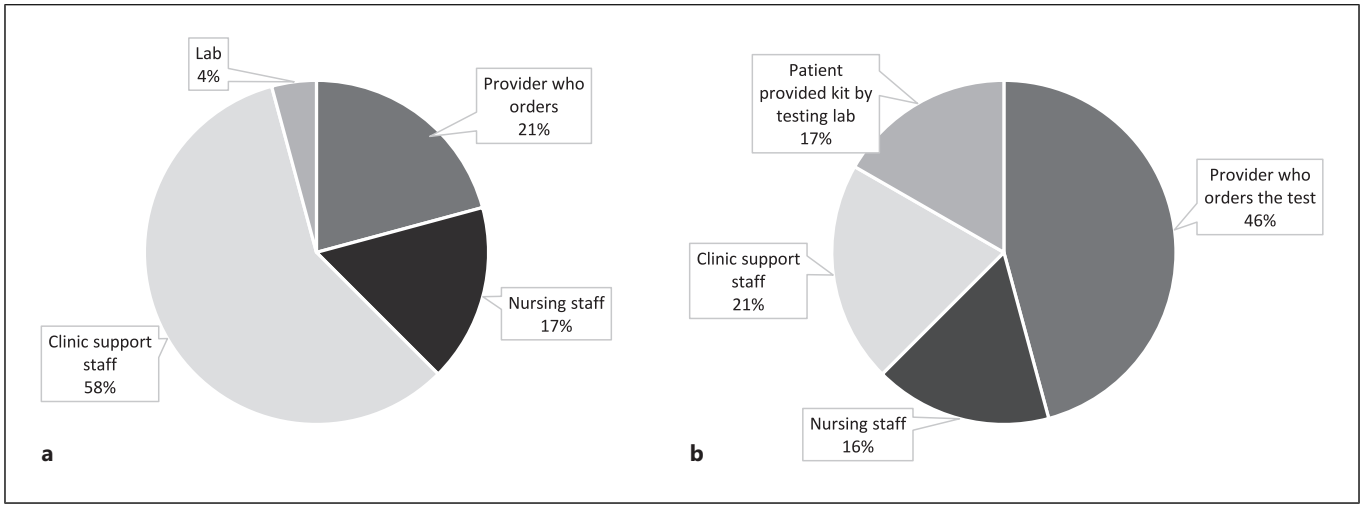

Fig. 2. Respondents were asked who in their division (n = 24) primarily handles the logistics of obtaining insurance authorization (**a**) and obtaining the samples for genetic testing (**b**).

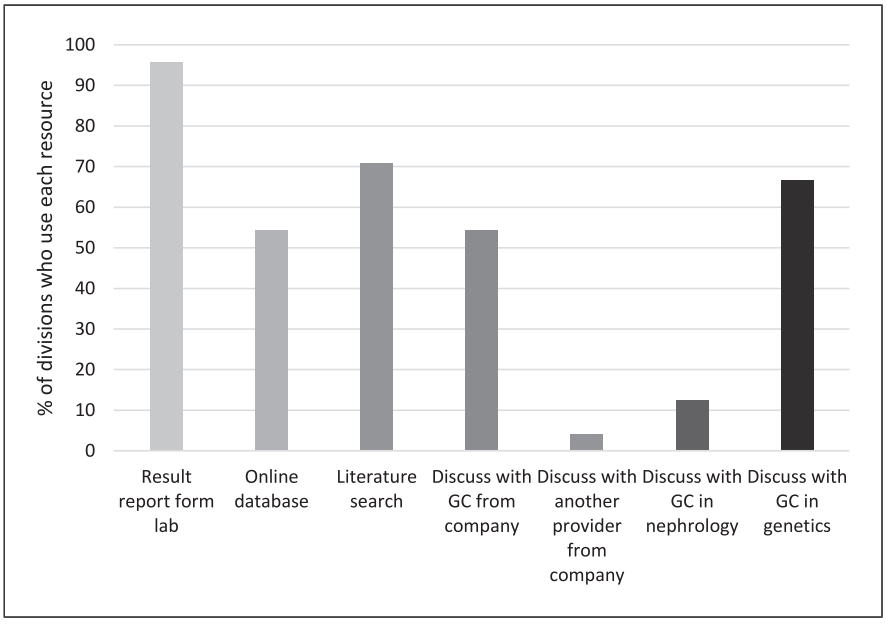

Fig. 3. Respondents were asked what resources are used by providers in their division (n = 24) to interpret the results of genetic testing. GC, genetic counselor.

There was not an obvious relationship with which sites had a nephrology genetics clinic, were already offering genetic testing, used more resources to interpret results, or had more support for logistics of obtaining samples and insurance approval. This indicates that there may be other factors not yet identified which are affecting the ability of sites to successfully return results.

Our results highlighted the need for support and education of providers in implementing our return of results process. In the open response questions, respondents reinforced the need for support, noting the need for education about use of genetic testing and expressing concerns about burdens on their division to take on this program. To address these concerns and provide more support for the nephrologists, our return of results working group plans to create educational materials about use of genetic testing clinically, genetics of nephrotic syndrome, and templates for documentation.

In the NEPTUNE return of results program, participants will have targeted variant testing to ensure the

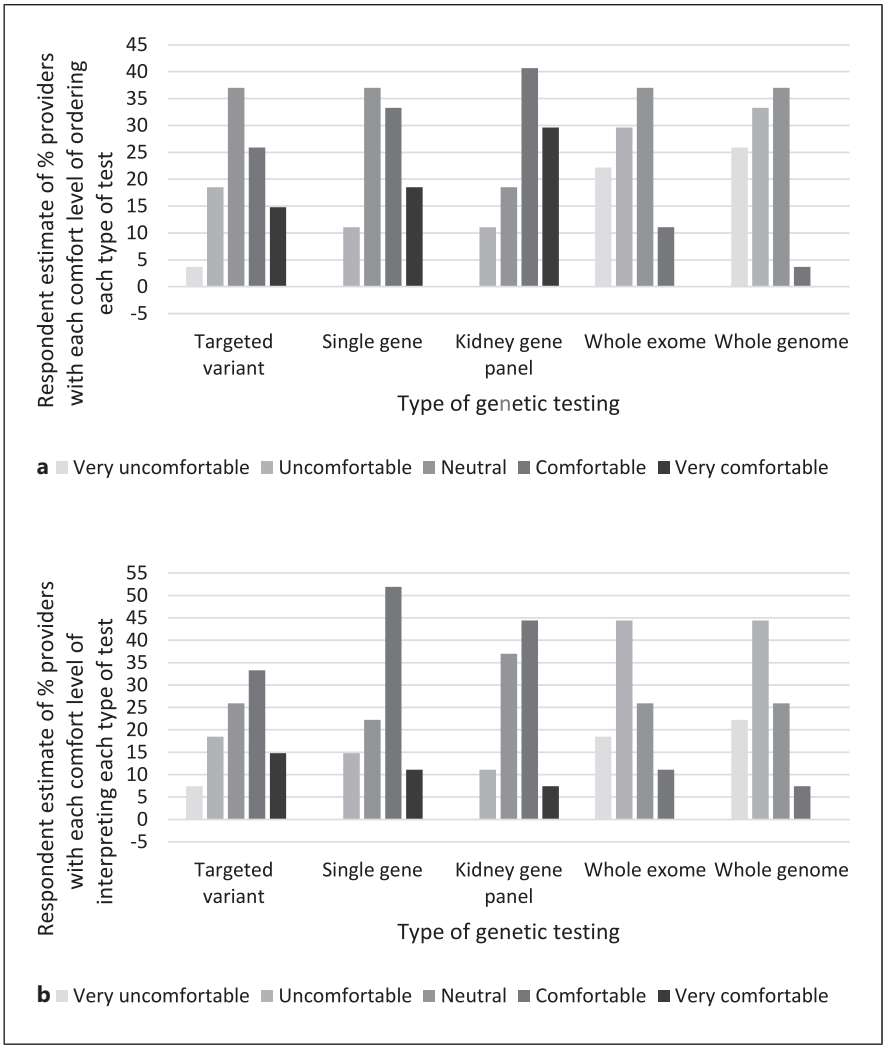

Fig. 4. Respondents were asked the comfort level of providers in their division (n = 27) with ordering (**a**) and interpreting (**b**) different types of genetic testing.

results meet CLIA standards. However, respondents noted that in less than half of divisions, providers were comfortable with ordering and interpreting targeted variant testing. Given the potential implications for cascade family screening as a result of this program, this may be another area of need for divisions in this process.

Beyond the focus on return of results, a number of our survey findings about genetic services and genetic testing in nephrology aligned with previous surveys. Similarly to previous genetic workforce surveys, we observed long wait times for genetic providers [12, 13]. While greater than 80% of institutions surveyed had genetics clinics available, we suspect that this is because NEPTUNE sites are at academic institutions, which aligns with the distribution of genetic providers across the country [12]. While it is encouraging that there were genetic providers at NEPTUNE sites, our survey respondents still noted limited access and availability. The number of providers may not be sufficient and there may be gaps in their available time and support to take on additional research patients who now need to be seen clinically for testing. Genetic providers who would assist with NEPTUNE return of results and with nephrology genetic testing would only be in nephrology genetics clinics or pediatric, adult, or general genetics clinics, whereas genetic providers in prenatal and other subspecialty genetic clinics would not be taking on these patients.

The prior US survey of nephrologists identified the biggest barriers to genetic testing being costs of tests, difficulty accessing testing, and need for logistical support [23]. Our results confirm this finding, demonstrating that 21% of providers were handling insurance logistics and 46% were handling obtaining samples themselves. It was surprising that only one site indicated that the laboratory performing the testing assisted with insurance authorization, especially given that commercial laboratories

often offer this service. Challenges with obtaining insurance coverage was noted by the physicians we surveyed and has been described specifically as something to address in the creation of a nephrology genetics clinic [27]. Clearly, this additional burden in the process of genetic testing needs to be addressed. As the scale of genetic testing increases, the lack of support resources will not be sustainable [19].

Our survey demonstrated that 89% of nephrology divisions at academic centers in the NEPTUNE study were conducting genetic testing. This compares to the prior US survey of nephrologists demonstrating that 72% of adult nephrologists were conducting genetic testing and the prior Australian survey of nephrologists demonstrating 63% were conducting genetic testing [23, 25]. We hypothesize that our number is slightly higher because we focused on academic divisions and not on individual providers. We expect that this number will differ significantly in other countries around the world. For example, in reviews of genetic testing for familial hypercholesterolemia and for movement disorders around the world, there was consistently more access to genetic testing in the US and in European countries, and limited access in African, Asian, and South American countries [30, 31]. Both of these analyses noted that in some countries, only certain hospitals or certain research studies will provide genetic testing, and even then the cost may be prohibitive because there is not consistent coverage [30, 31]. In China specifically, while genetic testing is widely available in urban areas and payment is usually covered, there is limited use of services overall because of shortage of technical personnel to carry out the tests and lack of public awareness and education in rural areas [32]. Given these realities, we recognize that the findings in our survey are not likely representative of the global landscape of genetic testing.

The types of genetic testing being done by nephrologists had not previously been investigated. The most common type of genetic testing was a kidney multi-gene panel (96%). Perhaps surprisingly, nephrologists were more comfortable ordering this panel than targeted variant testing and single-gene testing, which has not been noted in previous surveys. However, providers were more comfortable in interpreting single-gene testing and targeted variant testing, as opposed to ordering the test itself. We hypothesize that this difference in comfort results from lack of experience with these types of tests. It was not surprising that our respondents were less comfortable with WES and WGS, given that these are more complex and newer tests, yielding results beyond nephrology conditions.

In interpreting test results, survey respondents relied heavily on the results report from the laboratory. They also used online databases and took advantage of genetic counselors from both the testing company and their institution. Genetic education and training have been reported as a significant barrier to conducting testing among both nephrologists and other clinicians, but it was reassuring here that nephrologists were for the most part using multiple resources [19, 23–25].

We had the opportunity to compare pediatric and adult nephrologists' practices, finding that pediatric nephrologists appeared to conduct more genetic testing and were more comfortable doing so. This is consistent with both previous surveys of nephrologists discussed above, which found that pediatric nephrologists felt more confident with genetic testing and were ordering more testing [24, 25]. We uniquely highlighted the types of genetic testing in our comparison, finding that only pediatric groups were offering WGS. However, our survey only included six pediatric sites, all of which were at large academic institutions, which may limit the generalizability of these comparisons.

There are other limitations in the generalizability of this survey. Only one individual provider at each institution was asked to make an assessment for their entire division. We also only surveyed academic institutions in North America involved in NEPTUNE, leaving out other academic institutions, community hospitals, private practices, and international sites. These centers may have different experiences, resources, and relationships. There is still need for additional analysis on the scope of use of genetic testing and genetic literacy of physicians in nephrology across practice types.

We uniquely evaluated the ability of institutions to perform return of research genetic results for a multicenter nephrology research study. This is particularly relevant for return of results from multicenter studies with limited resources to organize such programs centrally. Our survey identified areas of need in return of results which we believe are generalizable for other cohorts. These needs will become even more apparent for research studies that choose to include return of secondary findings, which is recommended by the American College of Medical Genetics and Genomics, and will require even more time and resources to interpret results and counsel patients [33]. Given the strong recommendations from multiple national groups about the responsibility of research studies to return genetic results to patients, it is expected that even more return of results programs will be implemented in the near future [1, 8].

We also ascertained how well nephrology divisions were equipped to incorporate genetic testing clinically. We replicated previous findings of limited resources for genetic testing, and we also identified variability in comfort with different types of genetic testing. Overwhelmingly, we identified gaps in support and resources for implementing

genetic testing, which was made particularly clear in the open-ended responses by physicians in this survey regarding both insurance coverage and return of results capabilities.

While this survey was specifically being used to guide the NEPTUNE return of results process, the findings will be of relevance to other multicenter research studies, both within and outside of nephrology. Given that advances in genetics and research will result in increased use of genetic testing and an increase in return of research result programs, it is important to ensure that providers have the needed support and resources to handle all aspects of genetic testing in order to achieve their full benefits in healthcare and promise of precision medicine.

Statement of Ethics

This protocol was reviewed and was granted exemption by the Boston Children's Hospital Institutional Review Board, protocol number IRB-P00041589.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

J.E.F. led the design of the survey, analysis of results, and writing of the manuscript. L.W.D. helped with design of the survey and writing of the manuscript. C.L. organized distribution of the survey. M.K. helped with design of the survey, distribution of the survey, and writing of the manuscript. R.A.G. assisted with design of the survey and writing of the manuscript. J.S.R. assisted with design of the survey, analysis of results, and writing of the manuscript. M.G.S. and W.R.U. supervised the project.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding authors.

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