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Use of genetic risks in pediatric organ transplantation listing decisions: A national survey

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Abstract

There is a limited supply of organs for all those who need them for survival. Thus, careful decisions must be made about who is listed for transplant. Studies show that manifesting genetic disease can impact listing eligibility. What has not yet been studied is the impact genetic risks for future disease have on a patient's chance to be listed. Surveys were emailed to 163 pediatric liver, heart, and kidney transplant programs across the United States to elicit views and experiences of key clinicians regarding each program's use of genetic risks (ie, predispositions, positive predictive testing) in listing decisions. Response rate was 42%. Sixty-four percent of programs have required genetic testing for specific indications prior to listing decisions. Sixteen percent have required it without specific indications, suggesting that genetic testing may be used to screen candidates. Six percent have chosen not to list patients with secondary findings or family histories of genetic conditions. In hypothetical scenarios, programs consider cancer predispositions and adult-onset neurological conditions to be relative contraindications to listing (61%, 17%, and 8% depending on scenario), and some consider them absolute contraindications (5% and 3% depending on scenario). Only 3% of programs have formal policies for these scenarios, but all consult genetic specialists at least "sometimes" for results interpretation. Our study reveals that pediatric transplant programs are using future onset genetic risks in listing decisions. As genetic

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AUTHORS' CONTRIBUTIONS

MG, DC, and DM conceptualized the initial study idea. MG designed and created the initial survey draft and subsequent revisions, performed recruitment, data collection and analysis, and drafted the initial manuscript and subsequent revisions. DC contributed to survey design, critically reviewed and revised manuscript drafts, and approved the final manuscript as submitted. AK reviewed and revised the survey instrument and manuscript and approved the final manuscript as submitted. DM helped design the survey, reviewed and revised the study instrument, critically reviewed the data analysis, examined and revised each manuscript draft, and approved the final manuscript as submitted.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

testing is increasingly adopted into pediatric medicine, further study is needed to prevent possible inappropriate use of genetic information from impacting listing eligibility.

Keywords

bioethics; contraindications; genetic predisposition testing; organ transplantation; pediatric transplantation; predictive genetic testing

1 | INTRODUCTION

Decisions about who is listed for solid-organ transplantation are often contentious.[1] There is a severely limited supply of organs for the many patients who need them for survival.[2] We are now in an era where genetic testing is used both for diagnosis and to predict an individual's chance of developing a specific inherited condition in the future–for example, cancer or a neurological disease.[3] This power of prediction engenders practical dilemmas such as how aggressive prophylactic measures should be,[4] personal dilemmas such as how knowledge of genetic risks impacts quality of life in the asymptomatic stage,[5,6] and ethical issues such as the possibility of genetic risks affecting chances for life insurance.[7,8] An important ethical question that has not yet been addressed in the literature is how knowledge of these genetic risks impacts an individual's chances of obtaining a life-saving organ transplant. This question is important to address within the pediatric transplantation setting given the particular scarcity of organs that induces constant pressure on programs to optimize resources and given that genetic screening is becoming more broadly implemented into the care of children.[9–13]

Existing data suggest that some genetic traits (eg, those associated with neurodevelopmental delay) are being used in inconsistent and sometimes inappropriate ways to make life and death decisions about whether to list patients for transplant.[14–18] As more genetic information is made available to parents of children, there is likely to be an increase in information that may be irrelevant to listing decisions.[19] Given concerns about bias, how will transplant programs make life-saving decisions when confronted with this knowledge? This study seeks to understand how pediatric solid-organ transplant programs use genetic risk information, such as predispositions found through expanded genetic testing or predictive testing results, in their listing decisions.

2 | MATERIALS AND METHODS

2.1 | Subjects

In July of 2017, we identified pediatric liver, heart, and kidney transplantation programs in the United States through the OPTN online member directory. Excluding our institution's programs, we found a total of 202 such programs. For each program, we identified the names of the program directors and key clinicians involved in transplant listing decisions (physicians, advanced care providers, or nurses). We then searched the transplant program websites and used online search engines (Google, Mountain View, CA) to locate e-mail addresses for identified key personnel. We were unable to find a single e-mail contact for

thirty-nine programs. We found at least one e-mail contact for each of the remaining 163 programs. For all programs, we had at least the program director's e-mail. We e-mailed 526 personnel (201 liver, 149 heart, 176 kidney) to participate in the survey. Those who indicated that they were not involved in listing decisions could not complete the survey.

2.2 | Survey instrument

The survey instrument was designed to determine the views, experiences, and policies of transplant programs regarding how genetic risk information is used in the context of listing decisions. The survey framework was derived from previous surveys created by a member of our research team.[17,20] Questions and hypothetical scenarios were developed in consultation with members of our institution's pediatric liver, heart, and kidney transplant teams, as well our institution's pediatric genetics and bioethics departments. Cognitive pretesting of the survey was done on four members of our institution's and one member of an outside institution's pediatric transplant teams. Iterative revisions were made, which included clarifying questions and condensing hypothetical scenarios.

The survey contained 16 multiple-choice questions with space for optional open-ended comments. Three versions of the survey were created, one for each organ system, which differed only by minor wording changes (see Appendices S1–S3). There were three sections to the survey. The first collected program characteristics and information about the individual respondent including their role on the transplant team and expertise in genetics. The second included three hypothetical scenarios (Box), which involved transplant listing decisions for pediatric patients with known risks to develop genetic conditions unrelated to the transplant indication. Two of these scenarios involved candidates with known pathogenic variants for cancer syndromes (HBOC and LFS). The other involved a patient who had a parent with HD and thus a 50% chance of also having the disease. Other than the genetic risks, there were no other contraindications to listing in the scenarios.

As confirmed through piloting and cognitive interviewing, the only significant variable between our three scenarios was the genetic condition the patients were at risk of developing (HBOC, LFS, or HD). The conditions differed by their natural history, the quantitative risk of developing it, average age of onset, and the availability of effective surveillance and/or treatment. For each scenario, programs were asked whether they considered the genetic risk a relative or absolute contraindication to listing, or not a contraindication at all.

The final section of the survey asked questions about program's actual use of genetic risk information in listing decisions, including whether they had ever used secondary findings or family history of genetic conditions as a reason not to list a patient. They were asked if genetic testing was ever required and if their program had policies regarding the use of genetic test results in listing decisions.

2.3 | Data collection and analysis

The survey was distributed through Qualtrics (Provo, UT), beginning in December 2017. An organ-specific survey was sent to each participant through a unique, non-reusable link, depending on the organ system they worked with. Each participant was sent only one version of the survey. After several reminder emails were sent, we made follow-up phone

calls to the programs from which we had not yet received a response to encourage them to participate.

Based on an established methodology, we used programs as the unit of analysis, with the assumption that the individual respondent represented the views of his/her program. While we retained all responses to questions about the individual respondent (ie, role on the team, years practicing in transplantation), we used a different approach for questions relating to program characteristics, views, and experiences. The approach was as follows: When more than one individual from a single program responded, we reviewed responses question by question. We retained a single response when all duplicates were concordant and discarded all responses when at least one response was discordant (see Table S1).

Data were analyzed using SPSS, and descriptive statistics were used to summarize the findings. Optional, open-ended comments were analyzed to identify themes and are used herein to further describe the quantitative findings of this study.

2.4 | Human subjects oversight

The Institutional Review Board of Stanford University approved the study design and final survey design as exempt (Protocol #42240).

3 | RESULTS

3.1 | Response rate

We received a total of 83 individual responses, representing 69 of the 163 programs recruited (42%). Four of the 83 responses were omitted from analysis because respondents were not involved in listing decisions, leaving 79 responses to be analyzed overall. We had duplicate responses from eight programs (six with two responses, and two with three responses). Thus, 69 total programs are represented in analysis. Table 1 summarizes program and individual characteristics of respondents.

Our data captured a range of programs, with broad geographical representation and a tendency toward programs that perform more transplants. There was nearly equal representation from all organ systems. All UNOS regions were represented, with the largest proportion of programs from region 5 (15%) and the smallest from region 4 (3%). Half of the programs that responded performed 11 or more transplants last year. In terms of individual characteristics, our respondents tended to be well-experienced physicians, primarily organ-specific specialty physicians (hepatologist, gastroenterologist, nephrologist, or cardiologist). Sixty-six percent of directors were also specialty physicians or surgeons. Thirty-eight percent of respondents practiced in transplantation for over 20 years.

The survey is not powered to describe differences between organ systems; however, descriptive differences are displayed by organ in Table 2.

3.2 | Current use of genetics in practice

Sixty-four percent of programs responded that they have required genetic testing in the pretransplant evaluation based on specific clinical indications, whereas 16% of programs have required it irrespective of a specific clinical indication.

3.3 | Views on genetic risks and transplant listing

Responses to the hypothetical scenarios varied. Each scenario was structured to involve a patient between ages 18 months and 4 years who required transplant for either liver, heart, or kidney failure. The scenarios asked how different genetic test results would influence a program's decision to list the described patient. As detailed in Box, one scenario involved a patient who had a *BRCA1* pathogenic variant, predisposing to HBOC, an adult-onset condition. Another scenario (Box) involved a patient with a pathogenic variant in *TP53*, predisposing to LFS, a multiorgan cancer syndrome that can onset in childhood, but typically onsets in adulthood. The last scenario (Box) described a patient who was positive for a pathogenic variant that would cause HD, a progressive, fatal neurological condition, starting in their mid-30s to mid-40s. We asked whether the aforementioned genetic test results would be considered relative or absolute contraindications or would not be considered contraindications to listing.

Many programs would consider positive genetic test results to be *relative* contraindications to listing. For example, programs would use predispositions to hereditary cancers as relative contraindications to listing (8% for HBOC and 61% for LFS) and 17% percent of programs would use positive predictive testing for HD as a relative contraindication to transplant listing. Some programs would consider positive genetic test results to be *absolute* contraindications (5% for LFS and 3% for HD), meaning patients with these genetic results would not be listed for transplant.

An additional question was posed in the HD scenario. We asked programs to assume that the transplant candidate had a parent with HD and had not yet been tested themselves (thus had a 50% chance of having the disease allele). About a quarter of programs said they would require genetic testing before they would make a transplant listing decision.

3.4 | Program experience

In addition to asking what programs would *hypothetically* do with predictive genetic test results or secondary findings indicating predisposition to genetic conditions, we asked whether they had ever actually used such genetic risks as a reason not to list patients for transplant. Six percent of programs have used a secondary finding, or a pathogenic variant found through genetic testing that is unrelated to the indication for testing, to exclude patients from listing. One heart transplant program reported that they have used a pathogenic variant for an adult-onset condition pre-sent in the family, but unconfirmed in the patient, to exclude the patient from listing.

We also investigated whether programs had policies regarding the use of genetic test results in listing decisions. Only 3% of programs have formal policies, 76% have no policies at all, and the remaining programs indicated that they have informal policies. Despite a small

number of programs having any sort of policies, all programs reported that they sometimes (14%), usually (31%) or always (55%) use genetic specialists, such as genetic counselors or medical geneticists, to interpret genetic test results.

3.5 | Expertise

Respondents ranked their individual level of expertise in genetics from novice (level 1) to expert (level 5). We first asked about their genetics knowledge related to the organ system they transplant. We found the mean level of expertise in this area to be 3.4, with a standard deviation of 1.0. When we asked about genetics expertise in general, we found the mean level of expertise to be 1.9, with a standard deviation of 1.2.

3.6 | Supporting comments

Twenty comments were left. Most comments pertained to one of two main topics: (a) use of positive genetic test results in hypothetical scenarios and (b) requirement of genetic testing before listing decisions. Analysis of comments in response to hypothetical scenarios revealed two themes. First, several programs (n = 7) expressed that predisposition to cancer syndromes or adult-onset conditions are irrelevant to listing decisions, especially given that many good years will be gained from transplant before the genetic disease would onset. For example, one program said, “Given the likely years gained from transplant in comparison to adult recipients, would err on the side of proceeding with transplantation.” Second, two programs indicated a concern for immunosuppression and cancer risk in the Li-Fraumeni scenario. One program said: “Very difficult case; concerned that immunosuppression will further augment cancers.”

Eleven programs commented on the question about requiring genetic testing before listing. Two themes emerged. First, two programs said they would require genetic testing to diagnose the primary cause of liver disease. The remaining programs said they would require or desire testing if they suspected a lethal disease, a mitochondrial disease, or other multisystem disorder. For example, one program commented, “If mitochondrial hepatopathy is confirmed and child has systemic disease, that knowledge would impact transplant decisions.” Another program said they would require genetic testing “If we are concerned [the patient has] a disease that will be lethal and therefore disqualify from transplant.”

4 | DISCUSSION

Our findings show that clinicians are using genetic risks (such as cancer predispositions and positive predictive testing results for adult-onset neurological conditions) to make transplant listing decisions in the pediatric context. However, the relationship between such genetic risks and adverse transplantation outcomes or with impact on graft survival has not yet been established. This raises two concerns: that use of genetic risk information in this context may be premature, and that consequently, children may be inappropriately denied life-saving transplants.

As an example, surveyed programs indicated that cancer pre-dispositions would matter in the listing decision. We did not ask programs to explain why they would matter; however, one possibility raised in comments is that immunosuppression used in the transplant process

leads to an increased risk for cancer. Although immunosuppression is known to cause increased cancer incidence following transplantation,[21] there are very limited data both on how immunosuppression might impact cancer development for children with genetic predispositions and on whether this impact may be different between childhood and adult-onset predisposition syndromes. Thus, programs could be denying children for transplant based on a possible, not proven, increased risk for cancer.

Programs may also be denying transplant to children because of risks for conditions that will present after the limited lifespan of the transplanted organ. For example, our data revealed that adult-onset neurological conditions (such as HD) may impact a child's chances of being listed for a transplant, though it is undetermined why this is the case. It is known that presence of a neurological condition is an exclusionary criterion to listing for some transplant programs. Richards et al[17] found that 40% of US pediatric transplant programs would use severe or profound neurodevelopmental delay as an absolute contraindication to listing, even though those with neurodevelopmental delay have survival rates equivalent to others receiving transplant.[18,22] The reasons for not listing a child with a currently manifesting neurological condition, let alone a child who has not yet developed an adult-onset neurological condition are unknown, but raise questions about whether quality of life judgments may be at play, or if programs may be concerned that transplantation accelerates neurological disease. These topics lead to subjective viewpoints and are difficult to study.[23,24]

There may be conjectures that immunosuppression increases cancer risk post-transplant in children with genetic predisposition syndromes, that certain neurological conditions are accelerated by transplantation, and that either or both of these genetic risks could lead to worse post-transplant outcomes or worse organ survival. Yet such associations have not yet been demonstrated. Whether they should constitute valid contraindications to transplant, without further evidence, is unclear.

It is well known that genetic testing has increased in utility and ubiquity, particularly in pediatric medicine,[9–13] yet those making use of genetic results in this context are not genetics experts. Non-genetics healthcare providers are increasingly confronted with genetic information that they find difficult to interpret, and there is little formal training in medical school curriculum specific to genetics.[25–28] While it is encouraging that respondents in our survey self-report an intermediate to expert level of genetics expertise in their organ system, they reported a much lower level of expertise in genetics overall. This is problematic because many familial conditions and most secondary findings, which are identified up to 6% of the time through broad genomic testing,[29,30] are unrelated to the organ system that the patient is being treated for. Furthermore, genetic testing, especially broad genomic testing, has the potential to detect genetic variants with unclear clinical relevance (eg, variants of uncertain significance, or variants in genes with uncertain disease association and disease trajectories).[31] While all of our survey questions involved well-characterized diseases with established pathogenicity of variants, what programs may do with more ambiguous results is unknown. Reassuringly, most programs always use genetic specialists to interpret genetic test results; however, the shortage of genetic specialists to meet demand means that programs may not always have the resources to consult with genetics specialists in

complicated listing decisions.[32,33] Overall, programs may not be equipped to interpret the clinical significance and relevance of many genetic test results they will encounter.

Our findings suggest that genetic testing may be used to screen transplant listing candidates. Implementation of genetic screening into transplant evaluation is in a gray and vulnerable time. Outcome-association studies would be helpful to determine how specific genetic risks impact transplant success and longevity; however, there is a limited population of pediatric transplant recipients available for such study and these studies would require increasing the number of children who undergo genetic testing as part of their transplant evaluation. Now, when we lack clear associations but are encountering more transplant candidates with genetic screening results, there must be caution in how such results are used to determine access to life-saving transplants. This involves using what we do know about genetic diseases in general (irrespective of the transplant context), and seeking expert opinion from genetics clinicians. Using genetic risks in the transplant context without great care may lead to claims of discrimination against groups with certain genetic results and may play into existing concerns among minority communities (such as the deaf community) about the eugenic implications of genetic testing.[34,35] Such a backlash could undermine the implementation of genetic testing, such as broad genomic testing, and prevent the full realization of such a powerful biomedical tool in this context.

We propose that moving forward, we need a way to measure how genetic risks are being factored into listing decisions to understand the magnitude of the issue and the reasons programs are choosing not to list patients for some of these genetic risks. It is well known that the transplant listing process is inherently biased by virtue of it being a subjective, program specific process, with no standardization across all programs.[14,17] As broad genetic testing (like large, multigene panels or whole-exome sequencing) becomes more routine, more patients will present to transplant with genetic results or will have genetic testing included in their transplant evaluations. Most programs do not currently have policies to deal with these scenarios, and it is important that they consider introducing them.

We also raise the possible emergence of a novel genetic specialist role within the transplant evaluation context. When faced with a genetic test result, we suggest a collaborative role between genetic specialists and transplant physicians to determine the most probable risks to the patient and the best strategy for transplantation. Furthermore, we encourage clinicians to consider discussing the possible implications genetic test results may have for a transplant candidate as a part of the genetic testing informed consent process. This discussion will need to evolve as we are able to better define the possible implications.

Our study was limited in that it was a non-random sample. It can not be said to be representative of all pediatric transplant programs, as the sample size is insufficient and because we used individual respondents to represent whole program views and experiences. In addition, as self-reported data, this study likely under-reports the degree to which genetic risks are being used in making listing decisions. However, our study is primarily descriptive in nature and is sufficient to show that the identified genetic risks are sometimes being used in listing decisions.

In conclusion, we reveal that pediatric transplant programs are using genetic testing in their listing evaluation, and that genetic risks sometimes impact a patient's chance to receive a life-saving transplant. Using genetic testing and results in this way may be inappropriate due to a lack of outcomes data and consideration of factors that may prove irrelevant to transplant success. Clinicians handling genetic information in this context generally have an intermediate degree of genetics expertise and many are using genetic specialists for results interpretation, but there are still areas of insufficiency. More research is needed to understand the risks genetic predispositions pose in transplant and the reasons patients would be excluded based on such risks. This is especially relevant given the growing use of genetic testing in pediatric medicine, both as a screening and diagnostic tool. Lastly, programs should consider developing formalized policies that incorporate genetic specialists, surrounding how genetic testing and its results should be used in their transplant listing decisions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

HBOC	Hereditary Breast and Ovarian Cancer syndrome
HD	Huntington's disease
LFS	Li-Fraumeni syndrome
OPTN	Organ Procurement and Transplantation Network
SPSS	Statistical Package for the Social Sciences
UNOS	United Network of Organ Sharing

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Box 1

Hypothetical scenarios

BRCA1 pathogenic variant

A 3-year-old female patient presents to your service requiring transplantation for [liver/heart/kidney] failure. She has previously received whole-exome sequencing (WES), which analyzes the protein coding regions of an individual's DNA, where most disease-causing pathogenic variants are found. WES failed to identify a pathogenic variant to explain the patient's [liver/heart/kidney] condition. The testing did, however, reveal a secondary finding, or a clinically relevant pathogenic variant unrelated to the indication for testing. This secondary finding was in *BRCA1.*

Background

Pathogenic variants in the *BRCA1* gene cause HBOC, which is characterized by a ~50%–65% risk of developing breast cancer and ~35%–45% risk of developing ovarian cancer. The average age of cancer diagnosis is in the 40s–50s. Following the National Comprehensive Cancer Network recommendations significantly reduces the risk of developing ovarian cancer by ~90% (through prophylaxis) and results in >95% survival from breast cancer (through early detection). As expected, the patient is currently asymptomatic for HBOC syndrome.

Box 2

Hypothetical scenarios

TP53 pathogenic variant

An 18-month-old female patient presents to your service requiring transplantation for [liver/heart/kidney] failure. She has previously received whole-exome sequencing (WES), which analyzes the protein coding regions of an individual's DNA, where most disease-causing pathogenic variants are found. WES failed to identify a pathogenic variant to explain the etiology of the patient's [liver/heart/kidney] condition. The testing did, however, reveal a secondary finding, or a clinically relevant pathogenic variant that is unrelated to the indication for testing. This secondary finding was in *TP53*.

Background

Pathogenic variants in the *TP53* gene cause LFS. LFS is a hereditary cancer predisposition syndrome characterized primarily by soft tissue and osteosarcomas, female breast cancer, brain tumors, adrenocortical carcinomas, and leukemia, though other cancer types are seen. The average age of onset of an LFS malignancy is ~25 years old. Cancers can occur in childhood, with a 22% chance of developing a malignancy by age 5. There is an 80%–100% lifetime risk of cancer. While the National Comprehensive Cancer Network has effective screening measures that nearly prevents development of a fatal breast cancer, screening for the other LFS cancer types has questionable efficacy in detecting cancers early and therefore preventing mortality. The patient currently has no signs or symptoms of LFS.

Box 3

Hypothetical scenarios

Huntington's disease

A 4-year-old patient presents to your service requiring transplantation for [liver/heart/kidney] failure. You learn that the patient's father has HD, but the genetic status of your patient is unknown.

Background

HD is a progressive disorder characterized by lack of controlled movement, cognitive decline, and psychiatric disturbances. The average age of onset is 35–44 years and individuals usually die 15–18 years after onset. If a parent has HD, there is a 50% that their child will also have the disease. While symptom targeted treatment is available, there is no cure for HD and quality of life is very poor. Progression of the disease and mortality from the disease are inevitable.

TABLE 1

Program and individual characteristics

Program characteristics	**n (%)**
Programs recruited	163 (100%)
Organ	
Liver	43 (26%)
Heart	45 (28%)
Kidney	75 (46%)
UNOS region	
1 CT, ME, MA, NH, RI, VT	8 (5%)
2 DE, DC, MD, NJ, PA, WV	17 (10%)
3 AL, AR, FL, GA, LA, MS, PR	18 (11%)
4 OK, TX	12 (7%)
5 AZ, CA, NV, NM, UT	20 (12%)
6 AK, HI, ID, MT, OR, WA	4 (2%)
7 IL, MN, ND, SD, WI	14 (9%)
8 CO, IA, KS, MO, NE, WY	18 (11%)
9 NY, VT	16 (10%)
10 IN, MI, OH	16 (10%)
11 KY, NC, SC, TN, VA	20 (12%)
Programs responded and analyzed	69 (42%)
Organ	
Liver	23 (32%)
Heart	22 (31%)
Kidney	27 (37%)
UNOS region	
1 CT, ME, MA, NH, RI, VT	5 (8%)
2 DE, DC, MD, NJ, PA, WV	5 (8%)
3 AL, AR, FL, GA, LA, MS, PR	6 (10%)
4 OK, TX	2 (3%)
5 AZ, CA, NV, NM, UT	9 (15%)
6 AK, HI, ID, MT, OR, WA	3 (5%)
7 IL, MN, ND, SD, WI	6 (10%)
8 CO, IA, KS, MO, NE, WY	6 (10%)
9 NY, VT	4 (7%)
10 IN, MI, OH	7 (11%)
11 KY, NC, SC, TN, VA	8 (13%)
Number of transplants performed in 2017	
<4	6 (10%)
4–5	7 (11%)
6–10	18 (29%)
≥11	31 (50%)

Program characteristics	**n (%)**
Individual respondent characteristics	**n (%)**
Total number of respondents	83 (100%)
Total responses analyzed	79 (95%)
Role on transplant team (more than 1 per individual may apply)	
Director	32 (39%)
Surgeon	18 (22%)
Hepatologist, gastroenterologist, nephrologist, or cardiologist	43 (52%)
Advanced practice provider	2 (2%)
Nurse	2 (2%)
Years practicing in transplantation	
1–5	15 (20%)
6–10	13 (18%)
11–20	18 (24%)
>20	28 (38%)

TABLE 2

Survey questions and responses–genetics in transplant listing decisions

Question	Liver	Heart	Kidney	Total
Current use	n (%)			
Does your program ever require genetic testing for a specific clinical indication before listing?				
Yes	13 (72%)	15 (79%)	11 (46%)	39 (64%)
No	5 (28%)	4 (21%)	13 (54%)	22 (36%)
Does your program ever require genetic testing without a specific clinical indication before listing?				
Yes	4 (20%)	4 (21%)	2 (8%)	10 (16%)
No	16 (80%)	15 (79%)	22 (92%)	53 (84%)
Views				
How would you consider a *BRCA1* pathogenic variant in listing decision?				
Relative contraindication	1 (5%)	3 (15%)	1 (4%)	5 (8%)
Absolute contraindication	0	0	0	0
Not a contraindication	19 (95%)	17 (85%)	24 (96%)	60 (92%)
How would you consider a *TP53* pathogenic variant in listing decision?				
Relative contraindication	10 (56%)	11 (55%)	17 (71%)	38 (61%)
Absolute contraindication	0	3 (15%)	0	3 (5%)
Not a contraindication	8 (44%)	6 (30%)	7 (29%)	21 (34%)
How would you consider an HD pathogenic variant in listing decision?				
Relative contraindication	4 (20%)	4 (20%)	3 (13%)	11 (17%)
Absolute contraindication	0	2 (10%)	0	2 (3%)
Not a contraindication	16 (80%)	14 (70%)	21 (87%)	51 (80%)
Would you require genetic testing for child with parent with HD before listing decision?				
Yes	4 (21%)	7 (35%)	3 (13%)	14 (22%)
No	15 (79%)	13 (65%)	21 (87%)	49 (78%)
Experience				
Has your program ever used a secondary finding as a reason not to list?				
Yes	1 (5%)	3 (15%)	0	4 (6%)
No	19 (95%)	17 (85%)	24 (100%)	60 (94%)
Has your program ever used family history of an adult-onset, heritable condition as a reason not to list?				
Yes	0	1 (5%)	0	1 (2%)

Question	Liver	Heart	Kidney	Total
No	20 (100%)	19 (95%)	24 (100%)	63 (98%)
Program protocol				
Does your program use a genetic specialist to interpret genetic test results?				
Always	10 (56%)	18 (90%)	6 (25%)	34 (55%)
Usually	7 (39%)	1 (5%)	11 (46%)	19 (31%)
Sometimes	1 (6%)	1 (%%)	7 (29%)	9 (14%)
Never		0	0	0
What policies does your program have for genetics in listing decisions?				
Formal ones	0	2 (10%)	0	2 (3%)
Informal ones	4 (22%)	6 (30%)	3 (13%)	13 (21%)
None	14 (28%)	12 (60%)	21 (87%)	47 (76%)
Expertise	Mean ± standard deviation			
Level of expertise in genetics related to organ[a]	3.6 ± 0.9	3.2 ± 1.1	3.3 ± 1.0	3.4 ± 1.0
Level of expertise in genetics overall[a]	2.2 ± 1.3	1.8 ± 1.0	1.7 ± 1.0	1.9 ± 1.2

[a] Level of expertise reported on a scale of 1–5; 1 = novice, 5 = expert.