THE USE AND IMPACT OF RISK INDICES IN PEDIATRIC HEART TRANSPLANT DECISION MAKING

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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ORGAN TRANSPLANTS – PAST, PRESENT, AND FUTURE

Breakthroughs in the Organ Transplantation Field

In 1954, surgeon Joseph Murray transplanted a kidney between a set of identical twins in Boston, Massachusetts (UNOS, 2023a). This kidney was the first human organ to ever be successfully transplanted, marking the beginning of the organ donation and transplantation system in the United States. Following the kidney, the first liver, heart, and pancreas were successfully transplanted in the 1960s (UNOS, 2022). Despite these medical breakthroughs, however, the organ donation and transplantation system was far from efficient. Up until the 1970s, individual hospitals and organ procurement organizations managed everything independently. Many organs were discarded if they couldn't be used at local hospitals since no matching system existed to locate potential recipients elsewhere (UNOS, 2022).

In 1977, the first computer-based organ matching system, the United Network for Organ Sharing (UNOS), was created (UNOS, 2022). This matching and data collection system helped the organ donation and transplantation system in the United States grow to what it is today. In 2021, the United States surpassed 40,000 transplants in one year, and in 2022, the US became the first country to achieve 1 million total transplants (UNOS, 2022). Transplants of kidneys, livers, hearts, pancreata, intestines, lungs, and heart-lungs are now considered routine medical treatment (HRSA, n.d.). In the pediatric heart transplant field, over 400 children are now treated annually (Colvin et al., 2022).

Current Issues in the Pediatric Heart Transplant Field

While the number of pediatric heart transplants performed in the United States has steadily grown over the past few decades, the demand for organs heavily outweighs the supply.

In 2020, only 456 pediatric heart transplants were performed whereas 673 new pediatric candidates were added to the heart transplant waitlist (Colvin et al., 2022). Despite heavy demand, however, the graft utilization rate in the United States for pediatric hearts is rather low - with over 40% of eligible cardiac allografts ultimately being discarded or offered to other international transplant programs (Khan et al., 2016, "Results" section). Compounding the problem, children awaiting a heart face one of the highest waitlist mortality rates, 8%, in the recent era. (Zafar et al., 2015, "Results" section).

These alarming rates bring attention to the decision making practices of the cardiologists who decide whether to accept or refuse a donor offer for a specific recipient candidate. Currently, the process for evaluating a donor heart is mainly based on personal practice and institutional experience with significant inter- and intra-center practice variability (Baez Hernandez et al., 2020, "Discussion" section). Subjectivity plays a concerningly large role in these critical decisions. Moreover, new evidence suggests that transplant survival outcomes are significantly similar for donors perceived as "high risk" compared to "low risk" when assessing the same recipient, suggesting the current decision making practices are suboptimal (Riggs et al., 2020, Figure 3). Part of this, however, can be attributed to the intense time constraints cardiologists face. When a pediatric heart becomes available, cardiologists have limited time to decide whether or not they want to accept or refuse the donor offer for a specific patient – an hour if it is for the initial potential transplant recipient and 30 minutes for all other potential transplant recipients (HRSA, 2023, pg. 90). Research and studies have shown that a more comprehensive, standard, and data-driven approach to assessing the suitability of a potential donor may be beneficial for decreasing the organ discard rate and waitlist times without affecting post-transplant outcomes (Baez Hernandez et al., 2020).

One approach to both standardizing and expediting the assessment of a potential donor is to employ a risk index that utilizes significant donor and transplant variables to quantify the risk associated with a donor graft. This STS research will explore the use of risk indices in organ transplants to determine if one could be beneficial and suitable in the pediatric heart transplant field. It will also compare the differing perspectives of risk to assess which is most appropriate in the context of decision making in a health care setting. Furthermore, the research will analyze the current use of risk indices in other organ transplantations through a review of previous literature to predict how one might impact pediatric heart transplant decision making. Finally, Actor Network Theory (ANT) framework will provide insight into how this technology might impact other actor groups as well as the likelihood of its adoption.

CONFLICTING PERSPECTIVES OF RISK AND RISK ASSESSMENT

The Technico-Socio Perception of Risk

When deciding whether to accept or refuse a donor offer, cardiologists must assess the risk associated with that specific heart and transplant. However, the term risk tends to change meaning depending on the context. As Deborah Lupton states in her book titled *Risk*, in the context of science and medicine, risk is often viewed as "an objective reality that can be measured, controlled and managed," where scientists and doctors are typically "using mathematical models to measure and predict risk" (Lupton, 2013, p. 20). This perception of risk, which Lupton dubs "the technico-scientific perspective," praises objectivity and focuses on how well risk has been calculated, how accurate the 'science' behind these calculations is, and the level of seriousness in terms of possible effects (Lupton, 2013, Chapter 2).

In her article "The Policy Implication of Differing Concepts of Risk," Judith Bradbury raises concerns about how measurements of risk are often treated as objective facts despite the fact that most probability risk assessment practitioners acknowledge that estimates "incorporate the analysts judgment at many critical points" and, therefore, "cannot be viewed as value-free" (Bradbury, 1989, p. 382). In addition to this subjectiveness, expert knowledge is subject to change as new observations and evidence appears, reinforcing the idea that risk estimation and evaluation should not necessarily be treated as separate steps. One might question how much weight should be put on a risk index in decision making should one ever be established and accepted.

The Sociocultural Perspective of Risk

Critics of the technico-socio perspective, like Bradbury, lean more towards the sociocultural perspective which views risk not as a physical entity that exists apart from the humans who assess it, but instead as a social process. Therefore, risk cannot be viewed in isolation from these social and cultural processes, and it cannot be considered "value-free" since "the scientist's judgment involves the balancing of conflicting evidence" (Bradburry, 1989, p. 381). In other words, subjectivity is inevitable in risk assessment. This perspective does not deny the importance of data-driven scores in risk assessment, but believes these alone are not sufficient. The "objective" measurements of risk need to be integrated with, not separated from, the somewhat subjective processes of risk evaluation.

Bradburry argues that risk is multidimensional and too complex to be captured in a mathematical calculation alone. Instead of concentrating too much on quantified methods of risk assessment, it is better to "provide a firm theoretical foundation for an appropriate formulation of the policy problem of risk and a framework for solution" (Bradburry, 1989, p. 394). The focus of

improving risk assessment and management should be less on improving the models that predict and measure risk and more on supporting critical dialogue between differing perspectives and opinions.

MEASURING AND ASSESSING RISK IN ORGAN TRANSPLANTATIONS

The Use of Risk Indices in Organ Transplantations

Mathematical calculations to predict and measure risk do exist for organ transplantations. Risk indices are used to assist doctors in quickly assessing data while making more confident, standardized, and data-driven decisions. Risk indices also help practitioners "longevity match," allowing recipient candidates with longer estimated post-transplant survival times to be priortized when a low risk organ becomes available (HRSA, 2020). Organ-specific risk indices are calculated by utilizing relevant donor and transplant variables to predict the risk of graft failure and to quantify graft quality. While there are currently no widely accepted risk indices for hearts, there are indices in kidney, liver, and pancreas transplantations (Akkina et al., 2012). It is important to note that these indices are calculated for all transplants, not necessarily pediatric transplants.

One such index, the Kidney Donor Risk Index (KDRI), includes ten donor and four transplant characteristics, each found to be significantly and independently associated with graft failure or recipient death (Rao et al., 2009). According to the Organ Procurement & Transplantation Network (OPTN), the Kidney Donor Profile Index (KDPI), a remapping of the KDRI onto a cumulative percentage scale, has been provided with all kidney donor offers since 2012. The predictive power of the KDPI can be represented by the c-statistic of 0.6 – the probability that a randomly selected kidney that results in negative post-transplant outcome had a

higher risk score than a kidney that did not result in a negative post-transplant outcome (HRSA, 2020).

Another index, the Liver Donor Risk Index (LDRI), includes seven donor and two transplant factors, and aims to quantify the risk associated with a specific liver donor. (Feng et al., 2006). The Pancreas Donor Risk Index (PDRI) includes 10 donor factors as well as ischemic time and predicts one-year pancreas graft survival (Axelrod et al., 2010). Studies have shown that high PDRI values are associated with higher graft-failure likelihood and that the PDRI has surpassed other pancreas risk scoring systems like the pre-procurement pancreas suitability score (Blok et al., 2016). The creations of the KDRI, LDRI, and PDRI helped establish which variables likely influence overall transplant survival.

The Observed and Speculated Effects of Using Organ Donor Risk Indices

Before the KDPI, kidneys were classified as either extended criteria (ECD) – meeting certain criteria that makes graft failure likely – or standard criteria (SCD). In comparison, the KDPI allows for more precise measurements since it accounts for ten factors. KDPI scores range from 0 to 100 with a higher score suggesting higher levels of risk (Lee & Abramowicz, 2015). On one hand, this more precise tool is speculated to increase the utilization of marginal yet viable kidneys that would be discarded under the ECD/SCD dichotomy (Bae et al., 2016). This was exemplified through an ambidirectional study by the Antwerp University Hospital. The study found that the utilization rate increased by over five percent when the KDPI was introduced, even though the average KDPI score was lower in the control group where the KDPI was not used. (Philipse et al., 2017). On the other hand, concerns have been raised about the high granularity and precision of the KDPI limiting flexibility in interpretation and leading to a harmful “labeling effect” for high-KDPI organs. Gandolfini and colleagues speculated that

transplant programs may set a threshold for acceptable kidneys, leading to the automatic refusal of viable high-KDPI kidney offers (Gandolfini et al., 2014). The results of a retrospective study assessing transplants in the United States before and after the introduction of the KDPI support this speculation. This study found that in the group of high-KDPI kidneys that would have been previously labeled SCD, there was actually a significant decrease in graft utilization. However, there was no significant change in the overall discard rate of all kidneys. (Bae et al., 2016).

One potential explanation for this minimal impact on organ utilization is the low rate of index adoption. A survey sent to liver transplant physicians in 2014 found that 62% of respondents were familiar with the LDRI, but the vast majority believed the index does not adequately represent the organs' risk of graft failure. Many respondents argued that the LDRI includes donor factors that are irrelevant while excluding relevant factors. Other respondents expressed that the LDRI "cannot replace the judgment and technical skill of the transplant team" (Mataya et al., 2014). These survey results suggest that indices like the LDRI and KDRI are not widely being used due to a perception that they are misleading and inferior to the practitioners' own assessments.

Risk Indices in Pediatric Heart Transplants

While currently there are no widely accepted and used risk indices in the realm of pediatric heart transplantation, several groups have attempted to create indices with varying levels of predictive success. Zafar et al. created a donor specific risk index called the Pediatric Heart Donor Assessment Tool (PH-DAT) which utilizes five transplant and donor variables to predict 1-year mortality after transplantion. This cumulative risk scoring system has an acceptable predictive value with a c-statistic of 0.62. The creators of this scoring system believe that the PH-DAT "will likely lead to better utilization of currently available donor hearts" and

that “age-specific PH-DATs may result in a national standardized donor selection guide similar to that in kidney transplantation” (Zafar et al., 2018, “Limitations” section). While not specific to pediatrics, Weiss et al. also developed a donor risk index to predict short-term mortality in heart transplantations. Using univariate and multivariate analysis, they identified four donor variables to be used to calculate a 15-point donor risk score that would approximate the risk of short-term mortality. Cross-validation was employed to test the predictive power of this scoring system. For the validation cohort, which consisted of over 4,000 patients, each increase of one point increased the risk of one-year mortality by 13% (Weiss et al., 2012).

This data-driven standardization in decision making practices aims to increase graft utilization and improve transplant outcomes. Ironically, however, the variability in decision making practices may be inhibiting index adoption. A survey on current donor acceptance practices was sent to an international group of pediatric cardiac transplantation professionals in 2018. The results of this survey highlight the significant variability in decision making and donor acceptance practices among pediatric heart transplant professionals. The researchers behind this survey speculate that the variation likely stems from “a lack of robust scientific evidence” as well as “the evolution of practice based on clinical experience” (Godown et al., 2019). Currently, there are no standard guidelines for evaluating a donor heart, and this is likely resulting in “considerable inconsistencies in the types of donor hearts that are accepted by different transplant centers” as well as the “non-recovery of potentially useful organs” (Khush et al., 2015). Indices like the LDRI and the KDRI are not fully utilized because practitioners doubt the indices’ accuracy and believe their own judgment is superior. With such variability in donor acceptance practices among pediatric heart transplant professionals, it might be difficult to garner wide acceptance and confidence in a singular calculation.

ASSESSING THE SUITABILITY OF RISK SCORING METRICS IN THE FIELD OF PEDIATRIC HEART TRANSPLANTS USING ACTOR NETWORK THEORY

Using Actor Network Theory (ANT) in a Health Care Setting

It is important to understand the impacts a risk index might have on different groups of people as the perceptions of these groups will have substantial influence on whether the use of a donor-specific index has a place in clinical pediatric heart transplantation. Actor-Network Theory (ANT) framework can provide insight into these impacts. Actor Network Theory, developed by science and technology scholars Bruno Latour, Michael Callon and John Law, views systems as being made up of actors which can be "any entity—human or nonhuman—that in some way influences or perturbs the activity of a techno-social system (Crawford, 2020, "Summary" section). Nonhuman actors can include objects and concepts, and all actors have the ability to exert power over or change in other actors. This agency stems from the way actors are connected and related to each other in the network (Crawford, 2020). According to Kathrin Creswell in her article "Using Actor-Network Theory to Study Health Information Technology Interventions", ANT framework is commonly used to conceptualize the introduction of new technologies in health care settings in order "to examine specific aspects of technology implementation, to explore the effects of technological systems on human actors, and to explain why information systems may be rejected by users" (Creswell, 2019, p. 90).

In the transplant actor-network, the new actor being introduced is the technology of a risk index to quantify the risk associated with a specific pediatric heart transplant donor. Other main actor groups in this network include the recipient candidates and their families, the donors and their families, the cardiologists responsible for evaluating the donor hearts, and the organ

procurement organizations (OPO) who manage the deceased donor before acceptance. This technology may impact each of these groups in different ways, and therefore, each group will have a unique perception of it. Furthermore, within each of these main groups, subgroups may be impacted differently. For example, different racial groups or socioeconomic subgroups within the recipient actor group may have different experiences with the introduction of this new non-human actor.

Actor Group 1: The Recipient Candidates & Families

There are several ways in which the recipient candidates and their families could be affected by the introduction of a donor risk scoring index. As discussed earlier, it is uncertain whether risk indices increase or decrease graft utilization. If the introduction of a risk index were to increase the graft utilization rate without worsening transplant outcomes, then waitlist times, and consequently overall program mortality, would decrease. Recipients and their families would perceive this positively. However, if the introduction of a risk index prompted a harmful labeling effect that decreased the utilization of viable kidneys, then this new actor would be perceived negatively by the recipients and their families.

There is the possibility that the introduction of a risk index could decrease the overall graft utilization rate due to non-viable hearts being better detected. This would improve transplant outcomes; however, this would not improve, and could even exacerbate, the waitlist mortality issues. This scenario could be perceived either way - positively by recipients who are in relatively good health and won't face complications waiting longer for a viable heart, or negatively by those recipients who are in critical condition and can't afford the longer wait.

Actor Group 2: The Organ Donors & Families

Like the recipient candidates, how the introduction of a risk index affects the donor actor group highly depends on how the graft utilization rate would change. For many of the donor families, donation is the one silver lining to the tragedy of losing their loved ones. In her article, Raelynn Maloney helps tell the stories of how two families found comfort in organ donation. One donor father describes how "organ donation does not take away the pain, but knowing that you have helped others start new lives makes it a little more bearable" (Maloney, 1998, p. 342). Therefore, a decrease in the utilization rate could be emotionally taxing for recipient candidates and their families who will lose opportunities to see their donated organs help others.

Because this index would be calculated using donor and transplant variables, there are additional factors affecting the donor actor group compared to the recipient group. For example, both the KRDI and the LDRI include ethnicity as a factor (Feng et al., 2006; Rao et al., 2009). Specifically, African American ethnicity is seen as riskier in comparison to other ethnicities. If ethnicity were to be included in a risk index for pediatric heart transplants, this could be viewed unfavorably by African Americans who are likely to lose opportunites to donate. This is just one example of how specific donor sub-groups could be affected by the variables used to calculate the index.

Actor Group 3: The Cardiologists

As the actor group who is leveraging the risk index to evaluate a donor heart, how the cardiologists perceive this new technology will be essential in determining whether it will be adopted and integrated into the system. As mentioned before, the current decision making process varies both within and between transplant programs. Different cardiologists review different variables when assessing a heart, and there is a lack of consensus on which variables are actually significant. This variability means that for many cardiologists, any risk index is

likely to include factors they don't consider and exclude factors they do. Furthermore, the risk indices that currently exist for pediatric heart transplants have only moderate predictability power.

Considering both of these points, right now it is unlikely that cardiologists would heavily leverage a risk index in their donor evaluation. Like the LDRI, it will likely be used secondary – if at all – to the cardiologist's own assessment. Until a consensus grows on what variables are significant or the predictive power of existing risk indices increases, cardiologists are likely to continue to trust their own expertise over a calculated score. There is, however, the possibility that cardiologists may be open to a trial period of using a risk index in an attempt to standardize and streamline the decision making process.

Actor Group 4: The Organ Procurement Organizations (OPOs)

The responsibilities of Organ Procurement Organizations are "to assess donor potential, collect and convey accurate clinical information, and follow national policies for offering organs" (UNOS, 2023b). Therefore, it is the job of the OPO to accurately and continuously collect data on the donors they manage. This data is what is provided when offers are sent out to appropriate transplant hospitals. This also means the information used to calculate the risk index will need to be accurately collected and provided by the OPOs.

Since the OPOs have the responsibility of continuously collecting donor information, introducing a risk index could require more work on their part. In order for the index to be useful, all of the information needed to calculate it will need to be kept correct and up to date. As stated earlier, the KDPI is currently provided with all donor offers - meaning OPOs already routinely collect much of the information required by this risk scoring index. Therefore, it is unlikely that there will be much resistance from OPOs if they have to begin regularly collecting

similar data for a pediatric heart risk index. However, there is always the possibility that the OPOs will resist taking on any extra responsibility, no matter how small.

THE FUTURE OF RISK INDICES IN PEDIATRIC HEART TRANSPLANTS

As demonstrated by the efforts to create risk indices for almost all organ transplantations, there is value in quantifying the risk associated with a donor offer. Risk indices allow for more data-driven and standardized decision making as opposed to the subjective and variable practices that currently exist in the pediatric heart transplant space. Furthermore, risk indices have the potential to accelerate donor evaluation, a process which happens under intense time constraints. However, should a risk index be integrated into the heart transplant evaluation process, it should be employed as only one of many considerations. As explained through the sociocultural perspective of risk, risk calculations cannot be seen as value-free due to the subjective judgements of the experts who create them. A risk index should not be used as the sole determinant of whether an organ is refused or accepted, but instead as an additional tool for cardiologists to leverage.

A risk index will not be widely used, however, unless accepted by the actor groups in the network. As explored through Actor Network Theory, the groups with the heaviest influence on the adoption of a risk index include the recipient candidates and their families, the donors and their families, the cardiologists, and the OPOs. The donor and recipient candidates' perceptions of this new technology will be highly influenced by how successful a risk index is in increasing the graft utilization rate – specifically for marginal yet viable organs. However, currently there’s a lack of substantial evidence on how already established risk indices in other organ transplant fields have affected graft utilization rate as well as transplant outcomes. Therefore, it is hard to predict how these two actor groups will perceive the introduction of this new technology. As for

the OPOs, there is the possibility of resistance due to an increased responsibility for accurate and continuous data collection. However, the OPOs already have to provide similar information to calculate indices like the KDPI, so an additional risk index will likely not be seen as overburdening.

In the current state of pediatric transplant decision making, the most resistance is likely to come from the cardiologists responsible for evaluating the donors. Due to the high variability in decision making practices, it will be difficult to create an index that a majority of cardiologists accept. The index would exclude and include many variables that some practitioners do and don't consider. The LDRI, which has been established for many years, has had low utilization due to the perception that it is misleading and inferior to the practitioners' own assessments. Therefore, a risk index in pediatric heart transplants is unlikely to be used until greater consensus is reached on what variables are significant and until the predictive power of the indices strengthen.

As mentioned earlier, Bradburry – one of the supporters of the sociocultural approach to risk – argued that improving risk assessment should be more focused on supporting dialogue between differing perspectives and opinions as opposed to improving the predictive models that quantify risk (Bradburry, 1989). This calls into question the suitability of a risk index in pediatric heart transplants where, at this point in time, a strong predictive model doesn't exist. It might be, for the time being, that the most effective path forward is to improve the channels and means for practitioners to communicate, discuss, and share opinions in order to improve decision making practices, decrease variability, increase the number of successful transplants, and decrease overall program mortality. However, should the donor variables that are important to a

successful transplant become clearer and better agreed upon in the future, a risk index could be crucial to streamlining and standardizing the donor evaluation process.

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