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The 3-T Model of Informed Consent for Nonstandard Risk Donors: A Proposal for Transplant Clinical Practice

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Background. The risk of disease transmission from nonstandard risk donors (NSRDs) is low, and outcomes are similar or better relative to transplants performed with standard criteria donors. However, NSRDs have posed new ethical challenges to the informed consent (IC) process. Based on the shared decision-making model, coinciding with the 3 main timings of the IC process ([1] pretransplant assessments and waiting list registration, [2] time on the waiting list, and [3] time of the organ offer), we put forward a model (3-T Model) to summarize the knowledge on IC for NSRDs and to deliver conceptual and practical support to transplant providers on this emergent issue. **Methods.** We searched *PubMed* and analyzed data from our area to provide evidence and ethical arguments to promote standardization of the timing of patient information, degree of patient participation, and disclosure of donor risk factors throughout the 3 stages of the time continuum leading to the potential acceptance of NSRDs. **Results.** Each of the 3 timings carries special ethical significance and entails well-defined duties for transplant providers relative to patient involvement and information of the benefits and risks associated with NSRDs. Based on our framework, experience, and interpretation of the literature, we put forward a list of recommendations to combine standardization (ie, timing, content, and degree of patient participation) and individualization of IC. **Conclusions.** The 3-T Model may enable the prevention of physicians' arbitrariness and the promotion of patient-centered care. Future studies will assess the effectiveness of the 3-T Model in transplant clinical practice.

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INTRODUCTION

Improvements in surgical techniques, immunosuppressive regimens, and evaluation of donor-associated risks have made solid organ transplantation a safe and effective treatment for end-stage organ failure. However, because the supply does not meet the growing demand, strategies have been developed to expand the pool of deceased donor organs. The use of nonstandard risk donors (NSRDs) versus standard criteria donors (SCDs) is one of these. The risk associated with the SCD category is not zero. It refers to donors for whom no risk factors of diminished organ quality or disease transmission are detected during the donor evaluation process. NSRDs—previously classified also as “high-risk donors” or “increased risk donors”¹—carry a potential risk of infectious (especially human immunodeficiency virus [HIV], hepatitis C virus, hepatitis B virus [HBV] infections and also multidrug-resistant bacteria and other potentially transmissible pathogens) or malignant disease transmission to the recipient when associated with clinical or behavioral risk factors at donor screening or in the history of the donor.²⁻⁴ These should not be confused with expanded criteria donors who, in contrast, carry the potential for diminished quality of the graft and risk of inferior graft function.⁵ Most studies indicate a very low risk of disease transmission and similar or better outcomes with the use of NSRDs when compared with transplants performed with SCDs.⁶⁻¹³ However, NSRDs have posed new ethical challenges to the informed consent (IC) process regarding the timing of patient information, degree of patient participation in decision making, and disclosure of donor risk factors throughout the IC process leading to the potential acceptance of an NSRD offer.^{2,14-16} Research has found variability of IC practices for NSRDs across transplant centers in the European Union and beyond.¹⁷⁻¹⁹ Furthermore, NSRDs are still underused because of physicians’ or patients’ attitudes and misunderstanding of NSRD-related risks.^{15,19-22} Studies have advocated for standardization of disclosure practices relative to content, modality of communication, and amount of information to be delivered to transplant candidates at different time points of the transplant process, so as to prevent disparities across transplant centers and between providers at the same center.^{23,24} We put forward a model, named 3-T Model, which represents an effort to summarize the current knowledge on IC for NSRDs and to deliver conceptual and practical support to transplant providers on this emergent issue.

Standardization of the modality of communication is virtually impossible given the need to tailor educational strategies to the specific cognitive abilities, sociocultural needs, and health literacy levels of individual patients.^{16,25,26} Therefore, although we acknowledge that communicative strategies are critical for effective communication of the risks and benefits of the NSRD option to improve risk tolerance and understanding,^{15,22,27,28} these aspects are beyond the scope of this work.

Conceptualizing Informed Consent

It is well established that IC may not be reduced to a signature. In the presence of high-risk procedures, with low levels of certainty, and with two or more treatment alternatives, the

processes of IC and shared decision making (SDM) coincide.²⁹ As indicated in the Report of the International Bioethics Committee of United Nations Educational, Scientific and Cultural Organization, the features for obtaining consent depend on various factors such as the invasive character of the procedure, the potential benefits and side-effects, the possible impact for third parties (especially family members), the economic consequences, and, most importantly, the duration and the quality of the relationship between the provider and the patient. For instance, the Report highlights that “requesting and obtaining consent is not a one-time affair but it is often a process where discussion with the patient is needed at several succeeding points in time, through an ongoing dialogue.”³⁰ Accordingly, SDM has been conceptualized as a deliberative process developing over time where “clinicians and patients share the best available evidence when faced with the task of making decisions, and where patients are supported to consider options, to achieve informed preferences.”³¹ SDM entails (1) communicating the benefits and risks of treatment options based on clinical protocols and the best available evidence, and (2) eliciting what is most relevant for patients and their families.³² Multiple studies have emphasized that SDM is the most desirable and ethical model for decision making in transplant clinical practice.^{14,16,23,33,34}

In the specific context of decision making, the criterion of proportionality enables the balance of the patient’s clinical conditions with the patient’s interest.³⁵ The notion of proportionality is relevant to this type of clinical choice regarding patient care, both on the part of the patient and the physician (ie, “therapeutic alliance”). Proportionality must be evaluated distinctively for each individual patient through open dialogue, careful listening, and over a sufficiently extended period of time. Proportionality is therefore regarded as the most suitable criterion, which should be used to guarantee treatments that respect both clinical indications and patients’ preferences, consistent with the SDM model.^{36,37}

Based on these considerations, we define IC as “a relational process between physician and patient, where each of the actors has a say and which allows decisions to develop over time by jointly respecting clinical indications and individual patients’ subjective considerations, values, needs, preferences, specific life circumstances and goals” (our definition). The process of IC for NSRDs is no exception. Clinical indications and patients’ views regarding NSRDs do not necessarily match (ie, patients may view NSRDs negatively despite clinical appropriateness).^{15,16,21,38} Furthermore, as in other areas of clinical practice, uncertainty cannot be eliminated for clinicians or patients.³⁹ These aspects make patient participation critical to the process of IC for NSRDs and emphasize the importance of the relational dimension as a means to transcend the tension between beneficence/non-maleficence and patient autonomy (ie, respect for persons), which is inherent to IC, along the entire continuum of the transplant process.

Toward Standardization of Timing, Patient Involvement, and Disclosure of NSRD Risks: The 3-T Model for Transplant Clinical Practice

Although it remains the most desirable model for decision making in medical care, several factors may impede the implementation of SDM in transplant clinical practice. These include providers’ (un)willingness to engage in SDM,

late referral of patients to transplant centers and fragmented interactions with multidisciplinary provider teams, patients' views of NSRDs and their desire for autonomy, different degrees of risk aversion across transplant centers, providers, or transplant teams, patients' ability to process complex medical information because of declining cognitive status, ethnic/cultural background, socioeconomic factors,¹⁶ and providers' inability to communicate risk effectively and to foster active patient participation in decision making.²⁸ Because the risk factors regarding individual donors cannot be assessed and explained in a prompt, evidence-based fashion to the transplant candidate, opponents of SDM regarding communication about NSRDs argue that discussion of risks and benefits at the time of the organ offer can be difficult given the limited time available for decision making. However, although scholars advocate for preemptive decision making,^{1,2,14-16} none have provided ethical arguments in favor of standardization of timing of the IC process for NSRDs and the relevance of patient participation at different stages of the transplant process. The British National Health Service Blood and Transplant and the European Directorate for the Quality of Medicines and HealthCare identify three distinct moments of the process of IC in the general field of organ transplantation, namely (1) pretransplant assessments and waiting list (WL) registration, (2) time on the WL, and (3) time of the organ offer.^{5,40} In our model, the three timings coincide with the three stages of the SDM model by Elwyn et al,³¹ namely (1) choice talk (the moment the clinician makes the patient aware that reasonable options exist), (2) option talk (the time the clinician provides more in-depth information about available options), and (3) decision talk (the moment the clinician supports the process of deciding for the best solution according to patient's preferences).

MATERIALS AND METHODS

We searched *PubMed* to find evidence and ethical arguments to support the need for standardization of the timing of patient information, degree of patient participation, and disclosure of donor risk factors throughout the three timings of the IC process leading to the potential acceptance of NSRDs.

Furthermore, from the Northern Italy Transplant program (NITp) area, we extracted the data of the clinical outcomes of transplant to determine 1- and 3-y graft survival by organ (ie, kidney, liver, heart, and lung) and by donor risk category (ie, SCD; NSRD with potential risk of infectious disease transmission, NSRD with potential risk of malignant disease transmission) in the 2015–2020 period to provide additional support.

Ethics Statement

The analyzed data were collected from the NITp information system, an interregional registry collecting data of the entire transplant process (donation–procurement–transplant) drawn from the NITp interregional transplantation network. Data were available on yearly posttransplant graft survival. The retrospective analysis was approved by the NITp and included patients' data that were anonymized and de-identified directly in the NITp database before extraction for the analysis. The study was performed in compliance with the ethical principles of the Declaration of Helsinki (with amendments).

RESULTS

In our model (Figure 1), each of the three timings carries special ethical significance and entails well-defined duties for transplant providers relative to patient involvement and information of the potential benefits and risks associated with the NSRD option, as described below.

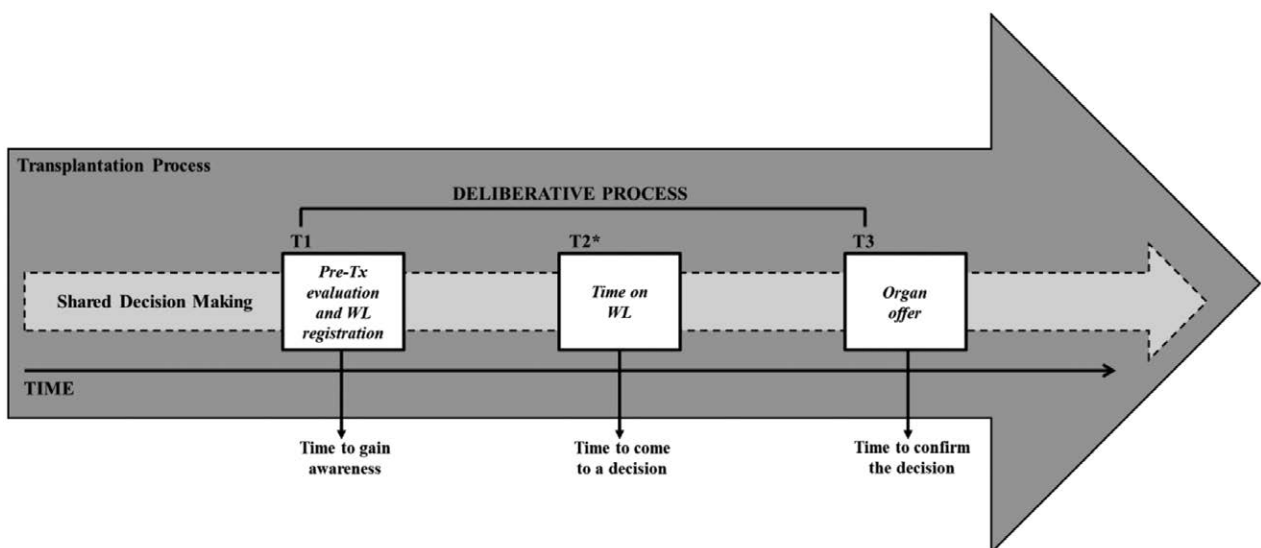


FIGURE 1. Informed consent process for NSRDs: the 3-T Model for transplant clinical practice. The model illustrates the features of informed consent for NSRDs in the general process of deceased donor transplantation. The 3-T Model highlights the relational and deliberative nature of informed consent for NSRDs, entailing that the patient must be informed about the NSRD option and of the entire process that will lead him/her to accept or refuse the NSRD organ in the event one should become available (T1); the patient must come to the decision of whether or not to accept the NSRD option after exposure of the patient to educational sessions and material and after formal assessment of the patient's understanding by the use of teach-back techniques (T2); and finally, if an NSRD becomes available, the organ is offered to the patient who decides whether or not to ultimately accept the organ offer based on the clinical and personal evaluation according to his/her subjective preferences, considerations, values, needs, specific life circumstances, and goals expressed earlier in the process and confirmed at the time of the NSRD offer (T3). *T2 should not be regarded as an isolated point in time but as a combination of multiple educational sessions according to the patient's subjective need for information and clarification. NSRD, nonstandard risk donor; T, time; Tx, transplant; WL, waiting list.

Time 1—Pretransplant assessments and WL registration: the time to gain awareness

Patients have the opportunity to make prospective choices without compromising the chance for transplant systems to successfully allocate organs at the time of the organ offer.²⁰ However, to do so by preventing the risk of disrespecting the autonomy of the patient, discussions of the risks and benefits associated with the NSRD option should be initiated early in the process of evaluation for transplant.^{5,14,16,24,40,41}

Studies have shown that patients do not sufficiently appreciate the differences among available options and the related outcomes in terms of WL mortality, likelihood of transplant, and organ quality.^{27,42} Furthermore, patients are frequently confused about the distinction between issues of organ quality and risk of disease transmission, stressing the need for thorough patient education to enable a valid IC.^{15,21,41,43,44}

The final decision regarding available options should therefore be deferred beyond the first phase of the SDM process to allow time for the patient to receive additional, more detailed information and education, to share their views and uncertainty with transplant providers, and to acquire additional experiential knowledge of the progression of their clinical and psychosocial condition later in the transplant timeline.^{31,39}

Based on these considerations, at the time of pretransplant evaluations, potential recipients should be informed that their consent to transplant will unfold through several discussions of the risks and benefits of different donor options, extending beyond the time of waitlisting, and ending at the time of their ultimate decision to accept or decline an NSRD offer.

Conversations regarding the transplant candidate's willingness to be considered for NSRD organs should include the best existing estimates of the patient's present and projected quality of life, together with information of the expected waiting time based on blood type and other relevant factors.¹⁵

The level of risk associated with NSRDs should be evidence-based and supported by figures of the experience of the transplant center, whereas national or broader-area data should be presented whether they are consistent with local facts⁴⁰ (NITp data are shown in Table 1).

Each transplant center should generate accurate and reliable data to guarantee an objective presentation of the risks and benefits associated with NSRDs and weigh them against the risks and benefits associated with SCDs and with those associated with declining an organ offer and remaining on the WL.²⁰ These considerations should be made on a case-by-case basis and tailored to individual candidates' clinical or psychosocial characteristics.

Although transplant systems and individual physicians are both accountable for information, transplant systems hold the responsibility of defining the general content of information, whereas physicians are required to adapt it and make it understandable to individual patients using tailored communicative strategies to enable a valid IC.^{16,25}

Time 2—Time on the WL: The Time to Come to a Decision

The time the transplant candidate stays on the WL should not be regarded simply as "chronological time" (*Kronos*) but also as "existential time" (*Kairos*), with the potential to play a critical role in the patient's decision making.

Patient's willingness to consider the NSRD option varies depending on numerous factors with variations across

TABLE 1.

One- and 3-y graft survival by organ and by donor risk category in the Northern Italy Transplant program area (2015–2020)

	Dx risk category	Tx (n)	1 y (%)	3 y (%)	P
Kidney	SCD	2308	95.8	94.2	0.3855
	NSRD-IDT	446	96.9	95.8	
	NSRD-MDT	97	97.7	97.7	
Liver	SCD	1255	91.0	87.9	0.8711
	NSRD-IDT	215	90.8	90.2	
	NSRD-MDT	61	90.8	90.8	
Heart	SCD	427	83.6	79.5	0.5937
	NSRD-IDT	78	77.3	75.8	
	NSRD-MDT	9	88.9	88.9	
Lung	SCD	290	82.8	74.5	0.0917
	NSRD-IDT	24	84.0	62.8	
	NSRD-MDT	1	–	–	

Survival analysis shows no significant differences between donor risk categories across different organ settings. No cases of infectious or malignant disease transmission from NSRDs were reported in the 2015–2020 period. The Northern Italy Transplant program area includes 6 regions: Lombardy, Veneto, Friuli-Venezia Giulia, Autonomous Province of Trento, Liguria, and Marche.

Dx, donor; NSRD, nonstandard risk donor; NSRD-IDT; NSRD with potential risk of infectious disease transmission; NSRD-MDT; NSRD with potential risk of malignant disease transmission; SCD, standard criteria donor; Tx, transplant.

different organ settings. Transplant candidates may experience inferior quality of life or decline of their clinical or psychosocial condition^{45–48} and, accordingly, their willingness to accept NSRDs may change over time.^{14,16,24,41} A study of liver transplant candidates revealed that variations may occur also based on transplant candidates' demographics, opinions on donor's high-risk behaviors, and information received by healthcare professionals.⁴³ A study on kidney transplant candidates found a significant association of multiple factors including longer waiting time for transplant, lower donor age, inferior donor HIV risk, potential recipient being on dialysis treatment, or being of an older age with a higher chance to consider the NSRD option. However, the study revealed that patients have an equal likelihood of accepting an NSRD kidney from a younger donor as from an older donor with an inferior chance of having HIV.¹⁵ Similarly, Ros et al⁴⁴ found that among kidney transplant candidates who had already received the same type of pretransplant education on different donor options, the majority regarded NSRDs as a valid alternative in the event of imminent death, poor quality of life on dialysis, and in case of reassurance of the good quality of NSRD kidneys.

Based on these considerations, the time on the WL is valuable for finding pertinent and practical application of the criterion of proportionality. In this context, what matters chiefly is the process leading to the decision more than the decision itself. Over time, through a deeper experiential knowledge of his/her pathology, understanding of its impact on his/her own life, and improved knowledge of the risks and benefits of the NSRD option, the patient may freely and deliberately come to a decision. For instance, the more the patient is well informed, the more he or she will be empowered to ask the physician for further information and decide whether to accept NSRDs at the time these types of donors should become available.

With this in mind, Elwyn et al³¹ recommend that the second stage of the SDM process (ie, option talk) should

include decision supports that may be in a brief format so as to enable use by clinicians and patients together or more extensive for use by patient and their families alone outside of clinical encounters. Empirical studies have shown that patient decision aids may be effective means to improve patient knowledge, decision making, and to foster SDM across different settings in organ transplantation. Research has shown a significantly higher knowledge of transplant,^{49,50} of HBV and HIV transmission, of the chance to receive a less-than-perfect SCD organ ($P=0.001$), higher willingness to consider acceptance of NSRD offers ($P<0.001$),⁵¹ improved knowledge of treatment options ($P<0.001$), more accurate expectations about risks and benefits ($P<0.001$), lower decision conflicts ($P=0.0007$), and longer-lasting decisions ($P=0.06$)⁵² in kidney, liver, and lung transplant candidates who were exposed to patient decision aids relative to those who were not, respectively. The choice made during the period on the WL may be either to accept or decline the NSRD option.

However, although it is important to start thinking sufficiently long in advance before transplant surgery to safeguard the patient from being psychologically overwhelmed at the time of the organ offer,⁵³ studies have shown that patients do not feel fully prepared to decide until they actually receive an NSRD offer.⁴⁴

Based on these considerations, *Time 2* should not be regarded as an isolated point in time but as a combination of multiple educational sessions according to the patient's subjective need for information and clarification. Therefore, provided that patients have received unbiased and equitable educational opportunities regarding NSRDs, and understanding has been formally assessed by asking patients to reformulate by use of "teach-back" techniques,^{31,54} potential recipients who turn down this chance will no longer be offered this donor type. Yet, they will be informed about the opportunity to change their position at any time point while on the WL and recommended to notify the transplant team should any change occur in their willingness to consider acceptance of NSRDs.

Patients who are willing to receive an NSRD offer will be reassured that, should an NSRD become available, (1) he or she will be in the position to ultimately accept or decline acceptance of these types of donor options, and that (2) in the unlikely but potential event of disease transmission, treatments will often be available for the recipient to diminish the risk or the severity of the transmitted infectious/malignant disease.

In the event of availability of an NSRD with an increased risk of infectious disease transmission, it will be anticipated to the patient that only the potential clinical risk of transmission of undetected HIV, HBV, hepatitis C virus, or other infections will be disclosed, whereas nonclinical information of the reasons of the potential presence of infectious diseases (ie, donor's behaviors, lifestyle, circumstances of death) will not be provided at the time of the organ offer.⁴⁰ Because these features do not affect the likelihood of infectious disease transmission, this type of information is not necessary for the patient to make an informed decision. Furthermore, there is an ethical duty to protect the donor's right to privacy and to prevent stigmatization of the nonclinical data of NSRDs with the potential to negatively influence the recipient's understanding.⁴³ Last, because some transplant candidates may

fear the acquisition of personality traits or behaviors of their donors,^{55,56} clinicians should prevent undesirable psychological reactions in the posttransplant period.

Time 3—Time of the Organ Offer: The Time to Confirm the Decision

Some clinicians contend that the ultimate decision is a clinical one, with little room for patient participation in decision making.⁵⁷ However, studies have demonstrated that, although some patients rely exclusively on trust in their physician(s),⁴³ most want to be involved in SDM in the event of an NSRD offer across different organ settings.^{23,27} For instance, Article 6 of the European Directorate for the Quality of Medicines and HealthCare document on *Safety, Quality and Ethical Matters Related to the Use of Organs, Tissues and Cells of Human Origin* states that "the ultimate responsibility for deciding whether to use a particular graft lies with the recipient's [transplant] team. [...] The doctor in charge should balance the risks and benefits and consequently, the [transplant] should only be performed if the benefits to the recipient outweigh the risks, and if consent or authorization has been given after information appropriate to the circumstances has been provided."⁵⁸

In the event of an NSRD offer, the risk of failing to undergo transplant in due time must be higher than the risk of infectious or malignant disease transmission. Although the risk of disease transmission is very low and the general outcomes of transplant with NSRD organs are comparable or better than those performed with SCDs,⁶⁻¹² (Table 1) the analysis of the risk–benefit ratio should be made on an individual, case-by-case basis.

Based on national and international guidelines for NSRD classification,^{1,2,5} and according to organ-specific allocation scores varying across countries, at the time an NSRD becomes available, organs are offered by regional or national organ procurement organizations to single-transplant teams. The transplant team holds ultimate responsibility for the decision of whether or not to use the NSRD organ and expresses a case-specific proportionality judgment to evaluate whether and to which of their waitlisted patients to propose the organ. For instance, over time, the physician or the member of the transplant team who participated in the relational process with the transplant candidate has acquired all of the elements that are necessary to evaluate the risk–benefit ratio based on clinical criteria as well as on the patient's subjective preferences, considerations, values, needs, specific life circumstances and goals expressed by the patient earlier in the process (ie, whether or not the patient has previously signed the specific IC form for NSRDs). Once the patient has received information from the physician, together they render the proportionality judgment explicit by evaluating whether to confirm the decision to accept.^{59,60}

In the logic of the criterion of proportionality, at the end of the process, the patient and the physician decide together. Although the physician should not shy away from giving the patient his or her opinion (ie, the physician does not hold a neutral position),⁶¹ it is recommended that physicians do not dwell in their own risk aversion when offering NSRD organs to their patient(s).^{12,22,62} For instance, because organ procurement organizations define the level of risk based on well-established protocols and determine the clinical appropriateness of the NSRD before offering organs to single-transplant teams,^{2,5} the physician should proceed with the NSRD offer in an unbiased fashion.²²

In case of inability to reach a shared decision, to respect the principle of proportionality, the ultimate decision of whether to ultimately accept lies with the patient.

DISCUSSION

The 3-T Model for transplant clinical practice highlights that SDM between patient and the transplant team requires time to be effective. It is necessary to implement a gradual process, respect for individual sensitivities, and an authentic ability to listen to the perspectives of others.

Transplant systems should hold the responsibility to define standardized content, timing, and degree of patient participation by providing specific indications to orient physicians in transplant clinical practice throughout the different stages of the transplant process.

Based on our framework, experience, and upon our interpretation of the literature, we put forward a list of recommendations regarding these aspects, which are listed in Figure 2.

Throughout the progressively unfolding process of SDM, the 3-T Model for transplant clinical practice may enable the integration of the conflicting concepts of standardization and individualization. On the one hand, standardization of the framework defining content, timing, and degree of patient participation prevents individual physicians' arbitrariness and, on the other, individualization promotes patient-centered care. Therefore, the 3-T Model orients physicians' actions, guarantees patient autonomy, and safeguards the whole "transplant community."

Research is needed to assess the effectiveness of the 3-T Model in transplant clinical practice in terms of clinicians' and patients' measurable outcomes including (1) satisfaction, (2) decision-making abilities (ie, improved knowledge and understanding of the benefits and risks of NSRDs, inferior decision conflicts, diminished risk aversion), and (3) NSRD utilization

across different organ settings. Furthermore, to enable the prevention of disparities, future studies should determine the effectiveness of the 3-T Model in more vulnerable groups of patients or substitute decision makers (ie, elderly or cognitively impaired patients, socioeconomically disadvantaged subjects, individuals who have migrated from other countries or who are from ethnic minorities, linguistically and culturally diverse individuals, and pediatric patients) to determine the need for targeted educational strategies to improve the process of IC. Studies on these aspects are warranted in the near future.

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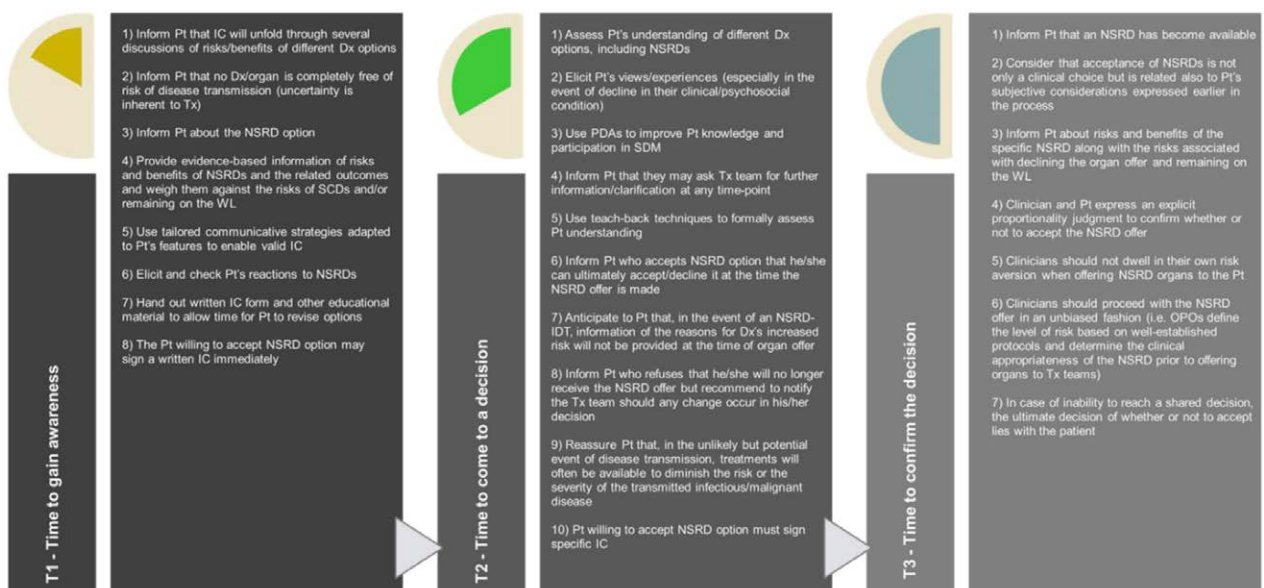


FIGURE 2. Recommended physician's actions at the three time points of the transplant process (Pre-Tx, WL, organ offer). Dx, donor; IC, informed consent; NSRD, nonstandard risk donor; NSRD-IDT; NSRD with potential risk of infectious disease transmission; OPO, organ procurement organization; PDA, patient decision aid; Pt, patient; SCD, standard criteria donor; SDM, shared decision making; T, time; Tx, transplant; WL, waiting list.

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