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# Increased-risk donors and solid organ transplantation: current practices and opportunities for improvement

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## Abstract

**Purpose of review—**The development and implementation of 'increased risk donor' (IRD) status by the Centers for Disease Control (CDC) was intended to guide patients and providers in decision making regarding risk of infectious transmission via solid organ transplantation. Several contemporary studies have shown underutilization of these organs. This review summarizes the issues surrounding IRD status as well as recent advances in our understanding of the risks and benefits of increased risk organs and their appropriate utilization.

**Recent findings—**Risk of window-period infection remains exceedingly low, and implementation of nucleic acid testing for HIV and hepatitis C virus (HCV) has resulted in decreasing risk of window-period infection often by an order of magnitude or more. Surgeons remain hesitant to utilize IRD organs. In addition, surgeon assessment of risk by donor behaviour was often discordant with known risks of those behaviours. Studies investigating outcomes of utilization of IRD organs suggest long-term mortality and graft survival is at least equivalent to non-IRD organs. Contemporary results suggest that IRD organs continue to be underutilized, particularly adult kidneys and lungs, with hundreds of wasted organs per year.

**Summary—**CDC IRD labelling has led to an underutilization of organs for transplantation. The risks associated with acceptance of an IRD organ are inflated by surgeons and patients, and outcomes for patients who undergo transplantation with increased risk organs are similar to or better than those for patients whom accept standard risk organs. The rate of transmission of window-period infection from IRD organs is exceptionally low. The harms regarding the utility of Public Health Service increased risk classification outweigh the benefits for patients in need of transplant.

### Keywords

donor; increased risk; organ supply; Public Health Service criteria

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Conflicts of interest

There are no conflicts of interest.

## INTRODUCTION

In 1994, the Centers for Disease Control (CDC) developed the Public Health Service (PHS) Guidelines for designation of what they deemed ‘increased risk’ organ donors based on a set of behaviours that increased risk of HIV transmission [1]. These guidelines were later updated in 2013 by the CDC to include criteria for assignment of increased risk status for hepatitis B virus (HBV) and hepatitis C virus (HCV) transmission in addition to HIV. The below criteria were intended to aid organ procurement organizations (OPOs), patients and providers in decision making regarding organ utilization, handling and testing [2].

1. MSM in the preceding 12 months;
2. Nonmedical IDU in the preceding 12 months;
3. People who have had sex in exchange for money or drugs in the preceding 12 months;
4. People who have had sex with a person known or suspected to have HIV, HBV or HCV infection in the preceding 12 months;
5. Women who have had sex with a man with a history of MSM behaviour in the preceding 12 months;
6. People who have had sex with a person who had sex in exchange for money or drugs in the preceding 12 months;
7. People who have had sex with a person who injected drugs by intravenous, intramuscular or subcutaneous route for nonmedical reasons in the preceding 12 months;
8. A child equal to or less than 18 months of age who was born to a mother known to be infected with, or at an increased risk for HIV, HBV or HCV;
9. A child breastfed within the preceding 12 months and the mother is known to be infected with, or at an increased risk for, HIV infection;
10. People incarcerated in prison or juvenile correctional facility for 72 consecutive hours in the preceding 12 months;
11. People on haemodialysis in the preceding 12 months;
12. Any patient who’s medical/behavioural history cannot be obtained or who’s blood specimen is haemodiluted.

With the implementation of these guidelines came concern from all stakeholders including OPO’s, surgeons and patients regarding the appropriate utilization of organs from increased risk donors (IRDs). The PHS stated in the initial 1994 recommendations that organs from ‘persons who meet any of the criteria… should be excluded from donation of organs or tissues unless the risk to the recipient of not performing the transplant is deemed to be greater than the risk of HIV transmission and disease’. This review will cover the current literature on infectious risk, utilization and the factors affecting utilization.

## VARIABILITY OF RISK IN INCREASED-RISK DONORS

At the time of the initial PHS publication, the risk of transmission of HIV from transplant organs was not well known. Furthermore, these estimates were based exclusively on HIV diagnosis by antibody detection. Recent meta-analyses by Kucirka *et al.* [3,4], in the contemporary era of antibody and nucleic acid testing, represent the most robust quantification of this risk. These studies demonstrate the risks of window-period infection from HIV and HCV to be highly variable depending on the particular criteria that the donor satisfied. For example, the risk of HIV window-period infection was found to vary from as high as 12.1 per 10000 donors for IDU donors tested by ELISA to as low as 0.9 per 10000 donors for incarcerated individuals tested by nucleic-acid testing (NAT). Risk of HCV infection followed a similar pattern, albeit with higher rates overall, ranging from 300.6 per 10000 donors for IDU donors tested with ELISA to as low as 0.8 per 10000 donors for incarcerated individuals tested by NAT. Importantly, since the publication of this study, the OPTN/UNOS Board of Directors has required NAT for HCV among all donors and NAT for HIV among IRD.

## RISK OF INCREASED RISK DONOR ORGAN ACCEPTANCE VS. REMAINING ON WAITING LIST

Clinicians must balance the risk of transmission of an infectious disease with the risk of remaining on the transplant list. Although studies in this realm are limited, a recent retrospective cohort study was completed investigating differences in mortality among patients listed for renal transplant who were offered IRD organs [5]. There was no difference in mortality between those who received IRD organs and those who were transplanted with non-PHS IRD organs, with a clear decrease in mortality compared with those who remained on the list after refusing a IRD organ. This corroborates a large retrospective study of the Scientific Registry of Transplant Recipients data showing a 48% lower risk of death at 6 months for patients who accepted IRD organs. These studies join results of a 2007 study that used a decision-analytic Markov model for transplantation of IRD organs [6]. The authors found that a policy requiring transplantation of IRD organs would lead to a decreased risk of HCV infections due to lower time of exposure to the known risk of HCV with ongoing haemodialysis. Multiple studies demonstrate that recipients of renal transplant with IRD organs had similar rates of mortality and graft loss compared with those of standard criteria donor organs [7,8]. Liver transplant outcomes following IRD organ transplantation share a similar outcome [9■■].

Risks at the population level clearly favour aggressive utilization of IRD organs. Critics of policy for transplanting all IRD organs voiced concerns regarding patient-specific risks and counsel at the time of organ offer. To this end, Chow *et al.* [10] utilized a Markov simulation design to create a web-based tool for assisting in understanding patient-specific risks of IRD acceptance. These findings underscore the clear mortality benefit associated with use of IRD organs.

## CURRENT UTILIZATION OF ORGANS FROM HIGH-RISK DONORS

The proportion of IRDs is currently between 20 and 27%, and rising in the wake of the opioid epidemic [11,12■]. In the period surrounding the publication of the updated PHS guidelines, several studies showed significantly decreased utilization of IRD organs [13,14]. In an effort to combat the underutilization of IRD organs, the OPTN published a guidance document in 2017 with tools to improve communication regarding the risks of accepting or declining an organ from an IRD [15]. Interestingly, data from a 2019 publication showed that adult heart and liver risk-adjusted utilization rates are currently no different for IRD organs compared with standard risk organs. However, adult kidney and lung utilization rates remain significantly lower in the most recent years of the study for IRD vs. standard risk organs [16■■]. Importantly, a review of data from all solid organ transplants from 2008 to 2016 by the OPTN Disease Transmission Advisory Committee found a total of 15 cases of HCV transmission from organ transplantation, of which only seven occurred from IRD in the NAT window period. Since the publication of the revised 2013 guidelines, there has not been a reported case of HIV transmission from organ transplantation [15].

## SURGEON UTILIZATION OF INCREASED RISK DONOR ORGANS

A national survey of over 400 transplant surgeons provided insight into surgeons' practices around IRD organs [17]. Surgeon responses mirrored the varied utilization rates by organs. Surgeons were much more likely to use IRD livers [odds ratio (OR) = 1.71] than kidneys (OR = 1.00) or pancreata (OR = 0.19). Surgeons believe that not all high-risk behaviour was equal as they were much more likely to utilize HRD organs from IDU and MSM compared to high-risk sex and HIV exposed. Surgeon-reported behaviour did not necessarily match with the data stratification of risk. Surgeons were much more likely to use organs from IDU (OR 1.71) vs. incarcerated individuals (OR 0.78), although data suggest that infectious transmission of HIV and HCV is more likely in IDU donors than incarcerated donors. Surgeons practicing in a hospital with a defined policy on IRD use and a defined IRD recipient profile had increased IRD utilization compared with those practicing in hospitals without.

## PATIENT ACCEPTANCE OF INCREASED RISK DONOR ORGANS

Patient attitudes toward IRD organ acceptance have a profound impact on IRD organ utilization. Patients have a poor understanding of the actual risks of infection from IRD organ transplantation (as do surgeons) and often underestimate the quality of the organs from IRDs [18]. Ros *et al.* [19] showed that patients were interested in receiving additional education regarding these issues, and generally felt unprepared to receive offers for IRD organs. A study published in 2019 investigated the attitudes that liver transplant candidates had towards IRD organ acceptance [20■]. The authors found that there was a significant difference in willingness to accept an IRD organ by sex, with women almost 20% more likely to accept than men. Patients with postsecondary education were less likely to be willing to accept an IRD organ. Patients were increasingly likely to accept the organ offer as the stated risk of transmission decreased and were shown to be more likely to be willing to accept an organ after they received various points of education on IRD organ acceptance.

The most striking result was that the overall acceptance rate for IRD organs was only 41%. These findings together suggest that, although patient attitudes toward IRD organs are a large barrier to acceptance, there are opportunities for transplant providers and institutions to impact this through increased education.

## UTILIZATION OF KNOWN HIV OR HEPATITIS C VIRUS INFECTED ORGANS

Significant advances have been made in the treatment of both HIV and HCV infection, with direct-acting antivirals (DAAs) curative in most HCV infections and antiretroviral medications essentially converting HIV into a chronic disease with a long-life expectancy. The implications of contracting HCV or HIV from IRD organ receipt are different than when the PHS guidelines were originally published. In a recent study by Cotter *et al.* utilizing data from the Scientific Registry of Transplant Recipients, it was found that over the 10 years prior to the study, over 800 HCV viraemic livers were transplanted into both HCV viraemic and nonviremic recipients with no significant difference in 2-year graft survival [21]. There was also an increase in the number of HCV viraemic organs transplanted into HCV nonviremic recipients, from just seven in 2008 to 107 in 2017. Graft survival for organs from viraemic donors increased significantly over the study period as well, likely due to posttransplant treatment with DAAs. In 2017, two landmark studies (THINKER 1 and THINKER 2) were published showing excellent 12-month outcomes following transplantation of HCV viraemic kidneys into HCV nonviremic recipients followed by treatment with DAAs [22,23]. These pilot studies suggest that utilization of kidneys from HCV viraemic donors may not be a barrier to transplantation, even when the recipient is HCV negative.

## CONCLUSION

The PHS guidelines for IRD labelling were published at a time when transmission of viral infection via organ transplant had potentially devastating outcomes for patients and the transplantation community. Over the 25 years since, the ability to detect these viral infections has greatly improved, decreasing the window period. Data have continued to mount suggesting that the PHS guidelines have led to a significant underutilization of organs at the population level. The benefit for preventing cases of organ transmitted viral infection has been limited to a dozen or so cases in contemporary transplant. Recent studies have shown that improvement has been made in underutilization for several organs, but this remains an ongoing public health problem.

The Department of Health and Human Services is currently in the process of updating recommendations in the PHS Guideline for Reducing Human Immunodeficiency Virus, Hepatitis B Virus and Hepatitis C Virus Transmission Through Organ Transplantation. In April of 2019, the Advisory Committee on Blood and Tissue Safety and Availability met and agreed on a series of recommendations to HHS regarding updates to the PHS guidelines. A robust discussion took place over 2 days and resulted in a total of 11 recommendations made. These recommendations included continuing to recognize and designate donors at augmented chance of transmission of viral infection, testing all organ donors for viral infection using NAT and funding a longitudinal collection of data by the OPTN regarding

donor and recipient risk as well as the impact of risk assessment on the donor pool and organ utilization. They also recommended changing the behaviour timeframe to 3 months from 12 months and removing several criteria from the IRD designation, including women who have had sex with men with a history of MSM behaviour, newly diagnosed sexually transmitted diseases, haemodialysis, children born to a mother at an increased risk for HIV/HBV/HCV and children breastfed in the preceding 12 months by a mother at an increased risk for HIV infection. Finally, they recommended changing the terminology of IRD, as there was concern that the current terminology caused cognitive bias, although new terminology recommendations were not made [24].

The literature suggests that PHS guidelines for IRD designation have resulted in substantial underutilization of organs, particularly adult kidneys and lungs, and that the actual risk of viral transmission is exceptionally low. The opioid epidemic has led to a substantial increase in the number of donors identified as increased risk even though the organs procured from these donors are often of higher quality than the average organ. With continued increase in opioid related deaths, combined with the major advancements in the treatment of blood borne infections, we should consider whether we need PHS guidelines to label donor organs increased risk at all.

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**KEY POINTS**

- Increased risk classification has led to a systematic underutilization of organs in the USA.
- Surgeon and patients have poor understanding of the actual risks of blood-borne viral infection from acceptance of increased risk organs.
- Recent advancements in the treatment of HCV and HIV have drastically altered the trajectory for patients with these infections, and prior estimates of risks and benefits of acceptance of increased risk organs are no longer valid.