How Do IRB Members and Ethicists Assess the Risk of Zoonotic Disease Transmission in Xenotransplant Pig Kidney Clinical Trials?

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INTRODUCTION

- First-in-human xenotransplant (XTx) pig kidney clinical trials may soon be launched and raise myriad ethical questions.[1]
- To approve a research protocol, Institutional Review Boards (IRBs) must conclude that the potential risks to participants are reasonable in relation to the anticipated benefits.[2]
- Concerns have been raised about risk of infectious (zoonotic) disease transmission from pig organ to recipient and from recipient to the broader community.[3]
- We assessed the extent to which the risk of zoonotic disease transmission to transplant recipients, transplant teams, or the general public would/should affect IRB risk/benefit assessment of a first-in-human XTx pig kidney trial.

METHODS

Design: Cross-sectional study

Setting: Medical centers, academic institutions, and non-academic institutions

Participants: IRB chairs, IRB members, and human subjects research ethics experts

Data Collection: Semi-structured telephone interviews (June 2022 – March 2023)

- Likert scale ratings of extent to which risk of zoonotic disease transmission to transplant recipients, the transplant team, or the general public *would* (for IRB members) or *should* (for ethics experts) affect IRB risk-benefit
- Open-ended rationale for decisions

Data Analysis:

- Descriptive statistics
- Thematic analysis (K > 0.80)

RESULTS

- N=23 participants (11 IRB chairs; 4 IRB members; 8 human subjects research ethics experts), 38% participation rate

Table 1. Extent to which risk of zoonotic disease transmission to transplant recipients, the transplant team, or the general public would/should affect IRB risk-benefit assessment of a XTx clinical trial

	Not at all n (%)	A little n (%)	Somewhat n (%)	Very n (%)	Entirely n (%)
Transplant Recipients			4 (17.4%)	18 (78.3%)	
Transplant Team	2 (8.7%)	7 (30.4%)	8 (34.8%)	5 (21.7%)	
General Public	1 (4.3%)	7 (30.4%)	4 (17.4%)	10 (43.5%)	

**Percentages do not sum to 100 because one participant did not provide scaled responses*

- To effectively assess the risk-benefit ratio, IRBs would need to know:
  - What infectious diseases might be transmitted
  - How transmission risk would be mitigated
  - Whether effective treatment therapies are available

Table 2. Factors that would/should influence IRB risk-benefit ratio assessment

Factors	Illustrative Quotes
What infectious diseases might be transmitted	• "It's going to depend on the nature of the infection. Is it viral, bacterial, fungal?" (7001) • "[W]hat was the biggest risk? You know, what were the top three infectious disease risks?" (7007)
How transmission risk would be mitigated	• "[A]re these clean animals? In what conditions are they grown?" (7006) • "Are we able to identify which organs have the fewest contaminants and don't carry with them physically contagious or lethal contagions?" (6004)
Whether effective therapies against the diseases are available	• "[W]e just don't have a great armamentarium for combating zoonotic infections… In that case with a transplanted organ with a zoonotic infection you may create a greater risk than the person came in with to begin with. (7015) • "We already think about these sorts of risks in transplants. We also need to think about the risks here, especially when we may not have effective therapies against the disease." (6001)

CONCLUSIONS

- Preliminary findings suggest that risk of zoonotic disease transmission to transplant recipients would/should affect IRBs' overall risk/benefit assessment of a proposed first-in-human XTx pig kidney trial to a greater extent than risk of transmission to transplant teams or to the general public.
- Future research should examine how IRBs assessed the risk of zoonotic disease transmission to each group in their review of actual XTx pig kidney clinical trial protocols in order to learn how they view these risks in relation to other XTx risks.
- Limitations: Perceptions reported reflect participants' consideration of hypothetical XTx trial participation rather than an actual trial.

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