

# *The Dilemma of Ethical Recipients of Xenotransplantation under the Biopsychosocialmedical Model*

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**Abstract:** In recent years, there have been continuous reports of new breakthroughs in clinical xenotransplantation, indicating that xenotransplantation is expected to become the main method of clinical transplantation. However, at present, clinical workers mostly focus on technological development and current clinical trial ethical principles, to some extent neglecting the psychological and social adaptability of individuals. The biopsychosocial medical model not only acknowledges the influence of biological factors on individuals but also recognizes the role of psychological and social factors in human health and disease. Therefore, this article discusses and analyzes the ethical issues of xenotransplantation recipients from the perspective of the biopsychosocial medical model: human integrity, consciousness, and personality changes; pre-transplant psychological cognition and acceptance level, post-transplant psychological adaptation; social rejection, fair distribution of transplantation rights. Corresponding solutions are provided, including the establishment of a personality database, popularization of relevant knowledge, strengthening medical insurance coverage, providing humanistic care, conducting psychological analysis, enhancing self-regulation awareness, encouraging social acceptance, formulating relevant social systems, rationalizing surgical costs, and issuing effective laws and regulations. It is hoped that the rationalization of xenotransplantation in the ethical field can be achieved as soon as possible, which can not only save and prolong the lives of patients, and provide a higher quality of life, realizing the inherent value of life, but also promote the development and improvement of xenotransplantation technology, advancing more humane applications.

## 1. Introduction

Xenotransplantation (XTx) is the transplantation of organs from one species to another to help maintain or prolong the life of the recipient.

The bold idea of XTx and clinical trials actually preceded those of allogeneic organ transplantation. As early as the 17th century, Western doctors boldly attempted to transplant sheep kidneys into patients with uremia<sup>[1]</sup>. However, due to the limited medical technology of the early human civilization, XTx was too difficult to implement. Subsequently, due to various problems

such as avoiding interspecies infections, relatively backward technology, and social controversies, allogeneic organ transplantation rapidly developed and matured, becoming the main way to save the lives of terminally ill patients. However, with the continuous maturation of allogeneic organ transplantation technology and the increasing demand from patients, allogeneic organ transplantation can no longer meet the supply needs. Therefore, clinical workers have once again begun research on XTx. Reasons for this include: First, XTx can not only provide sufficient donors for human transplantation but also avoid the problem of organ failure in treatment. Second, pigs have become the main research subjects for xenogeneic donors. Humans have found that compared with other animals, pigs not only best fit human physiological needs in transplantation but also have a relatively clear genetic background, which is conducive to the exploration and breakthroughs of XTx<sup>[2]</sup>. Third, gene editing technology is now maturing, providing conditions for compatibility between donors and recipients.

This has led to rapid development of XTx in recent years. In January 2022, the University of Maryland School of Medicine transplanted a genetically edited pig heart into a 57-year-old male with myocardial disease who relied on Extra Corporeal Membrane Oxygenation (ECMO). However, severe transplant dysfunction occurred after transplantation, and life support was withdrawn after 2 months, marking the crucial first step in determining whether animal organs can become human transplant donors<sup>[3]</sup>. Subsequently, the University of Maryland School of Medicine summarized the reasons for the failure of this transplantation and conducted a second pig heart transplantation surgery in September of the same year, but the patient died six months after transplantation due to rejection. In 2023, the Langone Transplant Research Institute at New York University transplanted a genetically edited pig kidney into a 57-year-old brain-dead patient, and the experiment found that even without experimental drugs and equipment support, the kidney could function in the patient's body for at least 32 days. As of March 2024, the West Jing Hospital in China transplanted a genetically edited pig liver into a brain-dead patient, and the liver could secrete bile normally after surgery, with no signs of hyperacute rejection<sup>[4]</sup>. In March of the same year, doctors in Boston, United States, announced that they had successfully transplanted a genetically modified pig kidney into a 62-year-old patient with kidney disease, marking the first time that a genetically modified pig kidney had been transplanted into a living human body. This rapid development and high attention to XTx suggest that it is likely to become the main method of clinical transplantation.

Today, clinical workers are more focused on the development of technology, to some extent neglecting the human psychological and social dimensions, and failing to consider changes in the social environment where humans are the subjects. However, to resolve the conflict between ethical principles and the implementation of XTx, we must begin to pay attention to the psychological and social adaptation of recipients. In the mid-20th century, George L. Engel, a professor of psychiatry and internal medicine at the University of Rochester School of Medicine, criticized the shortcomings of the biomedical model, believing that simple biological indicators cannot achieve a comprehensive assessment, diagnosis, and treatment of patients. Thus, a new medical model was proposed: the biopsychosocial medical model. Today, the biopsychosocial medical model has become the basic model of contemporary medicine, focusing on and evaluating patient-related social relationships and psychological factors that affect diseases in a connected and developmental perspective, meeting patient needs from basic to advanced levels<sup>[5]</sup>. This model not only recognizes the influence of biological factors on humans but also acknowledges the role of psychological and social factors in human health and disease, considering both the biological and social attributes of humans, achieving an organic unity of human social and natural attributes. Therefore, this article will analyze and propose corresponding strategies for the ethical dilemmas of XTx recipients from the perspectives of the biopsychosocial medical model in terms of biology, psychology, and society.

## 2. Ethical Issues of Xenotransplantation Recipients

### 2.1. Ethical Issues at the Physical Level of Recipients

Here we can consider transplanting a pig's heart into a human body. After transplantation, is the recipient still a complete human? Compared to disabled individuals, a person with an intact body structure and organ functions is considered complete. However, XTx precisely aims to address these issues. Therefore, we need to further consider the differences between humans and animals. Even though philosophers have been debating this topic endlessly, we must acknowledge the vast difference in consciousness and feelings that animals possess compared to humans<sup>[6]</sup>. Therefore, the integrity of the body needs to consider the unity of ideology and personal behavior.

Earlier studies on allogeneic organ transplantation found that transplant recipients experienced changes in food preferences, music, art, entertainment, and occupational preferences that followed the donors. There have even been cases where transplant recipients dreamt of being murdered and provided detailed descriptions, leading to the arrest of the actual perpetrator<sup>[7]</sup>. Therefore, even though it's unavoidable for donors and recipients to belong to the same species, recipients after XTx are likely to face similar issues. Due to the significant differences between donor and recipient populations, the types and degrees of changes may even exceed those in allogeneic organ transplantation.

Furthermore, a recent study indicates the potential and extensive connections between the heart and the brain. After controlling various covariates, researchers found significant correlations between cardiac magnetic resonance imaging features and the brain. They also determined that cardiac magnetic resonance imaging features are genetically related to various features and diseases in the brain, including stroke, dietary imbalance, and schizophrenia. Therefore, adverse cardiac indicators could greatly affect brain function and lead to brain abnormalities and neurological diseases<sup>[8]</sup>. Considering the correlation between the heart and the brain, the transplantation of animal hearts may severely disrupt brain physiology and modes of thinking, thereby altering the recipient's consciousness, memory, thoughts, and sensations.

Lastly, from the perspective of traditional Chinese medicine, it emphasizes the physiological function of the heart in governing consciousness. The "Su Wen · Ling Lan Mi Dian Lun" states, "The heart is the official of the monarch, and the spirit emerges from it." This means that the heart is the head of the organs, and the spirit arises from it, referring to human mental activities. If the heart functions normally, various outward manifestations of life that depend on human life, such as speech, facial expressions, eye contact, body movements, and pulse, will all exhibit abundant energy and a harmonious state<sup>[9]</sup>. The transplantation of xenogeneic hearts completely replaces the human heart. Therefore, the recipient's mental activities, including consciousness, sensations, perceptions, emotions, will, memory, and thoughts, may undergo significant changes.

### 2.2. Ethical Issues at the Psychological Level of Recipients

As a nascent and frontier technology in the clinical field, XTx must consider the thoughts and attitudes of recipients, which can provide clearer directions for the development of XTx technology. The main psychological issues of relevant recipients include their psychological cognition and acceptance before transplantation and their psychological adaptation ability after transplantation.

Since XTx is rapidly developing in clinical research, it must ensure the harmony between the applicability of the technology and the autonomy of the recipients. In the context of the information age, XTx is not unfamiliar to medical professionals. However, due to factors such as age, educational background, location, and occupation, the current dissemination and acceptance of XTx concepts and technology among recipients remain at a relatively low level. A survey

conducted in 2022 on the awareness of xenogeneic kidney transplantation among potential recipients showed that only 66.78% of the respondents were aware of xenogeneic kidney transplantation. Among them, 63.59% knew that the xenogeneic kidney transplant used a pig kidney, 57.47% knew that xenogeneic kidney transplantation research was in the preclinical trial stage, and 52.66% knew that the xenogeneic kidney transplantation used a pig kidney that had been genetically edited<sup>[10]</sup>. The data indicate that even though some people are aware of XT<sub>x</sub>, less than half of them truly understand it. Therefore, the degree of acceptance among relevant groups may also be affected. Therefore, the degree of acceptance among relevant groups may also be affected. The psychological acceptance of XT<sub>x</sub> is also related to factors such as economic status, age, gender, and educational level. A study on the concerns of Chinese kidney transplant recipients and candidates about using genetically edited pig kidneys showed that the concern level of respondents aged  $\geq 60$  was higher than that of those aged  $< 60$ . Compared with female respondents, male respondents had lower levels of concern. Furthermore, respondents with a university education or above were more concerned about various potential risks of XT<sub>x</sub> than those with a high school education or below<sup>[11]</sup>. This indicates that various factors influence the acceptance of XT<sub>x</sub> by recipients and candidates, and there may be significant differences among groups. The overall acceptance of XT<sub>x</sub> recipients and candidates needs to be improved.

Secondly, whether recipients have sufficient ability to psychologically adapt after transplantation. Psychological adaptation refers to an individual's self-adjustment process to alleviate stress and restore balance through correct psychological defense mechanisms after setbacks and blows<sup>[12]</sup>. After XT<sub>x</sub>, the psychological adaptation of recipients relies on self-defense mechanisms to readjust to the new body. In 1894, Freud first proposed the concept of defense mechanisms: "Individuals protect themselves from external harm by changing their cognitive perception of threatening events such as anxiety and pain, thereby maintaining psychological balance." Research has found that the less mature defense mechanisms may lead to more psychological disorders<sup>[13]</sup>. Therefore, recipients with immature defense mechanisms may develop anxiety disorders, depression, autism, and other psychological disorders when facing issues such as postoperative health recovery, various complications caused by new technologies, and unknown potential risks of XT<sub>x</sub>, even if they can overcome immune rejection.

### 2.3. Ethical Issues at the Social Level of Recipients

Returning to recipients within the social group inevitably involves the influence of social relationships and social life. Therefore, the main ethical issues of recipients at the social level include social exclusion and fair distribution of transplant rights.

Excluding people in need of transplantation, we cannot be sure that social groups including some medical workers and even some transplant relatives can fully accept XT<sub>x</sub>. Therefore, the primary problem faced by XT<sub>x</sub> patients when reintegrating into social life is social exclusion. Social exclusion refers to the phenomenon and process of excluding or rejecting certain social groups or individuals for some reasons, resulting from the failure to meet individual affiliation needs and social relationship needs<sup>[14]</sup>. Here, we specifically divide social exclusion into social psychological exclusion and social institutional exclusion. Social psychological exclusion in XT<sub>x</sub> is akin to the rejection that recipients receive because their transplantation behavior does not conform to the common values of the general public. The general public cannot understand the reasons for using XT<sub>x</sub> and may exhibit prejudice and discrimination due to the "non-human" nature of the donors used by patients. For example, stigmatizing xenotransplant recipients as having "the face of a human, the heart of a beast" may undermine the recipients' self-esteem, making it difficult for them to reintegrate into normal social life, including social interaction, interpersonal communication,

learning status, and work life. In addition, in the context of big data, recipients may not only need to endure pressure from public opinion but also face the problem of personal information and privacy leakage, greatly affecting the normal life of recipients. Institutional exclusion mainly manifests in the lack of relevant systems for XTx recipients. For example, based on considerations of immunological rejection reactions between organisms, the issue of how recipients of pig heart transplants donate blood needs to be addressed. The imperfection of the system prevents recipients from exercising their rights and fulfilling their obligations, gradually leading them to become marginalized individuals in society.

Furthermore, how to maintain fairness and justice in the transplantation rights in the human social domain. Since XTx aims to solve the shortage of allogeneic organ transplantation resources, from the perspective of patients waiting for transplantation, this will become the only way to save lives apart from allogeneic organ transplantation. However, the application of emerging high technology often comes with high costs. Economic factors often deter patients. For example, compared to any other medical service, organ transplantation, which can rapidly save human lives, is widely recognized as very expensive<sup>[15]</sup>. So, how can XTx effectively avoid similar situations and ensure that the development of high-tech is not only to save the wealthy but to ensure that the entire society has fair access to transplantation rights? On the other hand, due to the urgent demand of patients for treatment, some deviations from the normal trajectory have appeared in the medical system and the transplantation market<sup>[16]</sup>. This has led to situations where hospitals, both internally and in relation to external markets, or even among external markets, seek personal gains through improper means, seriously disrupting the fair allocation of transplantation resources and causing some patients to lose their rightful transplantation rights.

### **3. Measures to address the Ethical Issues of Xenotransplantation Recipients**

#### **3.1. Solutions at the Physical Level of Recipients**

Humans have proposed three hypotheses to explain changes in personality and consciousness after organ transplantation: psychological, biochemical, and electromagnetic energy. The psychological hypothesis suggests that these changes are fantasies produced by the recipients when facing the pressure of surgery. The biochemical hypothesis holds that the donor's organs store memories and personalities, which are transferred to the recipient through donated organs. The electromagnetic energy hypothesis considers personality-related information as electromagnetic energy, with the heart being the body's largest electromagnetic field. Information stored in the donor's heart is transferred to the recipient's electromagnetic field during surgery<sup>[17]</sup>. However, none of these hypotheses have been fully proven. Perhaps these hypotheses are all invalid, or perhaps there are other undiscovered factors. Personality changes may also result from the combined effects of these factors. However, it can be confirmed that we cannot apply the reasons for personality changes in allogeneic organ transplantation to solve the same difficulties faced by XTx.

Therefore, it is necessary for us to start categorizing XTx types and establish a comprehensive personality database for XTx recipients during the clinical trial stage. It is important to note that such actions are not discrimination against the XTx population but rather aim to compare whether the personality of recipients changes before and after transplantation, and thus select XTx technology types that better serve humanity. Subsequently, recipients should be followed up over time, and their personality conditions should be meticulously recorded. Based on the recorded results, an analysis should be conducted to determine whether relevant XTx procedures should continue to be implemented clinically.

Of course, such an approach inevitably involves sacrificing some patients. Therefore, before the trial, the risks of personality and consciousness changes should be explained to the recipients and

their families. Long-term or even lifelong follow-ups may be necessary, giving them sufficient time for consideration without rushing them to sign informed consent forms. If consent is obtained, recipients should be treated with respect and care during surgery and follow-up, as their brave step forward is a significant advancement for XTx. Furthermore, due to this crucial selection process, defining the integrity of the human body in XTx becomes simpler. Since screened XTx can minimize changes in recipient personality, the recipient's body naturally remains intact after transplantation.

### 3.2. Solutions at the Psychological Level of Recipients

Trengthening the dissemination of knowledge related to XTx concepts, advantages and disadvantages, reasons for implementation, basic operations, and other relevant knowledge through community health public welfare activities, academic lectures, news columns, and online self-media platforms can enhance the awareness of XTx among the transplant waiting population and individuals outside the medical field. This approach not only reduces the differences in acceptance among different groups but also improves the accuracy of subsequent acceptance research results, providing clearer directions for clinical trials. Additionally, the mutual influence of such relationships will facilitate the exploration of XTx technologies that meet human psychological expectations.

Furthermore, an analysis of the factors influencing public acceptance of XTx in China shows that in addition to factors such as gender, marital status, place of residence, religious beliefs, and vegetarianism, medical insurance status is the most significant factor influencing acceptance<sup>[18]</sup>. Therefore, we must plan and segment more inclusive and reasonable medical insurance systems based on the needs and economic levels of recipients, without affecting the implementation of surgical techniques, to avoid patients being left without insurance coverage.

To reduce psychological problems in transplant recipients, the most effective solution is to achieve the ideal state of XTx technology without sequelae. However, we need to move beyond idealization and propose more comprehensive solutions. Research on immature defense mechanisms shows that individuals facing greater stress from negative life events are more likely to use immature defense mechanisms<sup>[19]</sup>. Therefore, besides excluding uncontrollable factors of potential complications, transplant patients should be provided with sufficient life care and support. Sensitizing patients to positive living conditions will encourage them to use mature psychological defense mechanisms for self-regulation. Additionally, specific analysis and research on the paths of psychological problems in transplant recipients should be conducted, and professional psychological knowledge should be used for resolution. It is worth noting that patients with severe psychological disorders may require further consideration for medication. Their adaptability to medication should be assessed to avoid causing further physiological harm, such as hallucinations and delirium, while addressing the psychological problems of recipients.

### 3.3. Solutions at the Social Level of Recipients

Firstly, effective reduction of social exclusion can be achieved by accelerating self-integration into society. Research indicates that individuals can regulate themselves by increasing self-awareness. However, those rejected by society often do not actively strive to increase their self-awareness<sup>[20]</sup>. Therefore, patients can be encouraged to start working or participate in public welfare activities as soon as possible to find a sense of presence and value in society, promoting active integration into society. Secondly, we should promote social acceptance. A key aspect of social acceptance is to improve society's acceptance of XTx. Unlike the acceptance discussed earlier, this refers to the non-transplantation social population, including family members, friends, medical

personnel, colleagues, etc. Due to the complexity of social structures, such as differences in religion, educational background, and thinking patterns, we can only strive to ensure that XTx technology applications and effects are within the acceptable range of the majority of humanity to increase social acceptance levels. As long as the acceptance rate predominates, it will effectively address social exclusion issues. Finally, we need to anticipate relevant social system issues in advance, synchronize the formulation and improvement of systems that affect transplant recipients, and continually improve them in the later stages. For example, establish relevant blood donation systems for transplant recipients to reduce their sense of exclusion in social life and prevent the marginalization of the transplant population due to institutional exclusion.

Regarding the issue of high costs, although research on new technologies does incur substantial costs, compared to allogeneic organ transplantation, XTx has the advantage of a larger donor pool. Only by ensuring that the costs of XTx are reasonable and acceptable to the general patient population can the widespread clinical application of new technologies be promoted. Therefore, relevant personnel need to comprehensively assess XTx expenses to minimize the impact of economic factors on transplantation rights and prevent high-income patients from dominating essential resources. Additionally, fair distribution of transplant rights should be reinforced through institutional guarantees and legal safeguards. On one hand, systems should be formulated and implemented to maintain fair transplantation rights and increase awareness among transplant populations to prevent patients from missing transplantation opportunities due to lack of understanding of relevant systems. On the other hand, strong laws and regulations should be enacted to provide legal support for patients to maintain personal transplantation rights while regulating the XTx market to prevent medical personnel from profiting from the public and commercializing transplantation technology. Of course, as XTx technology advances, social supervision must be strengthened accordingly to strictly prevent the utilitarian use of transplantation.

#### 4. Conclusions

The original intention of XTx technology development is to address the shortage of organ supply, thereby saving human lives and benefiting human society. However, various problems are inevitable during the development stage. A crucial aspect of humanity, distinct from other species, is civilization. Therefore, besides life itself, we must follow the footsteps of clinical research and discuss and explore ethical and moral issues related to XTx, and propose solutions. The use of the Biopsychosocial Medical Model for analysis will make the issues clearer and more comprehensive. This model not only provides perspectives from biology, psychology, and society but also includes the connections between them. It is precisely this chain-like impact that indicates we should treat ethical issues with rigorous attitudes. Moreover, because recipients are the "protagonists" of transplantation, benefiting from it while bearing the greatest risks, this paper mainly discusses the ethical issues of XTx recipients from the perspective of the Biopsychosocial Medical Model. This includes issues such as human integrity, consciousness and personality changes, psychological cognition and acceptance levels, psychological adaptation, social exclusion, and fair distribution of transplantation rights. Corresponding solutions are provided, including establishing personality databases, disseminating relevant knowledge, strengthening medical insurance protection, and providing humanistic care, among others. In addition to the above ethical issues, there are many other ethical issues related to XTx, such as animal rights, theological and religious perspectives, and attitudes. These require scholars from various professional fields to conduct research and discussions on relevant issues. It is hoped that through the joint efforts of scholars from all sectors of society, we can gradually realize the rationalization of XTx in the ethical field, thereby promoting the comprehensive development of XTx and striving to provide higher quality of life

while saving and extending the lives of patients, thus realizing the inherent value of life.

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