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Abstract

The shortage of donor organs for transplantation is an international problem. One promising option to meet the need is xenotransplantation (XTx; e.g. pig-to-human). However, there are still questions surrounding XTx that must be answered before proceeding to clinical trials. The current work is a meta-analysis of articles published between 1985-2019 to analyze the factors most strongly associated with agreement and opposition towards the procedure. Although 80% (41/51) of the published studies were related to the opinions of patients, only three provided sufficient data for analysis. Thus, the bulk of what we really know about attitudes towards XTx comes from students, stakeholders, and hospital staff. The findings suggest that, before proceeding from the laboratory to clinical trials, more directed research is necessary from individual programs to achieve sufficient understanding of the attitudes of patients and the broader public, and the level of risk that is acceptable to these groups.

Key words: meta-analysis; public perceptions; xenotransplantation; medical professional perceptions

Abbreviations: xenotransplantation (XTx); Cumulative Index of Nursing and Allied Health (CINAHL); Odds Ratios (ORs);

Introduction

Given the shortage of organ donors, and the ever-increasing number of individuals needing organ transplantation, a worldwide dilemma for clinicians exists. Numerous approaches to address the donor organ shortage are currently under consideration. Xenotransplantation (XTx) (genetically-engineered pig-to-human) is one of the options that could potentially provide an endless supply of organs for patients with end-stage organ disease. However, there are still questions surrounding XTx that must be answered before proceeding to clinical trials and routine practice of the procedure.

Although porcine tissue has been used in numerous other medical treatments and procedures (1-7), no whole organ transplants have yet occurred. While the social impact of these tissue-only procedures has been minimal, with only limited concerns expressed by patients or the broader public, the acceptability of whole organ XTx is uncertain.

The importance of fully engaging the public prior to clinical testing has historical precedent. In 2002 and 2004, public consultations on XTx in Australia were flawed in both their design and process. By pre-emptively suggesting a desired outcome for XTx to be ‘allowed to proceed’, they failed in their ability to meaningfully engage and involve the citizens. This approach resulted in a complete moratorium on clinical trials of animal-to-human organ transplantation in Australia until 2009 (8).

The results of some of the more well-known prior XTx efforts have not always resulted in a positive perception about the procedure. One of the most controversial moments not only in XTx, but in medical history, which caused opposition by animal rights advocates, and some ethicists, theologians, scientists, and a section of the

medical community, occurred when surgeon Leonard Bailey transplanted a baboon heart into an infant known as Baby Fae (9). The fact that XTx efforts were attempted in the early part of the 20th century outside of any trial, proper navigation of any XTx clinical trial will be of utmost importance (10). Although nothing can be done about the prior actions, this does illustrate the importance of proper preparation to address the medical, as well as patient and public, beliefs and attitudes prior to the initiation of XTx clinical trials.

Understanding the basic science of XTx, and selection of the initial patients are both crucial to maximizing a successful XTx clinical trial. According to the World Health Organization (WHO) and the International Xenotransplantation Association (IXA), it is important to evaluate and determine if the existing knowledge is sufficient to recruit patients, with the reasonable expectation that the public is in full agreement to do so (11).

The purpose of the current meta-analysis is to combine and analyze data from several related, but independent, studies. Meta-analysis allows researchers to increase the sample size and statistical power, and to combine statistics from several studies to produce a single statistical test of significance for the entire body of literature that may have gone undetected in single papers (12-13). This allows researchers to form ideas about the overall effects. This being said, there are limitations to meta-analyses, such as the heterogeneity of subjects and conflicting data between studies (14).

To our knowledge, no meta-analysis of the social aspects and opinions concerning XTx exists. The goal of the present meta-analysis is to analyze the current data regarding the opinions of patients, physicians, and nurses to XTx. A primary goal

was to identify the factor most strongly associated with agreement with, or opposition towards, the procedure. Given the international interest, current literature involves citizens from various countries across the world. A secondary goal was to identify which aspects (psychosocial, religious, or medical) were most responsible for their perception about the procedure. The psychosocial challenges surrounding the patients in need of an organ and how it will impact their lives is of vital importance. This also extends to the medical staff who will care for these patients. Caring for future XTx patients will require a multidisciplinary team, with a comprehensive appreciation for psychosocial well-being.

Methods:

PubMed and Cumulative Index of Nursing and Allied Health (CINAHL) databases were searched for potential articles published between 1985 and 2019, inclusive. The search terms used were psychosocial factors, psychosocial, theological, ethical, and moral attitudes, and public perceptions to identify studies specifically related to patient, nursing, and physician attitudes to XTx. The initial review produced >200 references regarding patient, medical personnel, and the public attitudes, perceptions, concerns, or level of risk they would accept (Figure 1). Only a relatively small number of those studies resulted in peer-reviewed articles, most of them theoretical or value-based in nature. Of those published, some were in foreign languages, which resulted in only 51 being available through the university reference library. Of these, 41 surveyed patients, 9 surveyed nurses, and 1 surveyed physicians. Abstracts, articles published in foreign languages, and those that could not be located through the university online library services were excluded, a total of 19 papers were available and considered for meta-analysis.

Preliminary review of the 19 studies being considered, presented with considerable independent variable heterogeneity, and exhibited significant variability in the questions asked (15-34). However, the majority reported that, among those surveyed, >50% supported XTx (16-18, 20-24, 27-31, 33-34), with a range from a low of 37% (18) to a maximum of 83% (32). Of the 19 data-based studies, 12 were considered for inclusion in this study, but only eight provided original data in a usable format for meta-analysis (15, 20, 23, 26, 30-31, 33-34). Two of the 12 articles (22,32) were excluded because the data were very similar to attitudes toward xenotransplantation in other articles. Another article (21) was excluded because the data and population were the same as those presented in a previously published study. One study (16) was excluded because data on attitudes toward xenotransplantation were not specific enough to be analyzed. For example, key data were presented as follows "Assuming the xenograft could be transplanted with equal success as a human graft, more than 50% of both waiting list and transplant patients stated that they would readily accept a xenograft..." (p. 387). of those 19 articles yielded 8 that contained data that could be used to calculate effect sizes (Table 1).

Data were extracted and entered into Comprehensive Meta-Analysis 2.0 (CMA 2.0) for calculation of effect sizes. Data were reported in a variety of ways. Some of the studies reported findings through means and standard deviations, others correlations, while some listed Odds Ratios (ORs). Some data were presented as simple count data; for example, reporting the number of those in favor of XTx versus those not in favor. All data were converted to ORs for consistency, ease of interpretation, and as a

measure of effect size. Data extracted included a heterogeneous mixture of independent and dependent variables and corresponding statistics.

The study population column within Tables 2 and 3 were classified as either students, patients, professionals, public, hospital staff, or stakeholders. The comparison /independent variable (IV) column compared the dependent variable, in favor of XTx (Table 2) or not in favor (dis-favorability) towards XTx (Table 3). Confidence interval (CI) data were presented and reflects the level of heterogeneity of variance that was influenced by varying sample sizes. The null hypothesis was that the OR was 1, or the odds of favoring XTx were equal to the odds of not favoring XTx. The Z statistic is a measure of standard deviation units from the mean. The p value was a measure of the probability of having an odds ratio that is due to chance alone, and reported for those values <0.05.

Following calculation of effect sizes by CMA 2.0, data were tabulated and sorted according to effect size. ORs were sorted in descending order so that variables with the largest effect sizes in support of XTx were near the top (Table 2). Table 3 shows ORs sorted in ascending order, to highlight the relationships that are predictive of dis-favorability towards XTx.

Results:

The eight studies reflect a very diverse geographic area as reported in Table 1. Each of the studies provided the types of study participants, demographic information, followed by religion and perceived medical results. After that there was a great deal of heterogeneity about the questions, their format, and authors area of interest.

Table 2 presents the odds ratios in descending order for the variables that indicate their presence will result in support for XTx. The most important factors were: (i) personal experience with transplant (OR=16.8, p<0.01); (ii) perceived benefit of XTx (OR=9.83, p<0.01); (iii) partner's favorable attitude toward XTx (OR=5.80, p<0.01); (iv) area of the country in which the participant lived (OR=4.27, p<0.01); (v) favorable attitude of one's religion toward XTx (OR=3,22, p<0.01); (vi) a favorable attitude toward cadaveric donation (OR=2,58, p<0.01); and, (vii) whether or not one was a current organ donor (OR=2.48, p<0.01).

To illustrate the heterogeneity found in the independent variables studied, additional variables included: (i) year in school (i.e., students in advanced years were consistently more positive toward XTx than were students in earlier years-multiple comparisons); (ii) whether or not one had discussed treatment with the family; (iii) marital status; (iv) whether or not one might possibly need a transplant to cure an existing illness; (v) physicians vs. healthcare assistants; (vi) willingness to accept pig cells to cure an existing illness; (vii) favorable attitude toward cadaveric donation; (viii) status as a current organ donor; (ix) gender, (x) area of the country in which the participant lived; and (xi) several other demographic variables..

Table 3 presents the same odds ratio comparison, except from the perspective of the variables presence indicates less support for XTx. The belief that a porcine xenograft might alter one's self-image suggested the least support for XTx (i.e. OR=0.12, p<0.01). This effect was paralleled by a significant and inverse relationship (OR=0.23, p>0.01) between increased moral concerns and less approval of XTx. Comparison of income to expense, and perceived medical risk were also high in this list

of inverse relationships. The table also shows that year of education for nursing students (i.e., 3rd vs. 4th.) and physician status (professional vs. trainee) were inversely associated with less supportive attitudes toward XTx.

Variables that were not significantly associated with attitude toward XTx included education (OR=1.92, p=0.055), employment status (O =1.14, p=0.62), marital status (OR=1.17, p=0.19), and religion (OR=0.90, p=0.37). Only one of the included studies reported usable education-level data (30). From that study, odds ratios, calculated for each comparison, were as follows. On porcine xenotransplants, the high school versus university comparison yielded a non-significant odds ratio (OR=0.60, p=0.452). Similarly, primary and secondary vs. high school students, rating attitudes toward porcine xenotransplants did not significantly differ (OR=0.22, p=0.200). Primary and secondary students versus university-level participants on porcine xenotransplants were not significantly different at the .05 level (OR=0.13, p =0.057). Results on attitudes toward bovine xenotransplants were similarly non-significant across all three education-level comparisons.

Only one study reported usable data pertaining to employment status (31). Neither attitudes toward bovine xenotransplants nor attitudes toward porcine xenotransplants produced significant odds ratios (Bovine, OR=1.027, p=0.927; Porcine, OR=1.612, p=0.375). However, the combined effect of age did produce a significant combined test statistic (reported above).

Two studies reported usable data pertaining to the relationship between marital status and attitude toward XTx (20,31). The combined effect for these studies was not

statistically significant (OR=1.17, p=0.19). Religion, religious attitudes, and religious beliefs failed to produce a combined, significant effect on attitudes toward XTx (OR=0.90, p=0.37).

Discussion:

The initial review of the selected works presented with several issues that made a thorough and complete meta-analysis problematic.

First, the limited number of articles available for review was the most challenging factor encountered. Although there is no minimum or maximum number of studies necessary to conduct a valid meta-analysis, in this case the paucity of available studies reflected an absence of in-depth information, rather than the limitation of the procedure itself.

Second, the data presented, in most cases, were not in a format that lent itself to further comparative analysis. In some cases, only the most basic percentages were reported.

Third, the lack of any standardized approach to questioning respondents regarding their opinions. For example, of the final eight articles included in the meta-analysis, religiosity was addressed from several different perspectives: (i) one series of articles asked if the participant was Catholic, non-Catholic, or other (20,30,34); (ii) one article included four items pertaining to religiosity and moral concerns that were measured on a seven-point Likert scale (33); (iii) one article used a standardized religious fundamentalism scale (31); while (iv) another group coded religion as yes or no without showing the form of the questionnaire item (i.e., how the question was asked) (26). A bigger concern about the questions asked revolves around genetic

engineering. Only three of the studies reviewed had specific questions regarding genetic engineering. Here too, the nature of the questions were problematic making a cross-comparison extremely difficult.

All of these factors posed significant limitations for both comparing individual study data, and the amount of generalized information that can be drawn from it. The real irony of the meta-analysis was that, although 80% (41/51) of the published studies were of patients, only three included enough patient data to be included within the final meta-analysis (15,23,31) . Thus, the minority of studies were of students, stakeholders, and hospital staff, and it was these groups that provided the bulk of what we know about those who are in support of XTx as found in Table 2.

The same logic applies to the findings in Table 3, or those factors associated with a lack of support for XTx. Only two studies produced significant odds ratios about patient views that failed to support XTx (preferred human-to-dog and pig liver; and income to expense ratio, respectively) (23,31). All the other factors found significantly less likely to support XTx were among students, stakeholders, or hospital staff.

To date, numerous studies have been conducted and reported about patient attitudes and beliefs, but the bulk of the information that was useful for meta-analysis related to what ‘non-patients’ believe. The question then becomes, how reliable is any meta-analysis about patient views that include only three studies? More importantly, information about the broader public views and perceptions is almost non-existent when comparisons were attempted through meta-analysis.

When considered within the context of the WHO and IXA guidelines, we would suggest that, based on the current literature, there is insufficient information available

for an individual team to initiate clinical trials. In other words, before proceeding from the laboratory to the clinic, much more directed research is necessary by the individual program to identify patients, medical staff, and the broader local public's views, reactions, and level of risk they are willing to accept, prior to the conducting of clinical trials.

The findings from this work do not suggest the inadequacy of meta-analysis as a viable tool in preparation for clinical trials. In fact, they clearly indicate otherwise. It is reasonable to conclude that we do not have the depth of understanding about patient, public, and professional staff attitudes towards XTx as we may think. This is not an indictment of the existing work, but may be an indication of the need to use a more standardized and systematic approach is necessary to explore and report XTx perceptions and attitudes. The current analysis reflects that there are research groups who have already done so, and this may prove to be increasingly important as XTx moves from the laboratory to clinical trials.

References:

1. Buchbinder D, Buchbinder SB. Wound healing: adjuvant therapy and treatment adherence. *Venous Ulcers.* 2007: 91-93.
2. Carter JE, Holmes IV JH. The surgical management of burn wounds. *Skin tissue engineering and regenerative medicine.* 2016: 295-299.
3. Imahara SD, Klein MB. Skin Grafts. *Biomaterials for Treating Skin Loss*. 2009:72-77..
4. Herford AS, et al. Bone grafts and bone substitute materials. *Principles and practice of single implant and restorations.* 2014:80-86. .
5. Rogers JP, et al. Rotator Cuff Augmentation. *Biologics in Orthopaedic Surgery.* 2018:69-74.
6. Yun Shin S, et al. Periodontal Regeneration. *Stem Cell Biology and Tissue Engineering in Dental Sciences.* 2014:461-467.
7. Valdes-Gonzalez R, Rodriguez-Ventura AL, White DJ, et al. Long-term follow-up of patients with type 1 diabetes transplanted with neonatal pig islets. *Clin Exp Immunol.* 2010;162(3):537-542.
8. Cook PS. What constitutes adequate public consultation? Xenotransplantation proceeds in Australia. *Bioeth Inq*. 2011;8:67-70.
9. Daar AS. Analysis of factors for the response to xenotransplantation. Ann NY Acad Sci. 1998; 862:222-233.
10. Taniguchi S. Cooper DKC. Clinical xenotransplantation: Past, present, future. *Ann R Coll Surg Engl*. 1997:79(1);13-19.

11. Paris W, Mitchell C, Werkheiser Z, Lipps A, Cooper DKC, Padilla L. Public Perspectives Towards Clinical Trials of Organ Xenotransplantation. . In: Pathways to Clinical Xenotransplantation. David KC Cooper, ed. In press.
12. Egger M, Smith GD, Sterne JAC. Uses and abuses of meta-analysis. *Clinical Medicine.* 2001;1(6):478-84.
13. Gendelberg D, Slattery CA, Verma K. Guidelines on how to perform a meta-analysis in spine surgery: strengths and weaknesses of design. *Clin Spine Surg.* 2019;32(1):30-1.
14. Pace NL. Research methods for meta-analyses. *Best Practice & Research Clinical Anaesthesiology.* 2011;25(4):523-33.
15. Persson MO, Persson NH, Ranstam J, Hermeren G. Attitudes towards xenotranslantation-patients waiting for transplantation versus general public. *Transplan Int* 2001:14;334-342.
16. Schlitt HJ, Brunkhorst R, Haverich A, Raab R. Attitude of patients toward transplantation of xenogeneic organs. *Langenbecks Arch Surg*. 1999;384:384-391.
17. Deschamps JY, Roux FA, Gouin E, Sai P. Reluctance of French patients with type 1 diabetes to undergo pig pancreatic islet xenotransplantation. *Xenotransplantation* 2005;12:175-180.
18. Long T, Wray J, Myers L, Banner N. Attitudes of potential candidates for heart and heart-lung transplantation to xenotransplantation. *Prog Transplant*. 2002;12:280-228.

19. Kranenburg LW, Kerssens C, Ijzermans JN, Zuidema W, Weimar W, Busschbach JJ. Reluctant acceptance of xenotransplantation in kidney patients on the waiting list for transplantation. *Soc Sci Med*. 2005;61:1828-1834.
20. Rios A, Conesa C, Ramirez P, et al. Attitude toward xenotransplantation among residents. *Transplant Proc*. 2006;37:4111-4116
21. Persson OM, Persson NH, Ranstam J, Hermeren G. Xenotranslantation pubic perceptions: rather cells than organs. *Xenotransplantation* 2003:10, 72-79.
22. Mikla M, Rios A, Lopez-Navas A, et al. Looking for new alternatives:What nursing students of Lodz's medical University in Poland think about the use of organs coming from animals. *Transplant Proc* 2016: 48, 2476-2478.
23. Rubaltelli E, Burra P, Sartorato V, et al. Strengthening acceptance for xenotransplantation: the case of attraction effect. *Xenotransplantation*. 2008;15(3):159-63. doi:10.1111/j.1399-3089.2008.00474.x
24. Rios A, Martinez-Alcaron L, Sanchez J, et al. Population study about the attitude toward organ xenotransplantation in the population from Eastern Europe resident in southeast Spain. *Int J Artif Organs*. 2010;33:30-39.
25. Rios A, Martinez-Alcaron L, Ayala-Garcia MA, et al. Level of acceptance of a clinical solid organ xenotransplantation program among personnel in organ transplant-related services in Spanish, Mexican, and Cuban hospital centers. *Transplant Proc*. 2010;42(1):222-7. doi:10.1016/j.transproceed.2009.11.007.
26. Abalovich A, Matsumoto S, Wechsler CJ, et al. Level of acceptance of islet cell and kidney xenotransplants by personnel of hospitals with and without

experience in clinical xenotransplantation. *Xenotransplantation*. 2017: DOI: 10.1111/xen.12315.

27. Martinez-Alarcon L, Rios A, Pons JA, et al. Attitudes toward islet cell and tissue xenotransplantation among kidney and liver patients no the transplant waiting list. *Transplant Proc.* 2010;42:3098-3101. doi:10.1016/j.transproceed.2010.05.071.
28. Rios A, Febrero B, Lopez-Navas A, et al. Xenotransplantation of cells for diabetes: Is there a good acceptance rate among Spanish adolescents? *Transplant Proc.* 2011;43:55-57. doi:10.1016/j.transproceed.2010.11.007.
29. Martinez-Alarcon L, Rios A, Pons JA, et al. Attitudinal study of organ xenotransplantation in patients on the kidney and liver transplant waiting list in a country with a high rate of deceased donation. *Xenotransplantation*. 2011;18:168-175. doi:10.1111/j.1399-3089.2011.00673.x.
30. Mikla M, Rios A, Lopez-Avas A et al. Attitude of nursing students at the University of Lublin Poland toward xenotransplantation. *Transpl Proc* 2015:47;2583-2586.
31. Gungormus Z, Gungormus M. Effects of religious beliefs in selecting graft materials used in oral and maxiofacial surgery. Am Association of Oral and Maxiofacial Surgeons. 2017. Found at http://dx.doi.org/10.1016/i.joms.0217.07.160.
32. Rubaltelli E, Burra P, Canova D, et al. People's attitude toward xenotransplantation: affective reactions and the influence of the evaluation context. *Xenotransplantation* 2009:16; 129-134.

33. Amin L, Hashim H, Mahadi Z, Che Ngah A, Ismail K. Determinants of stakeholders' attitudes to xenotransplantation. *Xenotransplantation*.2018;25(6):e12430. doi:10.1111/xen.12430
34. Martinez-Alarcon L, Rios A, Santaines-Borreda E, et al. Student nurses at Spanish universities and their attitude toward xenotransplantation. *Xenotransplantation*. 2019;e12507. doi:10.1111/xen.12507.

Figure 1. Article Screening and Elimination Process

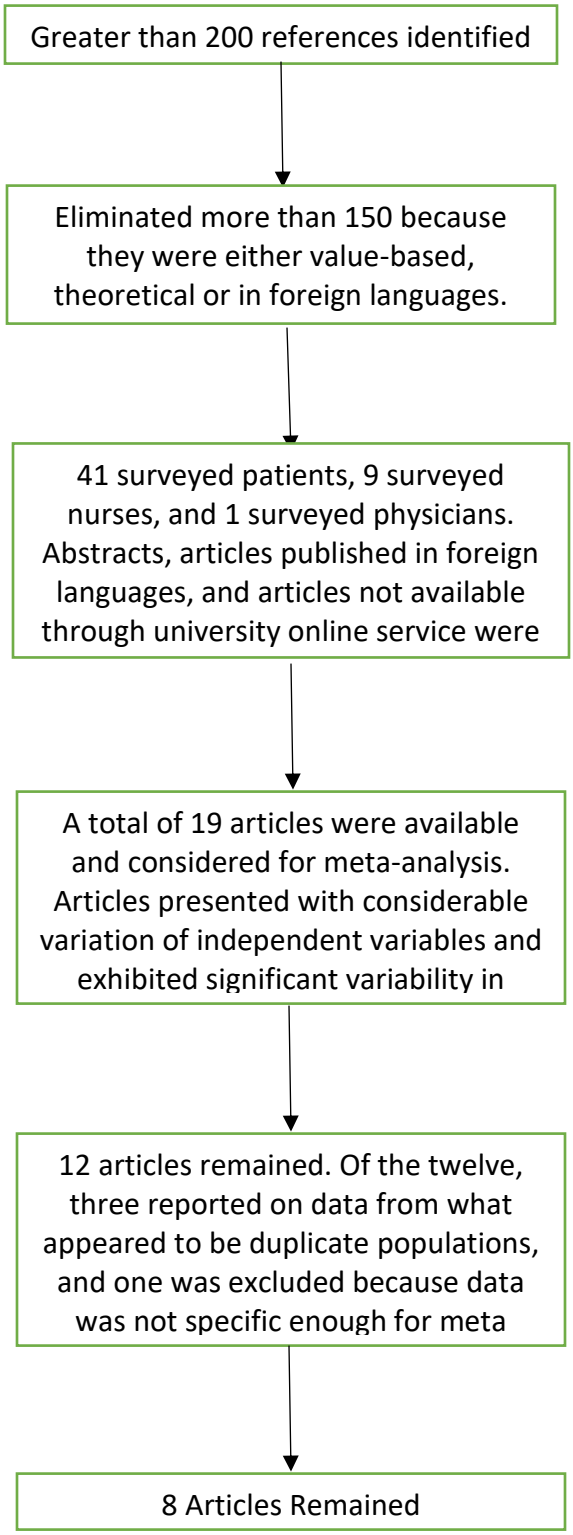
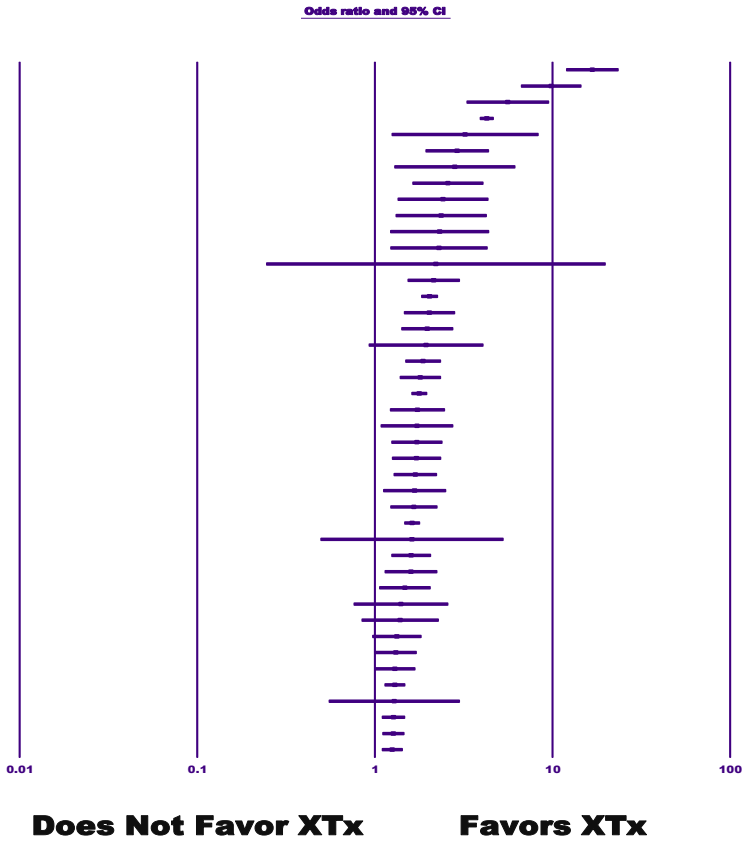


Table 1: Studies used for meta-analysis on attitudes to xenotransplantation

Country	N	Authors	(n=)
Spain	2	Rios, et al., 2006,	1,398
		Martinez-Alarcon 2019	8,913
Italy	1	Rubatelli, et al., 2008	271
Poland	1	Mikla, et al., 2015	325
Sweden	1	Persson, et al., 2001	994
Argentina	1	Abalovich, et al., 2017	104
Malaysia	1	Amin, et al., 2018	469
Turkey	1	Gungormus & Gungormus, 2017	203

Table 2: Odds Ratios for Independent Variables and Positive Attitudes Toward Xenotransplantation

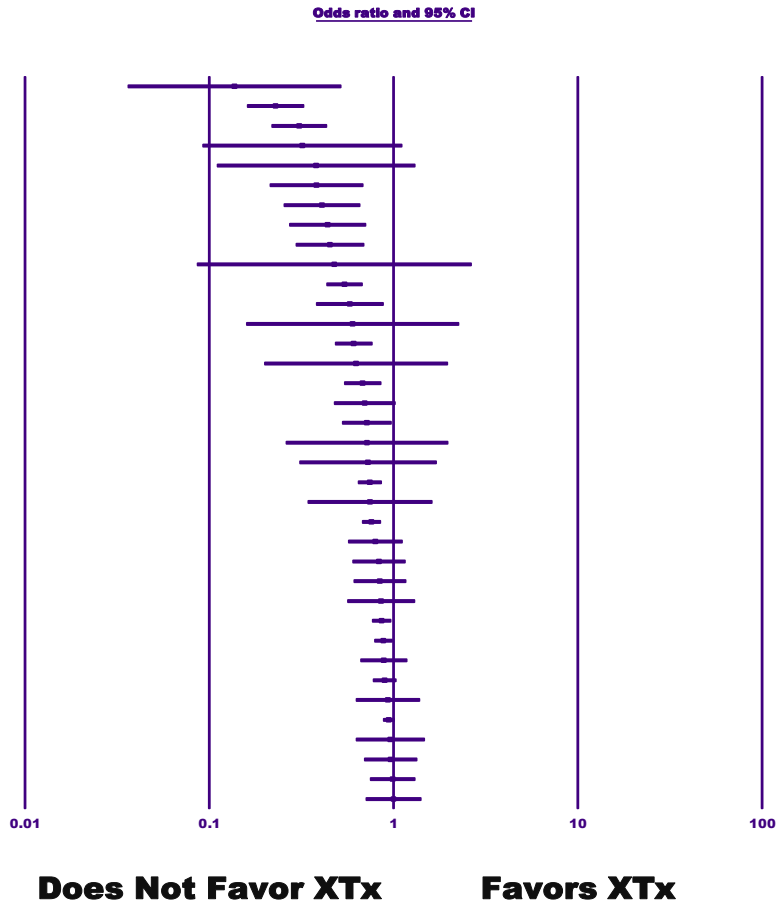
Study	Comparison	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Rios	Personal Experience with Donation	16.8	12.0	23.5	16.3	0.0
Amin	Perceived Benefit	9.8	6.7	14.5	11.5	0.0
Rios	Partner In favor of Xtx	5.6	3.3	9.5	6.3	0.0
Martinez	Eastern vs Northeastern	4.3	3.9	4.7	32.1	0.0
Rios	Religion In favor of Xtx	3.2	1.2	8.3	2.4	0.0
Rios	Physicians vs Assistants	2.9	1.9	4.4	5.1	0.0
Abalovich	E. P. vs T. (Cure Diabetes)	2.8	1.3	6.2	2.6	0.0
Mikla	Favors cadaveric donation	2.6	1.6	4.1	4.0	0.0
Mikla	Fourth Year vs. Other	2.4	1.3	4.4	3.0	0.0
Abalovich	E. P. vs T. (Accept Pig Kidney)	2.4	1.3	4.3	2.9	0.0
Abalovich	E. P. vs T. (Improve Diabetes)	2.3	1.2	4.4	2.6	0.0
Mikla	Nursing Course: Fourth vs. Fifth	2.3	1.2	4.3	2.6	0.0
G & G	Insured vs. Uninsured	2.2	0.2	19.9	0.7	0.5
Amin	Biotechnology Engagement	2.1	1.5	3.0	4.4	0.0
Martinez	Central vs Northeastern	2.0	1.8	2.3	12.9	0.0
Rios	Physicians vs. Ancillary Personnel	2.0	1.5	2.8	4.2	0.0
Amin	Attitude to Nature	2.0	1.4	2.8	4.0	0.0
Mikla	Social Interaction: Partner Opinion	1.9	0.9	4.1	1.8	0.1
Martinez	Second vs Third	1.9	1.5	2.4	5.4	0.0
Rios	Sex (Comp 1 = Male, Comp 2 = Female)	1.8	1.4	2.4	4.4	0.0
Martinez	Discussed this with family (yes vs no)	1.8	1.6	2.0	11.3	0.0
Rios	Physician vs Nurses	1.7	1.2	2.5	3.1	0.0
Rios	Prosocial voluntary activities	1.7	1.1	2.8	2.3	0.0
Persson	Diabetes and could be cured	1.7	1.2	2.4	3.2	0.0
Persson	Parkinson's disease could be improved	1.7	1.3	2.4	3.3	0.0
Persson	Patients vs Public: Human organ not available.	1.7	1.3	2.2	3.7	0.0
Rios	Nurses vs Healthcare Assistants	1.7	1.1	2.5	2.5	0.0
Persson	Animal Heart: Same Result and Risk	1.7	1.2	2.2	3.3	0.0
Martinez	Discussed with friends (yes vs no)	1.6	1.5	1.8	9.4	0.0
G & G	Urban vs. Rural	1.6	0.5	5.3	0.8	0.4
Martinez	Eastern vs. Central Area	1.6	1.2	2.1	3.6	0.0
Martinez	Central vs. Northern Area	1.6	1.1	2.2	2.7	0.0
Persson	Public: Human organ not available.	1.5	1.1	2.1	2.3	0.0
Rios	Hospital Professionals vs Control Group	1.4	0.8	2.6	1.1	0.3
Mikla	Nursing Course: Second vs. Third	1.4	0.8	2.3	1.3	0.2
Rios	Medical vs Ancillary Services	1.3	1.0	1.8	1.8	0.1
Rios	Single vs. Married	1.3	1.0	1.7	2.0	0.0
Persson	Animal Kidney Greater Result and Risk	1.3	1.0	1.7	1.9	0.1
Martinez	Eastern Area vs Northern Area	1.3	1.1	1.5	3.8	0.0
G & G	Employed vs. Unemployed	1.3	0.6	3.0	0.6	0.6
Martinez	Age: In favor, Not in favor	1.3	1.1	1.5	3.2	0.0
Martinez	Catholic vs, Non Practicing Catholic	1.3	1.1	1.5	3.3	0.0
Martinez	Possibly need transplant	1.3	1.1	1.4	3.3	0.0



Odds Ratios are sorted from high to low

Table 3: Odds Ratios for Independent Variables and Negative Attitudes Toward Xenotransplantation

Study name	Independent Variable	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Rubatelli	Animal vs. Human Liver	0.1	0.0	0.5	-2.9	0.0
Amin	Perceived moral concern	0.2	0.2	0.3	-8.2	0.0
Amin	Perceived risk	0.3	0.2	0.4	-6.7	0.0
Rios	Surgical vs infant maternity	0.3	0.1	1.1	-1.8	0.1
Rios	Medical vs infant maternity	0.4	0.1	1.3	-1.5	0.1
Mikla	Nursing course: third vs. fourth	0.4	0.2	0.7	-3.2	0.0
Rios	Temporary vs MIR	0.4	0.3	0.7	-3.7	0.0
Rios	Contract vs. Resident	0.4	0.3	0.7	-3.4	0.0
Rios	Permanent vs MIR	0.5	0.3	0.7	-3.7	0.0
G & G	Prim. & Sec. vs. HS	0.5	0.1	2.7	-0.8	0.4
Martinez	Partner's opinion about ODT	0.5	0.4	0.7	-5.3	0.0
Rios	Age	0.6	0.4	0.9	-2.5	0.0
G & G	Highschool vs. university	0.6	0.2	2.3	-0.8	0.5
Martinez	Southern vs northeastern area	0.6	0.5	0.8	-4.2	0.0
G & G	Eq. vs. More Inc. to Exp.	0.6	0.2	2.0	-0.8	0.4
Martinez	Publically vs privately funded	0.7	0.5	0.9	-3.3	0.0
Rios	Medical vs. Ancillary	0.7	0.5	1.0	-1.8	0.1
Rios	Professionals vs public	0.7	0.5	1.0	-2.1	0.0
G & G	Eq. vs. Low Inc to Exp	0.7	0.3	2.0	-0.6	0.5
G & G	Marital status	0.7	0.3	1.7	-0.7	0.5
Martinez	First vs second	0.7	0.6	0.9	-3.9	0.0
Mikla	Male vs. female	0.7	0.3	1.6	-0.7	0.5
Martinez	Southern vs northern area	0.8	0.7	0.9	-4.6	0.0
Mikla	Knowledge and attitudes	0.8	0.6	1.1	-1.3	0.2
Amin	Religious belief levels	0.8	0.6	1.2	-1.1	0.3
Rios	Surgical vs medical	0.8	0.6	1.2	-1.0	0.3
Rios	Infant maternity vs central lab	0.9	0.6	1.3	-0.7	0.5
Martinez	Yes vs. no	0.9	0.8	1.0	-2.5	0.0
Martinez	Yes, in favor vs yes, against	0.9	0.8	1.0	-2.2	0.0
Persson	Attitude toward animal heart	0.9	0.7	1.2	-0.8	0.4
Martinez	First vs third	0.9	0.8	1.0	-1.5	0.1
Rios	Temporary vs contract	0.9	0.6	1.4	-0.3	0.7
Martinez	In favor vs. not in favor	0.9	0.9	1.0	-1.6	0.1
Rios	Surgical vs. central laboratory	1.0	0.6	1.5	-0.2	0.9
Mikla	Discuss Xtx with family	1.0	0.7	1.3	-0.2	0.8
Rios	Not related vs. related to tx	1.0	0.7	1.3	-0.1	0.9
Rios	Maternity vs ancillary staff	1.0	0.7	1.4	0.0	1.0



Odds Ratios are sorted from low to high