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REVIEW ARTICLE

Exploring attitudes toward xenotransplantation: A scoping review of healthcare workers, healthcare students, and kidney patients

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Abstract

Background: Recent advances mean that formal clinical trials of solid organ xenotransplantation are increasingly likely to begin and patients requiring a kidney transplant could be the first participants. Healthcare workers and healthcare students constitute the current and future workforce that will influence public opinion of xenotransplantation. The attitudes of these populations are important to consider before recruitment for formal clinical trials begins.

Methods: This scoping review was reported according to the PRISMA extensions for scoping reviews checklist and the Joanna Briggs Institute methodology for scoping reviews. The Scopus, PubMed, and ScienceDirect databases were searched to identify articles that studied the attitudes of healthcare workers, healthcare students, or kidney patients toward xenotransplantation.

Results: The search generated 816 articles, of which 27 met the eligibility criteria. The studies were conducted in 14 different countries on five different continents. Participants from the 27 studies totaled 29,836—this was constituted of 6,223 (21%) healthcare workers, 21,067 (71%) healthcare students, and 2,546 (8%) kidney patients. All three groups had an overall positive attitude toward xenotransplantation. However, in studies where participants were asked to consider xenotransplantation when the risks and results were not equal to allotransplantation—the overall attitude switched from positive to negative. The results also found that Spanish-speaking populations expressed more favorable views toward xenotransplantation compared to English-speaking populations.

Conclusion: The results of this review suggest that while attitudes of the three groups toward xenotransplantation are—on the face of it—positive, this positivity deteriorates when the risks and outcomes are framed in more clinically realistic terms. Only formal clinical trials can determine how the risks and outcomes of xenotransplantation compare to allotransplantation.

KEYWORDS
attitudes, clinical trials, patients, risk, xenotransplantation

1 | INTRODUCTION

The lack of suitable donor organs has presented a problem ever since Joseph Murray performed the first successful kidney transplant in 1954.[1] While sourcing and transplanting solid organs from non-human animals was first attempted over 100 years ago, for a variety of reasons these experiments were unsuccessful. However, more recent scientific and clinical advances have led to renewed optimism about its potential. Since 2021, several kidneys and hearts from genetically engineered pigs have been transplanted into brain-dead human subjects for varying periods between three days and two months.[2–5] The rationale for conducting these kinds of studies has been to gather preliminary clinical information that involves living patients before initiating xenotransplantation clinical trials. In 2022 and 2023, two patients received pig heart xenografts, resulting in the patients living for eight and six weeks, respectively.[6–8] Progress is likely to continue for the foreseeable future in the hope that formal clinical trials of xenotransplantation can begin.

This review focuses on the following research question—"What is known about the attitudes of healthcare professionals, healthcare students, and kidney patients toward xenotransplantation?" Because the research question was broad and exploratory, and the purpose was to map and summarize the existing evidence, a scoping review approach was adopted. The objective was to understand how relevant stakeholders viewed xenotransplantation. These three groups were chosen because they all have a stake in the success of clinical xenotransplantation. First, healthcare workers and healthcare students constitute the current and future workforce that can impact, influence, and drive the public's health literacy and clinical decision-making. Furthermore, if formal clinical trials in xenotransplantation are approved, these persons will be responsible for caring for xenograft recipients. Second, it is important to understand the attitudes of patients in need of a kidney transplant—because whether they are willing to accept a xenotransplant will influence the extent to which xenotransplantation can address the shortage of kidneys for transplantation. A focus on patients requiring a kidney transplant is justified for two additional reasons: (i) they constitute the vast majority of patients on the organ transplant waitlist; and (ii) kidneys are a suitable organ for formal clinical trials because, if complications arise, the xenograft can be removed and renal replacement therapy can be recommenced.[9,10] Importantly, all three groups will likely play some role in the planning of formal clinical trials. This is essential for patients because their lived experience can provide meaningful insights that are often integral to designing effective clinical trials.

2 | METHODS

The scoping review followed the PRISMA extensions for scoping reviews (PRISMA-ScR) checklist and the Joanna Briggs Institute (JBI) methodology for scoping reviews.[11,12] The scoping review protocol was registered on the Open Science Framework registry (DOI: 10.17605/OSF.IO/2NYXP).

2.1 | Eligibility criteria

To warrant consideration for inclusion in the scoping review, articles needed to evaluate the attitudes of healthcare workers, healthcare students, or kidney patients toward xenotransplantation. The eligibility criteria were informed by the Population, Concept, and Context (PCC) framework (See Table 1). Peer-reviewed articles were included if they were published between the period of 1990 - July 2023; written in English; involved human participants; and evaluated the attitudes of adults on the kidney transplant waitlist and/or receiving dialysis, healthcare workers, or healthcare students (e.g., medical, nursing, or allied health students) toward xenotransplantation. The search parameters were chosen to capture articles published from the period when significant advances in genetically engineered pig research first occurred. Studies that used qualitative, quantitative, and mixed methods were considered.

2.2 | Search strategy

A search strategy including all search terms and Boolean operators was prepared with the guidance of a specialist librarian. A preliminary search was conducted to help identify appropriate keywords to use in the search. The following three databases were searched to identify relevant sources—Scopus, PubMed, and ScienceDirect. To help identify additional sources, a manual search was also conducted of relevant reference lists of studies identified in the database searches and relevant peer-reviewed journals. The final search results were exported to Mendeley (Mendeley Reference Manager). The following keywords and Boolean operators were used to identify appropriate sources for the review—xenotransplantation AND attitudes OR views OR beliefs OR perspectives AND kidney OR renal.

2.3 | Selection process

After retrieving the search results from the three electronic databases a total of 816 references were identified. Duplicates were removed and the remaining 796 titles and abstracts were screened by the first author against the eligibility criteria and identified those

TABLE 1 PCC framework.

Population	Adult patients on the kidney transplant waitlist and/or receiving dialysis, healthcare workers, or healthcare students, e.g., medical students.
Concept	Attitudes toward xenotransplantation.
Context	Any setting where the attitudes of the target population are assessed, e.g., hospitals and higher education institutions in any geographical region.

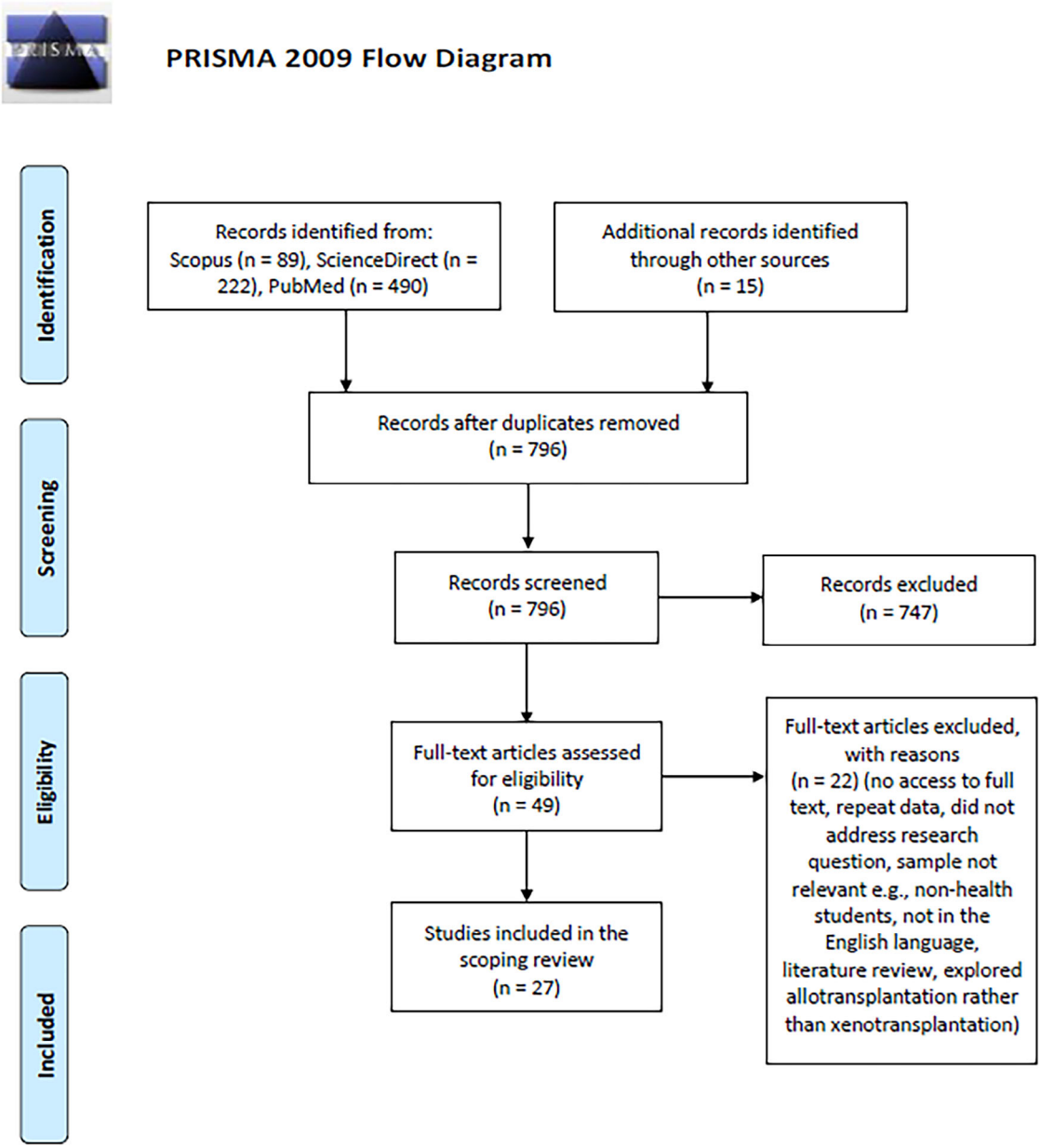

FIGURE 1 PRISMA flow diagram.

that would be included for full-text screening. Following the initial screening, 49 studies were identified for full-text screening and appraisal. The reasons for excluding a study were provided in the PRISMA flow diagram (See Figure 1). This process resulted in 27 studies meeting the eligibility criteria for inclusion in the scoping review.

2.4 | Data extraction

The following data was extracted from the included studies—authors, journal, country, year of publication, population studied, sample size, design and methods, and main findings. Several studies included participants in the study who were irrelevant to answering the research question, for example, patients on the waitlist for an organ other than a kidney, non-health students, or post-kidney transplant patients. In such cases, the sample (*n*) in the data extraction chart refers *only* to the sample in the study that met the eligibility criteria. However, in four studies it was not possible to distinguish the results between the different kinds of kidney patients,[13–16] but the data were still extracted because of its relevance to addressing the research question.

2.5 | Synthesis of results

The study results included in the review are presented in tables and in a descriptive narrative format.

3 | RESULTS

3.1 | Selection of sources of evidence

After duplicates were removed, 796 sources were left for the initial screening of titles and abstracts. Following this, the full text of 49 studies were screened and 27 were retained for inclusion in the review.

3.2 | Characteristics of source evidence

The characteristics of the studies included are presented in the data extraction chart (see Table 2), and 48% (n = 13) of them have been published since 2015 (Figure 2 provides the distribution of publication dates). 41% (n = 11) of sources were published in the journal *Xenotransplantation*. Figure 3 describes the number of studies conducted in each country with the majority conducted in Spain (n = 8, 30%). Most of the studies were cross-sectional surveys (n = 25, 92%) and the remaining studies were observational with a survey and in-depth interviews (n = 1, 4%), and a qualitative study with semi-structured interviews (n = 1, 4%).

Out of the 27 articles, 12 (44%) studied the attitudes of kidney patients; 8 (30%) studied the attitudes of healthcare workers; and 8 (30%) studied the attitudes of healthcare students. One study surveyed both patients and healthcare workers,[15] which is why the total percentage exceeds 100%. The total number of participants from the 27 articles was n = 29,836—this was constituted of n = 2,546 (8%) kidney patients, n = 6,223 (21%) healthcare workers, and n = 21,067 (71%) healthcare students. In studies where participants were given the option between different species of animals as the source animal, only the results that explicitly or implicitly included pigs were used. This is because pigs are the primary source animal for organs used in xenotransplantation.[17] Groups were deemed to have an overall positive attitude toward xenotransplantation if more than 50% of the sample viewed it positively and less than 50% would be considered negative. While the included studies varied in the questions posed, it was considered appropriate to understand and describe a willingness/unwillingness to accept a xenograft as equivalent to having a positive/negative attitude toward xenotransplantation.

3.3 | Healthcare workers' attitudes

The eight studies that explored the attitudes of healthcare workers toward xenotransplantation included a range of nurses, doctors, and other health workers from a variety of countries, clinical settings, and specialities with a total of 6,223 participants.[15,18–24] Healthcare workers had an overall positive attitude toward xenotransplantation in seven of the eight studies. The mean average positive attitude across all eight studies was 68% (SD = 10.8%). Acute care nurses in Australia were the exception, where 65% had an overall negative attitude toward xenotransplantation.[18]

In some cases, there was significant variation in the attitudes between the different healthcare workers. For example, in a study of Spanish doctors, nurses, and ancillary staff; doctors were the most likely to have a positive attitude toward xenotransplantation—89% versus 76% and 70%, respectively.[21] A similar pattern was recorded in a different study among healthcare workers in Spain, Mexico, and Cuba.[22] One study from France showed doctors had a narrowly less positive attitude than nurses; however, doctors were most likely to accept a xenograft in any circumstances, while nurses were the least likely.[19]

There was significant variability in the questions posed and information provided to participants and in most cases—where it was possible to determine—the overall positive results reflect a clinical scenario in which the results of xenotransplantation are considered equal to allotransplantation.[15,20–23] However, Padilla et al.[15] also asked healthcare workers—including nephrologists, transplant surgeons, and kidney nurses—whether they would accept or recommend a pig kidney xenograft to their patients as a bridge until a human kidney became available if the risks and results were inferior to those of an allograft—the positive attitudes dropped from 80% to 30%.

In one study from Argentina,[24] doctors and other healthcare workers with experience with islet xenotransplantation clinical trials were compared to those without that experience. It was found that healthcare workers with experience in clinical trials of xenotransplantation were more likely to have a positive attitude toward kidney xenotransplantation. If they needed a kidney transplant, 71% of clinicians with experience with clinical trials of xenotransplantation would accept a pig kidney xenograft rather than continue on dialysis; in contrast, only 51% of those without a similar experience would.

3.4 | Healthcare students' attitudes

Eight articles with a total of 21,067 participants explored the attitudes of healthcare students. The articles studied the attitudes of two different groups—medical students and nursing students. The three articles that studied the attitudes of medical students totaled 10,310,[25–27] and the five articles that studied the attitudes of nursing students totaled 10,757.[28–32] All the research exploring the attitudes of healthcare students has been conducted since 2015 and used cross-sectional surveys.

Healthcare students had an overall positive attitude toward xenotransplantation in seven of the eight articles, with a mean average of 66% (SD = 14.49). The exception to this was Dogan et al.'s study of nursing students in Türkiye,[32] where 65% would accept a xenotransplant from a halal animal, but only 35% would from a non-halal animal such as a pig. However, 40% of the nursing students thought that a xenograft from a non-halal animal would be acceptable *if* it were medically necessary.[32] Positive attitudes toward xenotransplantation from nursing students had an overall mean average of 62% (SD = 16.27) and ranged between 35% and 82% when the risks and results were deemed equal to allotransplantation. This was lower than the overall positive

TABLE 2 Data extraction chart.

Author(s), year	Journal	Country	Population studied	Sample size	Design and methods	Main findings
Mohacsi et al., 1995[18]	The Lancet	Australia	Acute care nurses	$n = 1{,}728$	Cross-sectional, survey	The nurses had an overall negative attitude toward xenotransplantation.
Ward, 1997[33]	The Lancet	Britain	Kidney patients receiving dialysis	$n = 850$	Cross-sectional, survey	78% were willing to accept a kidney from a pig.
Arundeii and McKenzie, 1997[34]	Xenotransplantation	Australia	Kidney transplant waitlist patients	$n = 137$	Cross-sectional, survey	Patients receiving hemodialysis were more likely than those receiving peritoneal dialysis to accept a pig xenotransplant: 55% versus 42%.
Mohacsi et al., 1997[13]	The Lancet	Australia	Kidney patients receiving dialysis or transplantation	$n = 113$	Cross-sectional, survey	Patients were more likely to agree with accepting an organ from a relative or someone genetically unrelated, compared to an animal organ: 61% versus 42%.
Schlitt et al., 1999[35]	Langenbeck's Archives of Surgery	Germany	Kidney transplant waitlist patients	$n = 248$	Cross-sectional, survey	~49% of patients on the waitlist for a kidney would accept a xenotransplant if the results were similar to an allotransplant.
Julvez et al., 1999[19]	The Lancet	France	Doctors, nurses, and technicians	$n = 304$	Cross-sectional, survey	All groups had an overall positive attitude toward xenotransplantation. Doctors were the most likely to accept a xenotransplant in any circumstances if they required a transplant.
Persson et al., 2001[36]	Transplant International	Sweden	Kidney transplant waitlist and dialysis patients	$n = 398$	Cross-sectional, survey	66% had a positive attitude toward receiving a kidney xenotransplant if the infection risk and results were equal to an allotransplant. When the infection risk and results of a kidney xenotransplant were more uncertain, positive attitudes dropped to 16%.
Martínez-Alarcón et al., 2005[14]	Transplantation Proceedings	Spain	Kidney and liver transplant waitlist patients	$n = 96$	Cross-sectional, survey and interview	If the results and risks of xenotransplantation were equal to allotransplantation, 83% would accept a xenotransplant. If the results involved greater risk than an allotransplant, then then only 33% would accept it.
Ríos et al., 2005[20]	Transplantation Proceedings	Spain	Doctors	$n = 171$	Cross-sectional, survey	If the results of xenotransplantation were equal to allotransplantation then 81% would be in favor of it.
Kranenburg et al., 2005[39]	Social Science and Medicine	Netherlands	Kidney transplant waitlist and dialysis patients	$n = 61$	Interventional, survey and semi-structured interviews	67% would rather wait four years for an allograft from a deceased donor than accept a xenograft. Willingness to accept dropped to 54% when information about xenotransplantation was provided.
Conesa et al., 2006[21]	Transplantation Proceedings	Spain	Doctors, nurses, and ancillary staff	$n = 428$	Cross-sectional, survey	If the results of xenotransplantation were equal to allotransplantation then 79% of the healthcare workers viewed it positively.
Ríos et al., 2010[22]	Transplantation Proceedings	Spain, Mexico and Cuba	Doctors, nurses, nursing assistants, and auxiliary staff	$n = 738$	Cross-sectional, survey	If the results of xenotransplantation were equal to allotransplantation then 66% of the healthcare workers viewed it positively.

(Continues)

TABLE 2 (Continued)

Author(s), year	Journal	Country	Population studied	Sample size	Design and methods	Main findings
Martínez-Alarcón et al., 2011[37]	Xenotransplantation	Spain	Kidney transplant waitlist patients	$n = 214$	Cross-sectional, survey	If the results were similar to allotransplantation then 76% had a positive attitude toward accepting a xenograft. If the results were worse than an allograft, the positive attitude dropped to just 8%.
Ríos et al., 2014[23]	Xenotransplantation	Spain, Mexico, and Cuba	Doctors, nurses, healthcare assistants, and ancillary staff	$n = 2618$	Cross-sectional survey	If the results were similar to allotransplantation then 61% of the healthcare workers had a positive attitude toward xenotransplantation.
Mikla et al., 2015[28]	Transplantation Proceedings	Poland	Nursing students	$n = 608$	Cross-sectional, survey	If the results of xenotransplantation were similar to allotransplantation then 62% had a positive attitude toward xenotransplantation.
Ríos et al., 2015[25]	Xenotransplantation	Spain	Medical students	$n = 9,275$	Cross-sectional, survey	If the results of xenotransplantation were similar to allotransplantation then 81% viewed it favorably. If the results were worse than an allograft, then only 8% would be in favor.
Mikla et al., 2016[29]	Transplantation Proceedings	Poland	Nursing students	$n = 325$	Cross-sectional, survey	55% had a positive attitude toward xenotransplantation.
Abalovich et al., 2017[24]	Xenotransplantation	Argentina	Doctors and hospital workers	$n = 196$	Cross-sectional, survey	Staff with experience of islet xenotransplantation clinical trials were more likely to have a positive attitude toward kidney xenotransplantation than those that did not: 71% versus 51%.
Balwani et al., 2018[38]	Transplantation	India	Kidney patients receiving dialysis	$n = 100$	Cross-sectional, survey	If the results were similar to an allotransplant, then 80% would accept a xenotransplant.
Martínez-Alarcón et al., 2019[30]	Xenotransplantation	Spain	Nursing students	$n = 8,913$	Cross-sectional, survey	If the outcomes were equal to allotransplantation then 74% had a positive attitude toward xenotransplantation. If the results were deemed to be worse than an allotransplant, positive attitudes dropped to 7%.
Padilla et al., 2020[15]	Kidney360	United States	Kidney patients, nephrologists, kidney transplant surgeons, and kidney nurses	$n = 203$	Cross-sectional, survey	If the results were similar to an allotransplant, then 69% of kidney patients would accept a xenotransplant versus 80% of healthcare workers. 42% of patients would accept a xenotransplant as a bridge.
Liu and Liu, 2021[26]	Xenotransplantation	China	Medical students	$n = 915$	Cross-sectional, survey	If the results were equal to an allotransplant, 64% would accept a xenotransplant when an allotransplant was also available. 70% would accept a xenotransplant if it shortened their time on the transplant waitlist.

(Continues)

TABLE 2 (Continued)

Author(s), year	Journal	Country	Population studied	Sample size	Design and methods	Main findings
Padilla et al., 2021a[16]	Xenotransplantation	United States	Patients with kidney disease or a kidney transplant	$n = 148$	Cross-sectional, survey	If the results of a xenotransplant were similar to an allotransplant, 91% of white kidney patients would accept it compared to 70% of black patients.
Padilla et al., 2021b[31]	Journal of Evidence-Based Social Work	United States	Nursing students	$n = 67$	Cross-sectional, survey	82% would agree to accept a pig xenotransplant if the results were equal to an allotransplant. 32% were still willing to accept a pig organ, even if the results would have worse results than a human organ.
Dogan et al., 2022[32]	Xenotransplantation	Turkey	Nursing students	$n = 844$	Cross-sectional, survey	65% would accept an animal organ from a halal animal, but only 35% would from a non-halal animal (e.g., a pig). 40% thought that a xenotransplant from a non-halal animal would be acceptable if it was medically necessary.
Safi et al., 2022[27]	Xenotransplantation	Lebanon	Medical students	$n = 120$	Cross-sectional, survey	If the results were equal to an allotransplant with a shorter waiting period, then 72% would accept a xenotransplant. If the outcomes were more uncertain then only 10% would accept a xenotransplant rather than wait for an allograft.
Akboğa and Hobek, 2023[40]	Xenotransplantation	Turkey	Kidney patients receiving dialysis	$n = 18$	Qualitative, semi-structured interviews	89% would accept a xenotransplant from a halal animal (e.g., sheep), while 66% would from a non-halal animal such as a pig.

attitude of medical students, who had an overall mean average of 72% (SD = 6.94) and ranged between 64% and 81%.

Four out of the eight studies assessed the attitudes of students when the risks and results from xenotransplantation were not considered equal to allotransplantation—in all four studies, the positive attitudes dropped markedly. For example, the levels of acceptance dropped from 81% to just 8% among Spanish medical students, while 50% were unsure, and 42% were against it in such cases.[25] Changes in positive attitudes and acceptance of xenotransplantation were observed in Spanish nursing students, dropping from 74% to 7%, with 49% undecided and 44% against.[30] Similarly, in nursing students from the United States, positive attitudes dropped from 82% to 32%,[31] and Lebanese medical students' willingness to accept a xenograft when the results were more uncertain dropped from 72% to just 10%.[27]

3.5 | Patients' attitudes

Twelve studies with a total number of 2,546 participants explored the attitudes of patients living with kidney disease who were receiving dialysis and/or on the transplant waitlist. Ten out of the 12 studies used a cross-sectional survey design;[13,14,15,16,33–38] one study was interventional, conducting two surveys and semi-structured interviews;[39] and one study adopted a descriptive qualitative approach using semi-structured interviews.[40]

In four studies, it was not possible to distinguish between pre- and post-transplant patients. For example, in Padilla et al.[15] the 163 kidney patients' results were grouped together, but 33% were on the transplant waitlist. This was also the case in Padilla et al.[16]—of the 148 patients, 32% were on the kidney transplant waitlist and 68% had already received a kidney transplant. In Martínez-Alarcón et al.[14] the number of patients on the kidney transplant waitlist was not recorded, however, the results between kidney and liver transplant waitlist patients were differentiated. Similarly, in Mohacsi et al.[13] 89 out of the 113 kidney patients were receiving dialysis and 24 had previously received a transplant but the results were grouped.

Kidney patients had an overall positive attitude toward xenotransplantation with a mean average positive attitude of 69% (SD = 13.93) with a range between 42% and 91%. The two studies that found an overall negative attitude toward xenotransplantation were some of the earliest studies.[13,35] Nevertheless, while the overall view was positive, patients consistently became much less positive when the risks and results were not comparable to allotransplantation. Four studies assessed attitudes when the risks and results were inferior to allotransplantation, and the overall attitude became negative in all four. For example, when Swedish kidney patients were told that the results of a kidney xenograft were more uncertain, the positive attitude dropped significantly from 66% to just 16%,[36] and from 83% to 33% in Spanish kidney transplant waitlist patients.[14] In a later study, the positive attitude dropped from 76% to just 8%, with 92% not in favor of a xenotransplant when it involved greater risks.[37] If the risks were not equal to allotransplantation, only 42% of kidney patients in a study from the

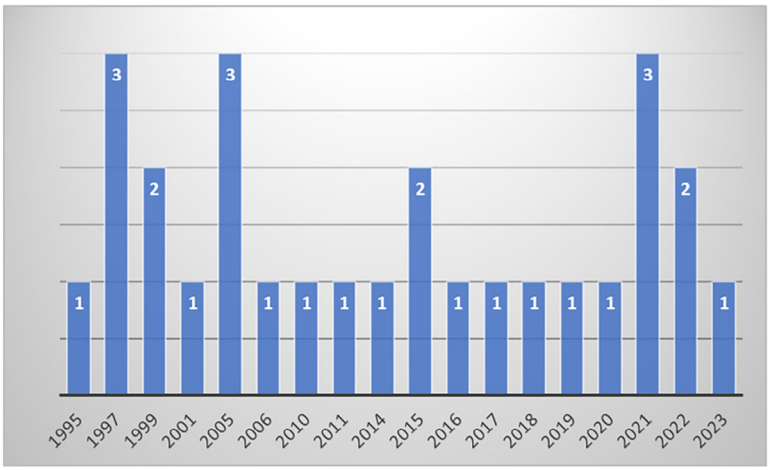

FIGURE 2 Publication date distribution.

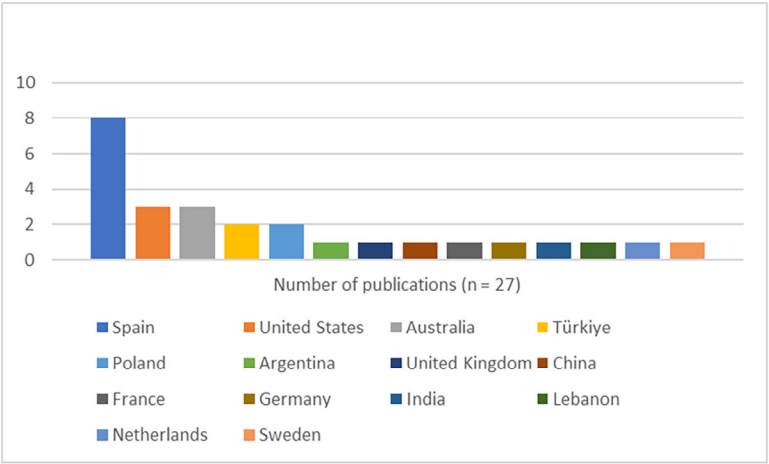

FIGURE 3 Country where the studies were conducted.

United States were willing to accept a xenograft, dropping from 69% when the risks were equal.[15]

One study by Padilla et al.[16] assessed the racial differences in attitudes toward xenotransplantation between White and Black kidney patients in the United States. If the risks and results were similar to allotransplantation 91% of White kidney patients would accept one compared to 71% of kidney patients who were Black. In a study of Turkish patients receiving dialysis,[40] nearly all the patients recorded that they had never heard of xenotransplantation, and positive attitudes reduced from 89% to 66% if the xenograft came from a pig. Similarly, 88% of kidney patients receiving dialysis in India had never heard of xenotransplantation but 80% would be willing to accept a xenograft, however, 100% of patients preferred an allograft.[38]

Four studies asked patients whether they would consider a xenograft as a bridge until an allograft became available. Martínez-Alarcón et al.[14] found that 98% of transplant patients were willing to accept a xenograft as a bridge and if it was functioning optimally, 98% would keep it rather than undergo allotransplantation if a human organ became available. However, this very high positive response is unlikely to be representative of kidney patients in general because the sample also included patients waiting for a liver transplant and these patients have no available alternative therapy equivalent to dialysis. In a later Spanish study, 44% of kidney patients would accept a xenograft as a bridge.[37] Of those who would accept a xenograft as a bridge, 90% would keep it if it continued to function optimally, even if an allograft later became available. Patients in Germany were asked if they would accept a xenograft as a bridge, presuming that function would only last a few years and ~30% would be willing to.[35] More recently, Padilla et al.[15] found that 41% of kidney patients were willing to accept a xenograft as a bridge until an allotransplantation became available.

There is some evidence that when patients are given more information about xenotransplantation it can affect their attitudes toward it. For example, kidney transplant waitlist and dialysis patients' positive attitudes dropped from 67% to 54% when they were given general information about xenotransplantation, making them more reluctant to accept one.[39] However, it is difficult to infer anything normative from this because it was unclear if the patients from the other studies were provided with any information about xenotransplantation. Nevertheless, the findings[39] are congruent with studies from other participant groups—animal technicians, researchers, and university students—which showed that positive attitudes fell when information about xenotransplantation was provided.[41] Interestingly—both before and after receiving information—more than half of the patients on the kidney transplant waitlist in the Kranenburg et al.[39] study ranked

xenotransplantation as their least preferable option. The patients were more willing to accept a kidney from a paid donor, deceased donor, or living donor during both of their interviews.

3.6 | Spanish versus English-speaking populations

Out of the 27 studies, the two largest language groups represented were from Spanish and English-speaking countries. To assess if a language-based difference in attitudes was present we compared the attitudes between the 16 studies in Spanish ($n = 9$)[14,20–25,30,37] and English ($n = 7$)[13,15,16,18,31,33,34] when the outcomes were considered equal to allotransplantation. Both language groups had an overall positive attitude toward xenotransplantation, however, the Spanish studies had a higher overall mean average positive attitude of 73% (SD = 10.2) versus 64% (SD = 19.5). While this finding may be representative of a more positive attitude toward xenotransplantation in Spanish-speaking populations, several limitations warrant caution when drawing this conclusion. For example, four out of seven studies in English-speaking countries were conducted in the 1990s, with a 23-year gap between the fourth and fifth studies.[13,15] The more recently published studies from English-speaking countries are notably more positive than the earliest studies. Furthermore, the studies from Spanish-speaking countries had significantly more participants—22,649 versus 3,246 and consequently limits the validity of any generalization.

4 | DISCUSSION

The findings show that patients on the kidney transplant waitlist and/or receiving dialysis, healthcare workers, and healthcare students all have an overall positive attitude toward xenotransplantation. While this is prima facie encouraging, the positive attitudes are contingent on xenotransplantation having equivalent risks and results to allotransplantation. This is because in *every* study participants were asked to consider xenotransplantation in a clinical scenario where the risks and results were *not* equal—the overall attitude switched from being positive to negative.[14,15,25,27,30,31,36,37] It is worth noting a methodological limitation in how the questions about risk were often phrased in these studies. For example, when a patient is asked whether they would accept a xenotransplant if it involves "greater risk" or "worse" outcomes than an allotransplant, there remains ambiguity about *how* different people could perceive and interpret their meaning.

This change is unsurprising because until formal clinical trials commence to assess the safety and efficacy of xenotransplantation it will remain impossible to know whether the risks and results will be congruent with allotransplantation. While xenotransplant decedent studies have been conducted,[2,3] their inherent translational limitations mean that only formal clinical trials will provide a definitive answer. Cooper and Kobayashi[42] have argued that the pathophysiological changes instigated by brain death mean that not only is the data gained from decedent studies limited but—because they can provide confusing results—could potentially negatively impact the introduction of clinical xenotransplantation. Similar clinical outcomes are unlikely to be achieved, at least initially, and risks are posed to recipients that are not present for allograft recipients. For instance, there is a longstanding debate surrounding the risk posed by xenozoonotic infection, and while it is likely low, this similarly cannot be determined definitively until formal clinical trials have commenced.[43–46]

There are especially strong reasons to view the overall positive attitudes of kidney patients with a degree of skepticism. When patients on the kidney transplant waitlist are one day asked to provide informed consent to participate in phase I clinical trials, it will not be presented as having equal risks and results—because it is those very clinical trials that are required to determine its safety and efficacy. While successful pre-clinical xenotransplantation research can be useful for gauging the likelihood of success, ultimately this can *only* be determined by robustly designed formal clinical trials. However, certain patients may welcome xenotransplantation if an allograft is unavailable and the alternative is dying very soon.

The World Health Organization and the International Xenotransplantation Association have highlighted the importance of public involvement and dialogue—because patients often feel excluded from decisions made by scientists, clinicians, and public policymakers.[47–49] Similar arguments have been made by leading transplant surgeons and xenotransplantation researchers—the opinions of patients are a vital step before beginning formal clinical trials.[9,15,50] After all, the significant investment in xenotransplantation research—[51] estimated at almost 500 million dollars in 2019—would be misguided if the target population were unwilling to accept a xenograft. Furthermore, if acceptance is limited to certain groups, then it could exacerbate existing transplant disparities. This is especially noteworthy given the disparities in the willingness to accept a xenograft between Black and White kidney patients in the United States.[16] Future studies should, therefore, seek to replicate these findings to see if they persist on a larger scale, and explore how this disparity should be understood and addressed.

An additional finding that this scoping review reinforced was the paucity of standardized surveys and questionnaires and significant variability in the assumptions and kinds of questions asked, especially around the presentation of risk and parity with standard therapies. The one exception is the PCID-XENOTx-Ríos, which is a validated questionnaire developed by the International Collaborative Organ Donation Project about xenotransplantation in Spain.[52] This problem was identified by Mitchell et al.[53] in their meta-analysis of patient attitudes toward xenotransplantation; only three studies provided sufficient data for comparison, despite identifying 41 studies on the attitudes of patients. The lack of consistency in the survey tools means that the literature currently provides a limited understanding of the attitudes of those who will be most closely involved in clinical xenotransplantation. Researchers should, therefore, create and validate their survey tools or utilize existing validated survey tools such as the PCID-XENOTx-Ríos to create a larger and more homogeneous body of evidence that can be, for example, subject to meta-analysis. While we identified a more favorable attitude toward xenotransplantation from Spanish-speaking

populations compared to English-speaking populations, the available data limits making a generalizable claim. For example, this difference could merely reflect a more positive attitude toward transplantation in general.

4.1 | Limitations

The scoping review has the following limitations. First, while the review was intended to be as comprehensive as possible, some relevant articles could have been missed. Second, the objective of the review was to assess *how* xenotransplantation was viewed and did not focus on the variables that could influence why the groups had the attitudes they did.

5 | CONCLUSION

In summary, all three groups had an overall positive attitude toward xenotransplantation. However, this comes with a notable caveat—when the risks and results are inferior to allotransplantation then all three groups shifted from an overall positive to a negative attitude. Moreover, while the evidence indicates that kidney patients would be less likely to accept a xenotransplant if its outcomes were inferior to an allotransplant, there is a limited understanding of the circumstances and contexts they would be willing to accept one. Importantly, the review included only one qualitative study; so, while the existing quantitative data provides a valuable overview of attitudes toward xenotransplantation, it is limited by the dearth of an adequate body of qualitative data that can provide a deeper and richer understanding. Future research should therefore continue to survey the attitudes toward xenotransplantation but also complement this data by using qualitative methodologies.

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