

Should you need an organ... Flemish secondary school students' attitudes toward xenotransplantation and transgenetic organ donation

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Abstract

Background: The supply of human organs available for transplantation remains grossly inadequate globally. Animal-to-human transplantation, and even more so humanized organ grown in animals, holds promising results for the start of clinical trials in humans. Very little is known about the public's willingness to accept different xenotransplantation techniques. This study aims to determine attitudes toward human-to-human transplantation, animal-to-human transplantation, and chimera-to-human transplantation in the Belgium context.

Methods: Secondary school students from Flanders, Belgium, were surveyed between January and June 2019. Socio-demographic details likely to influence participants' attitudes were gathered. Participants were presented with three hypothetical cases (human-to-human transplantation, animal-to-human transplantation, and chimera-to-human transplantation) and asked about their willingness to accept the particular organ. Their risk appetite to accept organs with potentially worse outcomes than the status quo was also evaluated.

Results: Seven hundred forty-one complete questionnaires were analyzed. It can be concluded that Flemish secondary school students favored the techniques of xenotransplantation to a lesser extent than allotransplantation; however, most of them did consider it a good solution for organ shortage. Compared to animal-to-human transplantation, chimera-to-human transplantation showed a more positive attitude among the respondents when considered a good organ transplantation solution.

Conclusion: Flemish secondary school students favored the techniques of xenotransplantation to a lesser extent than allotransplantation; however, most of them did consider it a good solution for organ shortage. In comparison to animal-to-human transplantation, chimera-to-human transplantation showed a more positive attitude among the respondents when considered a good solution for organ transplantation.

KEYWORDS

Belgium, chimera, organ donation, public perception, transplantation, xenotransplantation

1 | INTRODUCTION

While organs donated from fellow human-beings, that is, allotransplantation, have been established as the treatment of choice for a variety of (patients with) end-stage organ diseases, this source of organs is never enough. In the United States, one person is added to the national waiting list every 9 min. At the same time, 30 persons per day are removed from the waiting list because they have become too sick to be transplanted or have died without a lifesaving organ.¹ Around 1200 persons are currently waiting for an organ transplant in Belgium, and between 80 and 120 patients die each year while waiting for a lifesaving organ.² Despite various strategies to increase donor availability or the optimization of "higher-risk," "marginal," or "extended criteria" organs,³ the supply of organs remains grossly inadequate globally.

Successful xenotransplantation, that is, cross-species transplantation, holds the potential of a near unlimited supply to solve the ever-growing organ shortage. Progress in xenotransplantation suited for clinical application has generally progressed slowly over the last 50 years, but recent advances in genetically-engineered pigs and new immunosuppressive therapies have revitalized xenotransplantation's potential.⁴ Genome editing tools like TALEN and CRISPR/Cas9 are employed to perform multiple gene knockouts, insert human transgenes in pigs, and create specific animal organ knockouts to be substituted with humanized organs.⁵ Data on laboratory studies using pig organs in nonhuman primates suggest that animal-to-human transplantation may soon be ready to be tested in human clinical trials.^{5,6} While the Covid-19 pandemic has brought concerns about the possible introduction of zoonotic infections to the foreground for the public, experts are not concerned and remain optimistic about the future of clinical xenotransplantation.⁷ More so, the pandemic has again highlighted the need for public engagement and education on xenotransplantation.⁷

All prominent ethical guidance papers and international institutions involved with xenotransplantation regulation have always advocated early public engagement and education. In the 2008 Changsha Communiqué, the World Health Organization considers public education on xenotransplantation's potential risks and benefits as one of its key recommendations.⁸ The International Xenotransplantation Association, supported by the International Transplantation Society, stressed in its 2003 position paper the importance of understanding public perception and education to optimize xenotransplantation's clinical success.⁹ The ethical principles of respect for persons, beneficence, and justice necessitate individual and public involvement in all experiments conducted in humans.¹⁰ In the case of xenotransplantation, however, public views on the use of animals and transgenetic animals or chimeras could also have significantly influenced the public's acceptance of xenotransplantation trials.

However, a recent systematic review has shown that very little is known about public perceptions of xenotransplantation.¹¹ A study conducted in Japan observed 60% of the public and 84% of researchers supported the creation of human-swine chimeras, and 81% of the pub-

lic and 92% of researchers supported the creation of human-swine chimeric embryos.¹² In a study conducted by Stem Cells Transitional Medicine regarding public support in the US for human-animal chimera research, it was seen that over 44% of participants have some knowledge about chimera research and support the use of chimera organs.¹³

A study focusing on teenagers' views suggested that the acceptance of xenotransplantation in this specific age group varies considerably depending on the country, with acceptance rates ranging from 40% to 75%. In the same study, university students were seen to have more favorable attitudes varying from 64% to 92%.¹⁴ In a survey conducted among the Spanish Gypsy ethnic population group, 74% of the participant said they would accept an animal organ if they needed it and, 60% favored cadaveric donation.¹⁵

Because local authorities regulate xenotransplantation,^{8,9} there is a need for population-specific studies. To our knowledge, no public perception study has been done in the Belgium setting yet and, only a few studies worldwide have analyzed public attitudes toward organs from animals that have undergone multiple gene knockouts and support humanized organs. Therefore, the aim of this study is to determine attitudes toward human-to-human transplantation, animal-to-human transplantation, and chimera-to-human transplantation in the Belgium context. For this study, we focused on adolescents' attitudes attending the last 2 years of secondary school in Flanders (Belgium).

2 | METHODS

2.1 | Participants

In the region Flanders (Belgium), secondary education consists of 6 years (Grades 7–12). Students are divided during the 6 years into three different tracks: the academic, technical, and vocational track. The academic track (ASO) prepares students for higher education, the technical track (TSO) contains theoretical and technical training, and the vocational track (BSO) concentrates upon practical education and prepares students for a specific vocation. Participants were recruited through secondary schools using a convenience sampling method. Only students from the last two (academic and technical tracks) or three (vocational track) years were included. Students in these years are typically between the ages of 16 and 19 years. Data were collected from February 1, 2019 to June 30, 2019.

2.2 | Survey

The anonymous written questionnaire (addendum I) first gathered participants' socio-demographic data, such as gender, age, religion, and educational track. The rest of the questionnaire, divided into three sections, focused on human organ transplantation, xenotransplantation, and xenotransplantation with organs of human-animal chimeras. Each of the three sections first provided some background on the particular technique, whereafter, we evaluated participants' prior knowledge

TABLE 1 Social-demographic variables

Age (n = 709)	Observed frequency n (%)
Median	17.00
Range	15–21
Gender (n = 709)	
Male	310 (43.7%)
Female	397 (56.0%)
No answer	2 (0.3%)
Education (n = 709)	
ASO	266 (37.5%)
TSO	169 (23.8%)
BSO	272 (38.4%)
No answer	2 (0.3%)
Religious? (n = 709)	
Yes	355 (50.1%)
No	347 (48.9%)
No answer	7 (1.0%)
Religion (n = 355)	
Protestant	10 (2.8%)
Roman Catholic	315 (88.7%)
Muslim	15 (4.2%)
Other	13 (3.7%)
No answer	2 (0.6%)
Extent of religiosity (n = 355)	
Active	17 (4.8%)
To a certain extent	98 (27.6%)
Not active	237 (66.8%)

about the presented methods. To evaluate participants' willingness to accept the various techniques, we presented one or more hypothetical cases per technique. Finally, participants were asked to indicate to what extent they agreed with several statements using a Likert scale. If more than one question was not answered in one or more of the three sections, the questionnaire was excluded.

2.3 | Statistical analysis

The consistency of categorical data was checked with either the chi-square test or Fisher's exact test. The Mann–Whitney test was used to detect differences in attitudes for the variables gender and religiosity. The Kruskal–Wallis test was used to determine differences in attitude for the variables education, religion, and extent of religiosity. A correlation test was used to examine the correlation between the answers to xenotransplantation and transplantation statements with organs of human-animal chimeras. A two-sided p -values of <0.01 were considered statistically significant. Statistical analyses were performed using SPSS 26.0.

2.4 | Ethical approval

This study protocol and questionnaire were approved by the Research Ethics Committee UZ/KU Leuven (MP007957). Voluntary participation and participant's right to withdraw at any time were discussed with participants before they completed the questionnaire, and researcher contact details were provided to them.

3 | RESULTS

3.1 | Participants

Seven hundred forty-one questionnaires were returned. Thirty-two were excluded due to leaving more than one question blank per section. Therefore, 709 questionnaires were included for further analysis (Table 1). The median age of the respondents was 17 years (range 15–21). The wider than expected age range for the grades included in this study can be ascribed to outlier students that have either progressed faster (2) or slower (13) than normal schooling standards. Outlier aged students were not excluded from the analysis as the form part of the peer-group. It was observed that 43.7% of the participants were male, and 56.0% were female (Table 1). Of all respondents, 37.5% attended classes in general track (ASO), 38.4% in vocational track (BSO), and 23.8% in technical track (TSO). Approximately half of the participants (50.1%) said they were religious, of which 88.7% were Roman Catholic, 4.2% Muslim, and 2.8% Protestant. Of note among the religious respondents is that only 4.8% indicated that they were actively religious, and 66.8% stated that they did not actively practice their religion.

3.2 | Attitudes toward human-to-human organ transplantation

The majority (95.3%) had prior knowledge of human-to-human organ transplantation (Table 2). Participants with prior knowledge were also more willing to undergo organ transplantation (88.3% vs. 65.6%, $p = 0.001$). More than half of the students (56.7%) did not think that receiving an organ would change their personality; however, 16.1% thought it would (Table 3). Fifty-three percent indicated that organ transplantation would influence their view on life and death. Women were more likely to agree with this statement regarding views on life and death than men were (57.6% vs. 47.1%, $p = 0.003$). More than three quarter (77.7%) of the participants thought organ transplantation is accepted by their family and friends, while only 5.4% thought this would be a problem.

Only one-tenth of the respondents (10.3%) stated that they would not psychologically be able to live with someone else's organ, but 61.2% did not foresee prospects of psychological harm in organ transplantation. Participants from the general track (ASO) expressed less concern about the psychological impact (70.9%) compared to respondents from the technical track (TSO) (66.3%) and the vocational track (BSO) (48.9%, $p < 0.001$).

TABLE 2 Prior knowledge and attitude toward human-to-human organ transplantation

(n = 709)	Yes	No	I am not sure	No answer
	n (%)			
Did you hear about organ transplantation before your participation in this study?	676 (95.3%)	32 (4.5%)		1 (0.1%)
Suppose you need an organ transplant within 3 months to survive, and you are on the transplant list (waiting list for all persons waiting for an organ). You are told a human organ is available for you.	616 (86.9%)	11 (1.6%)	79 (11.1%)	3 (0.4%)
Would you accept this human organ?				

For the analysis, the answers "no" and "I am not sure" were joined.

TABLE 3 Statements about organ transplantation

Statements (n = 709)	Totally disagree	Disagree	Neutral	Agree	Totally agree	No answer
	n (%)					
I think receiving an organ would change my personality.	188 (26.5%)	214 (30.2%)	189 (26.7%)	93 (13.1%)	21 (3.0%)	4 (0.6%)
I think receiving an organ would influence my view on life and death.	59 (8.3%)	76 (10.7%)	197 (27.8%)	275 (38.8%)	101 (14.2%)	1 (0.1%)
I think receiving an organ would not be accepted by my family/friends.	356 (50.2%)	195 (27.5%)	118 (16.6%)	20 (2.8%)	18 (2.5%)	2 (0.3%)
I would not be psychologically capable of living with an organ of someone else.	179 (25.2%)	255 (36.0%)	201 (28.3%)	43 (6.1%)	30 (4.2%)	1 (0.1%)

For the analysis, the answers "totally disagree" and "disagree" as well as "agree" and "totally agree" were joined.

3.3 | Attitudes toward animal-to-human transplantation

The majority of students (71.1%) had never heard of xenotransplantation before (Table 4). More men than women (34.5% vs. 24.2%) already had prior knowledge ($p = 0.003$). Despite the low level of prior knowledge, 36.1% of participants would accept an animal organ if the risks and results of xenotransplantation were comparable to those of organ transplantation with human organs. Approximately half of the participants (50.4%) doubted the technique, and 13.3% would refuse to accept an animal organ. Technical track (TSO) students had a more positive attitude than general track (ASO), and vocational track (BSO) students did ($p < 0.001$). Additionally, 53% of the respondents with prior knowledge would accept an animal organ ($p < 0.001$).

If there were greater risks and worse results, only 12.8% would be willing to accept an animal organ. Slightly more than half (55.7%) would doubt, and 31.2% would refuse. If a participant would accept an animal organ in case of similar risks and results, 27% of them would also accept in case the risks were higher, and the results were indicated to be worse; 95.1% of the people who refused or were doubting in the first case of human-to-human transplantation, also in the second case of animal-to-human transplantation ($p < 0.001$).

A fourth (25.8%) of the participants thought that receiving an animal organ would change their personality, and 44.1% disagreed (Table 5).

Participants from the vocational track (BSO) were more likely to agree that xenotransplantation would change their personality (33.9%, $p < 0.001$). About half (48.8%) of the participants said they thought they would not feel less human after xenotransplantation, while 27.9% would. One-fifth (20.7%) of the students thought their family or friends would not accept xenotransplantation, while 41.3% thought this would not be a problem.

From the total number of respondents, 32.3% thought xenotransplantation was an animal unfriendly technique, compared to 34.7% of the participants who did not think so. More women than men (39.9% vs. 23.2%) indicated that they found this technique animal unfriendly ($p < 0.001$). A fourth of the respondents (24.3%) thought they would not be able to cope with living with an animal organ psychologically, and 39.5% thought they would have no problems with it. Around 73.8% were worried about the risks associated with this technique. Only 9.6% did not worry about it. Finally, 41.9% believed xenotransplantation to be a good solution for the organ shortage, and 16.2% did not.

3.4 | Attitudes toward chimera-to-human transplantation

The majority of students (87.3%) have not heard of chimeras before (Table 6). More men than women (16.2% vs. 9.3%) belonged to the

TABLE 4 Prior knowledge and attitude toward animal-to-human transplantation

(n = 709)	Yes	No	I'm not sure	No answer
	n (%)			
Did you hear about xenotransplantation before your participation in this study?	204 (28.8%)	504 (71.1%)		1 (0.1%)
Suppose you need an organ transplant within 3 months to stay alive, and you are on the transplant list. <u>The results and risks of animal and human organ transplants are similar.</u> Currently, there are no human organs available. The animal organs are immediately available. Would you (in anticipation) accept the animal organ?	256 (36.1%)	94 (13.3%)	357 (50.4%)	2 (0.3%)
Suppose you need an organ transplant within 3 months to stay alive, and you are on the transplant list. With animal organ transplants, <u>the results are worse, and the risks are greater</u> compared to human organ transplants. There are currently no human organs available. Animal organs are immediately available. Would you (in anticipation) accept the animal organ?	91 (12.8%)	221 (31.2%)	395 (55.7%)	2 (0.3%)

For the analysis, the answers "no" and "I am not sure" were joined.

TABLE 5 Statements about animal-to-human transplantation

Statements (n = 709)	Totally disagree	Disagree	Neutral	Agree	Totally agree	No answer
	n (%)					
I think receiving an animal organ would change my personality.	157 (22.1%)	156 (22.0%)	210 (29.6%)	121 (17.1%)	62 (8.7%)	3 (0.4%)
I would be afraid to show animal features.	321 (45.3%)	178 (25.1%)	98 (13.8%)	62 (8.7%)	49 (6.9%)	1 (0.1%)
I would feel less human.	155 (21.9%)	191 (26.9%)	160 (22.6%)	152 (21.4%)	46 (6.5%)	5 (0.7%)
I think receiving an animal organ would not be accepted by my family/friends	117 (16.5%)	176 (24.8%)	263 (37.1%)	102 (14.4%)	45 (6.3%)	6 (0.8%)
I think it is animal unfriendly.	110 (15.5%)	136 (19.2%)	230 (32.4%)	126 (17.8%)	103 (14.5%)	4 (0.6%)
I would not be psychologically capable of living with an animal's organ	116 (16.4%)	164 (23.1%)	257 (36.2%)	114 (16.1%)	58 (8.2%)	0 (0.0%)
I would be worried about the risks associated with this technique.	22 (3.1%)	46 (6.5%)	116 (16.4%)	292 (41.2%)	231 (32.6%)	2 (0.3%)
I believe it would be a good solution for the organ shortage.	40 (5.6%)	75 (10.6%)	292 (41.2%)	213 (30.0%)	84 (11.8%)	5 (0.7%)

For the analysis, the answers "totally disagree" and "disagree" as well as "agree" and "totally agree" were joined.

TABLE 6 Prior knowledge and attitude toward transplantation with organs of human-animal chimeras

(n = 709)	Yes	No	I am not sure	No answer
	n (%)			
Did you hear about chimeras before your participation in this study?	88 (12.4%)	619 (87.3%)		2 (0.3%)
Suppose you need an organ transplant within 3 months to stay alive, and you are on the transplant list. <u>The results and risks of a transplant with an organ from a chimera are similar to a human organ transplant.</u> There are currently no human organs available. The chimera organs are immediately available. Would you accept an organ from a human-animal chimera?	274 (38.6%)	136 (19.2%)	297 (41.9%)	2 (0.3%)
Suppose you need an organ transplant within 3 months to stay alive, and you are on the transplant list. <u>When transplanting with an organ from a chimera, the results are worse, and the risks are greater compared to human organ transplants.</u> There are currently no human organs available. The chimera organs are immediately available. Would you accept an organ from a human-animal chimera?	81 (11.4%)	257 (36.2%)	370 (52.2%)	1 (0.1%)

For the analysis, the answers "no" and "I am not sure" were joined.

TABLE 7 Statements about transplantation with organs of human-animal chimeras

Statements (n = 709)	Totally disagree	Disagree	Neutral	Agree	Totally agree	No answer
	n (%)					
I think receiving a chimera organ would change my personality.	163 (23.0%)	193 (27.2%)	223 (31.5%)	91 (12.8%)	37 (5.2%)	2 (0.3%)
I would be afraid to show animal features.	246 (34.7%)	181 (25.5%)	166 (23.4%)	72 (10.2%)	43 (6.1%)	1 (0.1%)
I would feel less human.	165 (23.3%)	196 (27.6%)	195 (27.5%)	114 (16.1%)	36 (5.1%)	3 (0.4%)
I think receiving a chimera organ would not be accepted by my family/friends	124 (17.5%)	176 (24.8%)	267 (37.7%)	96 (13.5%)	45 (6.3%)	1 (0.1%)
I think it is animal unfriendly.	102 (14.4%)	119 (16.8%)	209 (29.5%)	160 (22.6%)	117 (16.5%)	2 (0.3%)
I think one should not combine animal DNA with human DNA.	77 (10.9%)	126 (17.8%)	250 (35.3%)	127 (17.9%)	126 (17.8%)	3 (0.4%)
I would not be psychologically capable of living with an animal's organ	113 (15.9%)	155 (21.9%)	230 (32.4%)	140 (19.7%)	68 (9.6%)	3 (0.4%)
I would be worried about the risks associated with this technique.	31 (4.4%)	49 (6.9%)	127 (17.9%)	291 (41.0%)	209 (29.5%)	2 (0.3%)
I believe it would be a good solution for the organ shortage.	59 (8.3%)	90 (12.7%)	308 (43.4%)	176 (24.8%)	74 (10.4%)	2 (0.3%)

For statistical analysis, the answers "totally disagree" and "disagree" as well as "agree" and "totally agree" were joined.

group with prior knowledge ($p = 0.006$). If this procedure had similar results and risks as transplantation with a human organ, 38.6% would be willing to accept an organ from a chimera. A fifth (19.2%) would refuse, and 41.9% would have doubts. More men than women would accept such an organ ($p = 0.003$). In BSO, there was the least acceptance ($p < 0.001$). More religious than non-religious persons would be willing to take an organ of a chimera (44.5% vs. 33.1%, $p = 0.002$). Among the respondents with prior knowledge, 20% more people responded positively ($p < 0.001$).

In case of worse results and greater risks, 11.4% would be willing to receive a chimera organ, and 36.2% would refuse. Almost twice as many men as women (15.5% vs. 8.3%) would still accept a chimera organ if there were more risks ($p = 0.003$). If one would accept an organ of a chimera in case of similar risks and results, 27.7% would also accept one in case of more significant risks and worse results. Of the people who refused or doubted the first case, 98.8% also did in the second case ($p < 0.001$).

Half of the students (50.2%) did not think receiving an organ from a chimera would change their personality (Table 7). Similarly, half of the respondents (50.9%) stated that they would not feel less human after the transplantation. The technique itself was considered animal unfriendly by 39.1%. More women than men (46.3% vs. 29.9%) indicated concerns for animals ($p < 0.001$), as well as more non-believers ($p = 0.008$). More than a third of the students (35.7%) thought that one should not combine animal and human DNA, while 28.6% were not concerned. More women than men (43.3% vs. 25.9%) were against DNA recombination ($p < 0.001$). Non-religious students also took more issue with DNA recombination than religious students did (41.3% vs. 30.1%, $p = 0.003$). Less than a third (29.3%) thought they could not psychologically cope with living with a chimera organ. Approximately

70.5% were concerned about the risks associated with human-animal chimera transplantation.

3.5 | Animal-to-human transplantation versus chimera-to-human transplantation

In order to determine whether there was a link between the answers to the statement about allotransplantation and the two different xenotransplantation scenarios, a correlation test was done. For all the statements, a significant correlation was seen with a p -value < 0.001 . Thus, people who would not accept a human organ would also not do so for an animal organ in 96.7% of the cases if similar results and risks ($p < 0.001$) as well as in 97.8% of the cases if worse results and more significant risks ($p < 0.001$) (Table 8). Among those who would refuse a human organ, 92.2% would not want an organ of a chimera if similar results and risks ($p < 0.001$) as well as 96.7% if worse results and risks ($p = 0.009$).

4 | DISCUSSION

This study was the first published public perception study undertaken in Belgium. Although several studies have been done to determine the public acceptance of xenotransplantation and even fewer determining the acceptance of transgenetic organs, a recent systematic review illuminated the difficulty of comparing individual studies to determine factors associated in favor or against xenotransplantation.¹¹ This difficulty is due to these studies' non-standardized approach and results in the decreased ability to draw generalizations from these studies¹¹ including this one. The aim of this study was to determine

TABLE 8 Influence and correlation of attitude with human-to-human transplantation – animal-to-human transplantation – chimera-to-human transplantation

		Case animal-to-human transplantation: <u>similar risks and results</u> compared to transplantation with human organs (n = %)				
		Yes	No	I am not sure	No answer	p-value
Case allotransplantation	Yes	252/614 (41.0%)	51/614 (8.3%)	311/614 (50.7%)	5/709 (0.7%)	<0.001 ^a
	No	0/11 (0.0%)	8/11 (72.7%)	3/11 (27.3%)		
	I am not sure	3/79 (3.8%)	34/79 (43.0%)	42/79 (53.2%)		
		Case animal-to-human transplantation: <u>greater risks and worse results</u> compared to transplantation with human organs				
		Yes	No	I am not sure	No answer	p-value
Case allotransplantation	Yes	88/615 (14.3%)	166/615 (27.0%)	361/615 (58.7%)	5/709 (0.7%)	0.001 ^a
	No	0/11 (0.0%)	7/11 (63.6%)	4/11 (36.4%)		
	I'm not sure	2/78 (2.6%)	46/78 (59.0%)	30/78 (38.5%)		
		Case chimeras-to-human transplantation: <u>similar risks and results</u> compared to transplantation with human organs				
		Yes	No	I'm not sure	No answer	p-value
Case allotransplantation	Yes	267/614 (43.5%)	91/614 (14.8%)	256/614 (41.7%)	5/709 (0.7%)	<0.001 ^a
	No	0/11 (0.0%)	10/11 (90.9%)	1/11 (9.1%)		
	I am not sure	7/79 (8.9%)	34/79 (43.0%)	38/79 (48.1%)		
		Case chimeras-to-human transplantation: <u>greater risks and worse results</u> compared to transplantation with human organs				
		Yes	No	I am not sure	No answer	p-value
Case allotransplantation	Yes	78/615 (12.7%)	200/615 (32.5%)	337/615 (54.8%)	4/709 (0.6%)	0.009 ^a
	No	0/11 (0.0%)	10/11 (90.9%)	1/11 (9.1%)		
	I am not sure	3/79 (3.8%)	44/79 (55.7%)	32/79 (40.5%)		

^aChi quadrat test.

For the analysis, the answers "no" and "I am not sure" were joined.

the attitudes of participants, related to the different transplantation techniques. There are some interesting points to consider from this study.

4.1 | Attitudes toward human-to-human organ transplantation

In our study, almost all respondents had previous knowledge of human-to-human organ donation and transplantation, but it is unknown if respondents had direct or familial experience with the matter. A vast majority indicated their willingness to accept the technique if they were waiting for a lifesaving organ and had a 3-month prognosis. A similarly high prior knowledge and acceptance rate is found in the only other contextually comparable study by Coucke et al, who studied Flemish primary health care physicians' attitudes toward organ donation and transplantation.¹⁶ While these studies' comparability is low in terms of respondents' age and level of education, they both align with Belgium's above global average status regarding the recruitment of fellow residents to donate their organs posthumous. They, furthermore,

aligned with expected public attitudes for a country with a so-called presumed consent organ donation law.^{17,18}

4.2 | Attitudes toward xenotransplantation

Both xenotransplantation techniques were in comparison to human-to-human transplantation, mostly unknown techniques to respondents. A degree of scenario transference from human-to-human transplantation seemed to have influenced the respondents, as a remarkable 36%–39% were willing to accept the priorly unknown techniques of animal-to-human transplantation or chimera-to-human transplantation. In a study conducted by Febrero et al in the southeast of Spain, it was seen that 44% of the teenagers favored the technique of xenotransplantation.¹⁴ A seemingly higher rate of acceptance of xenotransplantation (51.4%) was found among university students in Italian (51.4%) and Polish (55%) studies,^{19,20} but the lack of more studies among teenagers and students limits age comparisons.

In our study, we evaluated participants' willingness to accept xenotransplantation if the technique would hold further or more severe

risks than human-to-human transplantation. The acceptance rate fell dramatically to around 12%. The questions on risk aversion phrased in a hypothetical scenario are interesting as they may support Persson et al.'s conclusion that it is difficult for a healthy person to judge the various possibilities of treatment in the event of suffering a life-threatening disease, which requires an organ transplant.²¹ Rubaltelli et al. raise further caution to the interpretation of these results. They demonstrated that participants' affective reactions would be influenced when human-to-human transplantation and xenotransplantation are compared directly, as supposed to separately.²² One should also recognize the potential bias brought about to participants in our study as the specific questions were phrased to focus only on the possible involvement of more risks associated with xenotransplantation. A recent publication shows that xenotransplantation will hold fewer risks or at least different kinds of risks than human-to-human transplantation. The benefits of xenotransplantation, like the absence of a waiting period and superior organ quality, were not explored in this study.²³

4.3 | Animal-to-human transplantation versus chimera-to-human transplantation

Overall, our results demonstrated that if the risks were potentially identified similar to both xenotransplantation and organs from chimeras, most of the respondents favored both the techniques (41% for animal-to-human transplantation and 43.5% for chimeras-to-human transplantation). Thirty-two percent of participants agreed the xenotransplantation technique is animal unfriendly, and 39.1% thought human-animal chimeras are animal unfriendly as well. However, approximately the same percentage agreed that it would be a good solution for organ shortage (41.8% for xenotransplantation and 35.2% for human-animal chimeras).

It was examined whether there was a connection with the attitude toward human-to-human transplantation with the two xenotransplantation techniques. Participants who would not accept a human organ would also not do so for an animal organ in 96.7% of the cases if similar results and risks and 97.8% of the cases if worse results and greater risks. Surprisingly, it was also observed that regardless of having the least prior knowledge about human-animal chimeras, there was more acceptance rate observed for the human-animal chimeric organ, especially when participants had to suppose if they were on a waiting list. This observation may be due to a general teenager curiosity and openness to new things, coupled with their tendency to underestimate risks.

We found no other studies that explicitly compared participants' attitudes in the two different scenarios of animal-to-human transplantation and chimera-to-human transplantation. However, in some studies on xenotransplantation, the attitude toward genetic modification in donor animals was questioned. In one study among the Korean population, 63% of participants held a positive attitude in this regard.²⁴ In de Bona et al.'s Italian study, 51.4% of students had favorable attitudes toward animal genetic modification for the purpose of transplan-

tation to humans.¹⁹ Besides, several studies have already been conducted on the public's opinion concerning research with human-animal chimeras and human-animal embryos. In a poll in 2007 among the British general public, 35% replied they thought hybrid embryos could be created for research; 48% were opposed to this.²⁵ Additionally, an American online survey issued shows 22.6% had opposed chimeric research.¹³ Another survey of the Japanese population showed opposition to research with human-animal chimeras of about 50%.²⁶ Conversely, a year later, another study among the Japanese population appeared in which 81% were in favor of the creation of human-pig embryo chimeras, and more than 60% were in favor of the creation of human-pig chimeras.¹² In our study, only 28.6% were in favor of transgenetic organ development.

4.4 | Limitations of the study

Some limitations were already discussed above, but some further limitation requires mentioning. First, the respondents chosen for the survey were from a particular educational background and age group, which were secondary students. Therefore, our results cannot be generalizable to the general population. Second, the study was conducted prior to the start of the global COVID-19 pandemic with no other major epidemic due to a zoonotic infection that occurred recently in Europe. The general public's understanding of the risks and consequences of zoonotic infections would likely have shifted since the study was conducted.⁷

5 | CONCLUSION

It can be concluded that Flemish secondary school students favored the techniques of xenotransplantation to a lesser extent than allotransplantation; however, most of them did consider it a good solution for organ shortage. In comparison to animal-to-human transplantation, chimera-to-human transplantation showed a more positive attitude among the respondents when considered a good solution for organ transplantation. As not many previous surveys have been conducted regarding secondary school students' attitudes, we cannot compare the results to other studies except for higher age levels or the general population.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest associated with this research study.

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