

## **ARTICLE**



# Public attitudes in the clinical application of genome editing on human embryos in Japan: a cross-sectional survey across multiple stakeholders

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Recent advances in genome editing technology are accompanied by increasing public expectations on its potential clinical application, but there are still scientific, ethical, and social considerations that require resolution. In Japan, discussions pertaining to the clinical use of genome editing in human embryos are underway. However, understanding of the public's sentiment and attitude towards this technology is limited which is important to help guide the debate for prioritizing policies and regulatory necessities. Thus, we conducted a cross-sectional study and administered an online questionnaire across three stakeholder groups: the general public, patients and their families, and health care providers. We received responses from a total of 3,511 individuals, and the attitudes were summarized and compared among the stakeholders. Based on the distribution of responses, health care providers tended to be cautious and reluctant about the clinical use of genome editing, while patients and families appeared supportive and positive. The majority of the participants were against the use of genome editing for enhancement purposes. Participants expressed the view that clinical use may be acceptable when genome editing is the fundamental treatment, the risks are negligible, and the safety of the technology is demonstrated in human embryos. Our findings suggest differences in attitudes toward the clinical use of genome editing across stakeholder groups. Taking into account the diversity of the public's awareness and incorporating the opinion of the population is important. Further information dissemination and educational efforts are needed to support the formation of the public's opinion.

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## INTRODUCTION

A recent genome editing method, the clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated protein 9 (Cas9), is a molecular technology of high precision. Genome editing is expected to significantly influence clinical practice through its ability to modify disease-causing genetic alterations and regulate gene expression. Thus, genome editing research is being conducted widely across many countries, including efforts to understand potential application in altering the genome of human embryos [1, 2]. However, concession for its use on human embryos still has various unresolved technological and ethical considerations despite its legitimate potential for promoting health and preventing disease [3, 4].

The movement is widespread to enact punitive legislation to regulate the clinical use of genome editing on human embryos. Several countries prohibit the clinical use by law or through medical regulations with penalties of imprisonment or

fines [5–9]. In Japan, several guidelines on gene therapies, guidelines on research using human embryos for reproductive therapies and guidelines on research using human embryos involving genome editing prohibit translation of genome edited embryos to the human uterus [10–12]. However, questions have been raised about effectiveness in compliance with guidelines since they are not legally binding and there are no specific penalties. In view of these issues, the Japanese National Expert Committee expressed the need to assemble a law to ensure effective regulatory mechanisms.

Understanding the opinions and ideas from a wide range of stakeholders is critically important in the process of formulating ethical and sustainable legal regulations [13]. The World Health Organization indicated the need for a comprehensive, multi-directional, multistakeholder dialogue on the future of human genome editing [14]. Studies surveying the beliefs, attitudes and ethical considerations toward gene therapy and genome editing

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in humans have been pursued by several countries, including the United States and the United Kingdom [15]. Some studies were also conducted across multiple countries to identify factors that influence the acceptability of gene therapy and genome editing in humans [5, 16]. Based on these results, perceptions appeared positive, particularly about the use of genome editing for medical reasons and fatal diseases. These studies have described that the risks and benefits need to be clearly communicated if the technology is to be accepted by the general public. However, previous studies on this topic in Japan are scarce, and the assembly of opinions from a broad range of stakeholder groups are insufficient to move the discussion forward regarding the extent of evidence that is needed on safety and other issues before clinical use of genome editing on human embryos can be considered acceptable [17-19]. Therefore, we conducted an exploratory study intended to capture the attitudes of multiple stakeholders and to point out descriptive differences that may contribute to future policy discussions.

The objective of this study was to understand the current attitudes towards the clinical application of genome editing on human embryos in three different populations of stakeholders and to explore the differences between these groups.

## MATERIALS AND METHODS Study setting and population

We conducted a cross-sectional survey using an online system between August and December 2020 which was approved by the Institutional Review Board of the National Center for Child Health and Development (Application #2020-039). We obtained informed consent from all participants via an online survey system before asking them to complete the questionnaire.

The study targeted three primary populations: the general public (GP), patients and patients' families (PT), and health care providers (HCP). The inclusion criteria for all three groups were adults aged 18 years or older. The GP were recruited using a web marketing research panel provided by Macromill Inc. (Tokyo, Japan) from among those who met the inclusion criteria. The number of respondents was adjusted in advance so that the gender and age distribution would be evenly distributed, and the survey was conducted until the target number was reached. The PT were recruited from the Japan Patients Association (92 affiliated organizations) [20], and the Approved Specified Nonprofit Corporation the Support Network for NANBYO Children of Japan (68 affiliated organizations) [21]. Members of these organizations include people who suffer from rare or incurable diseases. Preventing the transfer of heritable traits to the next generation through genome editing and in vitro fertilization may be a pertinent topic of interest for this population. The patients or family members of patients were invited to participate in this study through newsletters provided by the organizations and email-based distributions requesting members to participate in the questionnaire. The HCP included medical doctors or other health care providers who were recruited through one of the four clinical/academic societies that have relevance to this topic of genome editing (the Japan Society of Obstetrics and Gynecology, the Japan Pediatric Society, the Japan Society of Perinatal and Neonatal Medicine, and the Japan Society of Human Genetics). Based on estimated membership counts at the start of this survey, there was approximately 300,000 members among PT, and approximately 40,000 among HCP, in which there may have been some overlap in membership. Since PT and HCP were recruited using passive recruitment methods such as e-mail and web-based advertising, it was not possible to determine a response rate.

## Questionnaires

We sent the same questionnaire to the three groups, except for certain attribute questions that were specific to the populations (See Supplementary information), using web survey systems (Macromill, Inc., Tokyo, Japan, and Research Electronic Data Capture; REDCap). The questionnaire consisted of 17 closed-ended questions divided into three sections, and two videos were provided that included basic information about genome editing to help standardize baseline understanding of the technology. On the basis of Japanese National Expert Committee statements [6, 8, 10], the contents of the videos comprised an overview of genome editing technology including genome terminology and basic methods, and an

objective description of documented benefits and risks of the technology in Japanese. Each video was viewed through the web survey system, and were 3.5 min and 2 min in duration, respectively. The participants were asked to watch these videos prior to completing Section 2 and Section 3. Prior to full implementation, the questionnaire and videos were pilot tested among representatives of the GP, PT, and HCP populations to confirm that the information was objectively presented without potentially biasing the responses, and whether any expressions were difficult to understand. We collected their feedback using open-ended questions, and the comments referring to potential objectivity and bias concerns were addressed in a revised questionnaire and videos ensuring consistency with National Expert Committee statements.

Section 1 (8 items) of the questionnaire included demographic information such as gender, age, marital status, religious beliefs, and prior knowledge of genome editing; Section 2 (4 items) described four scenarios where genome editing in humans may be relevant to families, including adult-onset disease (Case 1), childhood-onset lethal disease (Case 2), embryonic lethal disease (Case 3), and enhancement use (Case 4), and the attitude of respondents were assessed using a 5-point Likert scale (i.e., strongly agree, agree, neutral, disagree, strongly disagree) with an option to select "Unable to decide or do not want to answer"; Section 3 (5 items) surveyed participant attitudes regarding when they considered clinical use of genome editing on human embryos acceptable based on, (1) the degree of efficacy that needs to be demonstrated (referred to as "Degree of Efficacy"), (2) the degree of risk (referred to as "Degree of Risk"), (3) the extent of evidence on safety based on animal studies (referred to as "Safety Evidence - animal studies"), (4) the extent of evidence on safety based on human studies (referred to as "Safety Evidence - human studies"), and (5) situations that may be considered acceptable (referred to as "Acceptable Conditions"). The participants were asked to select one option that was closest to their thoughts (full questions and possible responses are shown in the supplementary information).

## Statistical methods

Responses to each question were shown descriptively with numbers and percentages provided within each group. The 5-point Likert scale responses in Section 2 were summarized into three categories: Agree (includes Strongly agree and Agree), Neutral, and Disagree (includes Disagree and Strongly disagree). The survey was considered completed when all questions were answered; thus, there were no missing data for analysis. As a descriptive study performed in three separate stakeholder populations, distributions of responses were observed in each, and differences were qualitatively interpreted without statistical hypothesis testing. Stata version 16.0 (StataCorp LLC, College Station, TX, USA) was used for data analysis.

## **RESULTS**

We collected a total of 3511 responses (2060 GP, 497 PT, and 954 HCP). Demographic characteristics of the participants among the three groups are shown in Table 1. There were equal numbers of men and women in GP, but more women in PT and more men in HCP. Similarly, the age distribution of GP was uniform as dictated by the design, but PT and HCP showed a peak age group of 40 to 49 years old. The proportion of participants who were married and have children in GP were smaller than that of PT and HCP. As expected, HCP showed the highest educational background. Educational level of PT appeared to be slightly higher than GP. More than 80% of participants among the three groups answered that they have no religious beliefs (85.2% of GP, 83.7% of PT, 82.3% of HCP). Knowledge of genome editing was the highest in HCP (96.4%), followed by PT (67.4%) and GP (46.6%). About half of GP reported not knowing about genome editing (51.8%).

Responses to specific genome editing scenarios (Case 1 to 4) described in Section 2 of the questionnaire are shown in Table 2. From Case 1 to Case 3 (adult-onset diseases, childhood-onset and embryonic lethal diseases), the most common response was "Agree" to the use of genome editing among GP and PT with the proportion agreeing higher in PT (56.1% to 60.2%) compared to GP (40.9% to 47.2%). In contrast, "Disagree" received the highest proportion of responses among HCP (38.8% to 42.1%). For Case 4

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**Table 1.** Demographic characteristics of participants among stakeholder groups

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	GP (N = 2060)	PT ( <i>N</i> = 497)	HCP (N = 954)
Gender			
Male	1030 (50.0)	189 (38.0)	536 (56.2)
Female	1030 (50.0)	304 (61.2)	405 (42.5)
Prefer not to disclose	0 (0.0)	4 (0.8)	13 (1.3)
Age group (years)			
18 to 29	412 (20.0)	16 (3.2)	34 (3.6)
30 to 39	412 (20.0)	83 (16.7)	202 (21.2)
40 to 49	412 (20.0)	159 (32.0)	330 (34.6)
50 to 59	412 (20.0)	129 (26.0)	251 (26.3)
60 or older	412 (20.0)	109 (21.9)	133 (13.9)
Prefer not to disclose	0 (0.0)	1 (0.2)	4 (0.4)
Marital status			
Married	1279 (62.1)	400 (80.5)	773 (81.0)
Not married	756 (36.7)	89 (17.9)	156 (16.4)
Prefer not to disclose	25 (1.2)	8 (1.6)	25 (2.6)
Have children?			
Yes	1095 (53.2)	390 (78.5)	687 (72.0)
No	949 (46.1)	102 (20.5)	246 (25.8)
Prefer not to disclose	16 (0.8)	5 (1.0)	21 (2.2)
Highest educational attain	ment		
Junior high school	51 (2.5)	10 (2.0)	n/a
High school	564 (27.4)	93 (18.7)	n/a
Vocational school	350 (17.0)	78 (15.7)	n/a
University or college	971 (47.1)	261 (52.5)	487 (51.1)
Graduate school	93 (4.5)	42 (8.5)	450 (47.2)
Other	0 (0.0)	7 (1.4)	13 (1.4)
Prefer not to disclose	31 (1.5)	6 (1.2)	4 (0.4)
Relationship with patients			
Patient	n/a	217 (43.7)	n/a
Guardian	n/a	245 (49.3)	n/a
Partner	n/a	12 (2.4)	n/a
The survivor	n/a	2 (0.4)	n/a
Other	n/a	21 (4.2)	n/a
Prefer not to disclose	n/a	0 (0)	n/a
Medical profession	11/4	C (C)	11/4
Pediatrician	n/a	n/a	203 (21.3)
Neonatologist	n/a	n/a	71 (7.4)
Obstetrician	n/a	n/a	75 (7.9)
(reproductive	11/ a	II/a	73 (7.9)
medicine)			
Obstetrician (other than reproductive	n/a	n/a	215 (22.5)
medicine)			
Gynecologist	n/a	n/a	112 (11.7)
Other	n/a	n/a	273 (28.6)
Prefer not to disclose	n/a	n/a	5 (0.5)
Religious background			
A religious person	242 (11.7)	69 (13.9)	136 (14.3)
Not a religious	1756 (85.2)	416 (83.7)	785 (82.3)
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Prefer not to disclose	62 (3.0)	12 (2.4)	33 (3.4)
Prior knowledge of genom	ne editing		
Able to describe genome editing	130 (6.3)	73 (14.7)	479 (50.2)
Have heard of it, but unable to describe	831 (40.3)	262 (52.7)	441 (46.2)
Have never heard of genome editing	1067 (51.8)	161 (32.4)	31 (3.3)
Prefer not to disclose	32 (1.6)	1 (0.2)	3 (0.3)
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 $\mathit{GP}$  general public,  $\mathit{PT}$  patients and patient families,  $\mathit{HCP}$  health care provider

Data are shown as n (%).

**Table 2.** Attitude among stakeholder groups towards the use of genome editing according to four different case scenarios

genome editing according to four different case scenarios							
	GP (N = 2060)	PT (N = 497)	HCP (N = 954)				
Case 1 (Adult-onset disease): The disease develops in adulthood and is untreatable leading to a slow decline in daily activity, finally to become bedridden. A couple is strongly hoping to use genome editing to have a child who will not develop the disease.							
Agree	843 (40.9)	279 (56.1)	341 (35.7)				
Neutral	626 (30.4)	126 (25.4)	211 (22.1)				
Disagree	505 (24.5)	77 (15.5)	385 (40.4)				
Unable to decide or do not want to answer	86 (4.2)	15 (3.0)	17 (1.8)				
Case 2 (Childhood-onset lethal disease): The disease develops as a serious medical condition at birth and is untreatable leading to death before reaching adulthood. A couple is strongly hoping to use genome editing to have a child who will not develop the disease.							
Agree	973 (47.2)	299 (60.2)	373 (39.1)				
Neutral	556 (27.0)	112 (22.5)	192 (20.1)				
Disagree	443 (21.5)	73 (14.7)	370 (38.8)				
Unable to decide or do not want to answer	88 (4.3)	13 (2.6)	19 (2.0)				
Case 3 (Embryonic lethal disease): Due to genetic abnormalities, a couple is infertile and is undergoing fertility treatment. They are strongly hoping to use genome editing to increase their chances of conceiving and giving birth.							
Agree	925 (44.9)	286 (57.5)	324 (34.0)				
Neutral	595 (28.9)	126 (25.4)	214 (22.4)				
Disagree	474 (23.0)	73 (14.7)	402 (42.1)				
Unable to decide or do not want to answer	66 (3.2)	12 (2.4)	14 (1.5)				
Case 4 (Enhancement use): A couple is strongly hoping to use genome editing to have a child that possesses a specific desired trait (e.g., athletic ability, ideal body shape, etc).							
Agree	171 (8.3)	11 (2.2)	13 (1.4)				
Neutral	389 (18.9)	26 (5.2)	30 (3.1)				
Disagree	1442 (70.0)	459 (92.4)	904 (94.8)				
Unable to	58 (2.8)	1 (0.2)	7 (0.7)				

*GP* general public, *PT* patients and patient family, *HCP* health care provider Data are shown as n (%); full case scenarios is viewable in the supplementary materials

(genome editing for enhancement purposes), more than 90% of participants in PT and HCP disagreed with its use; among GP, the majority similarly disagreed, but at a lower proportion (70%) compared to the other groups. Across the four case scenarios, the proportion of participants in GP who answered "Neutral" or "Unable to decide or do not want to answer" tended to be higher than the other two groups.

Table 3 shows the results of Section 3 of the questionnaire, which asked for opinions on the acceptable clinical use of genome editing on human embryos in relation to 5 pertinent issues. Overall, the proportion answering that genome editing on human embryos should not be used regardless of the degree of efficacy, risk, and available evidence tended to be higher in HCP (22% to 32%) and the lowest in PT (approximately 16%). Regarding "Degree of Efficacy", more than half of participants across the three groups answered that genome editing may be acceptable if it can cure or eliminate most of the symptoms. But, one-third of HCP answered "Regardless of the degree of effectiveness, it should not be used", with smaller proportions observed in GP and PT. When asked about the "Degree of Risk" that is acceptable for clinical use, the most common answer across the 3 groups was "If the risk is negligible, it is acceptable",

Table 3. Attitudes among stakeholder groups regarding criteria for when genome editing on human embryos may be considered acceptable

	GP	PT	НСР
	(N = 2060)	(N = 497)	(N = 954)
Degree of Efficacy: The degree of efficacy that is required before accepting genome editing in human	n embryos for cli	inical use.	
The cause of the disease can be completely removed.	572 (27.8)	166 (33.4)	206 (21.6)
It cannot remove the cause of the disease, but it can greatly alleviate the symptoms.	480 (23.3)	136 (27.4)	275 (28.8)
It cannot remove the cause of the disease, but it can provide some symptomatic relief.	296 (14.4)	68 (13.7)	83 (8.7)
Regardless of the degree of efficacy, it should not be used.	449 (21.8)	80 (16.1)	306 (32.1)
Unable to decide or do not want to answer.	263 (12.8)	47 (9.5)	84 (8.8)
Degree of Risk: The degree of risk that is required before accepting genome editing in human embry	os for clinical us	se.	
If efficacy is assured, no matter how high the risk, it is acceptable.	43 (2.1)	11 (2.2)	10 (1.1)
It is acceptable if the level of risk is known in advance.	474 (23.0)	171 (34.4)	250 (26.2)
If the risk is negligible, it is acceptable.	839 (40.7)	199 (40.0)	361 (37.8)
Regardless of the level of risk, it should not be used.	485 (23.5)	82 (16.5)	278 (29.1)
Unable to decide or do not want to answer.	219 (10.6)	34 (6.8)	55 (5.8)
<b>Safety Evidence- animal studies:</b> The most important criteria for considering that genome editing in testing stage.	human embryos	is safe at the	animal
Only the target gene can be reliably edited.	442 (21.5)	207 (41.6)	346 (36.3)
It has been confirmed that there are no adverse effects on the next generation.	880 (42.7)	184 (37.0)	346 (36.3)
Regardless of the level of safety, it should not be used.	490 (23.8)	79 (15.9)	210 (22.0)
Unable to decide or do not want to answer.	248 (12.0)	27 (5.4)	52 (5.5)
<b>Safety Evidence- human studies:</b> The most important criteria for considering that genome editing in testing stage.	human embryos	is safe at the	human
Sufficient safety has been confirmed in animal eggs.	103 (5.0)	42 (8.5)	70 (7.3)
Sufficient safety has been confirmed in human embryos.	1070 (51.9)	311 (62.6)	522 (54.7)
Regardless of the level of safety, it should not be used.	561 (27.2)	79 (15.9)	288 (30.2)
Unable to decide or do not want to answer.	326 (15.8)	65 (13.1)	74 (7.8)
Acceptable Conditions: Disease circumstances for which genome editing in human embryos is considerable.	lered acceptable		
If there is no treatment other than genome editing.	750 (36.4)	223 (44.9)	424 (44.4)
If there is no treatment other than genome editing, but there are treatments that may alleviate symptoms.	228 (11.1)	82 (16.5)	103 (10.8)
Treatments other than genome editing are available, but the success rates are low.	200 (9.7)	62 (12.5)	78 (8.2)
Treatments other than genome editing are available, and their success rates are high.	133 (6.5)	9 (1.8)	8 (0.8)
No child should be born from genome edited human embryos regardless of treatment availability.	462 (22.4)	80 (16.1)	279 (29.3)
Unable to decide or do not want to answer.	287 (13.9)	41 (8.2)	62 (6.5)

GP general public, PT patients and patient families, HCP health care provider Data are shown as n (%)

accounting for about 40% of respondents. Regarding the extent of acceptable evidence from animal and human studies on safety, more than half of the respondents in all groups answered that safety needs to be confirmed in human embryos. Regarding "Acceptable conditions", the highest proportion among the three groups (36.4 to 44.9%) responded "if there is no treatment other than genome editing". For all of the five pertinent issues covered in Section 3 of the questionnaire, the proportion answering "Unable to decide or do not want to answer" was highest in GP compared to PT and HCP.

## **DISCUSSION**

This cross-sectional study is the first to compare the attitudes regarding clinical application of genome editing in human embryos among three stakeholder groups using the same questionnaire. In this study, we found that PT had the most positive view of genome editing in human embryos, while HCP appeared the most cautious and reluctant. We also observed that a relatively large proportion of people from three different

stakeholders considered genome editing on human embryos to be acceptable if it were the fundamental treatment of high efficacy with minimal risk, and safety issues have been confirmed in humans before clinical application. However, the attitudes toward clinical use of genome editing were different depending on the purpose.

In common across all groups, the pattern of answers regarding agreement to the use of genome editing appeared similar even if the timing of onset and severity of the disease differed as represented by the three scenarios presented (Case 1 to 3). In Jedweb et al.'s [16] survey of attitudes toward genome editing of human embryos among approximately 1500 participants from the general public in 67 countries, the proportion in favor of clinical application was nearly 80%, higher than our results. In our study, the percentage agreeing to its use was about 60% at most, suggesting that differences may be influenced by country-specific characteristics and cultural background; approximately 80% to 90% of the participants in Jedweb's study was from the United States, Australia, Canada, and United Kingdom. In contrast to our study which included only Japanese, the higher percentage

reported in the previous multi-national study may be a reflection of influences originating from various ethnicities, religions, and cultural spheres [4, 22].

With regard to enhancement, all groups showed a high percentage of disagreement with the use of genome editing on human embryos. A number of previous studies on genome editing technologies for enhancement purposes have reported similar results to our survey [5, 13, 16, 23–26]. Although there are both pros and cons to the clinical use of genome editing, the view that it should not be used for the purpose of enhancing the properties and abilities of healthy individuals was clearly expressed. Notably, the proportion among GP who agreed with enhancement use appeared higher than among PT and HCP. We speculate that PT and HCP might have a stronger rejection against enhancement than GP because PT and HCP may have greater awareness of the need to devote focused attention to overcome devastating genetic diseases. These observations highlight the importance of consensus building as opinions and attitudes related to this topic of genome editing may vary across a wide range of stakeholders in Japan.

In observing the patterns of responses across the three stakeholder groups, if the technology were to show a high degree of efficacy, the PT group showed the highest proportion of participants who would accept the clinical application. The HCP group showed the highest proportion expressing that "Regardless of the degree of efficacy, it should not be used". This result is reasonable because patients and their families with genetic diseases are the primary beneficiaries, and expectations would be high for the development and safe clinical application of genome editing technology. Consistent across all three groups was the strong sentiment that the technology should be safe and pose minimal risk in clinical use. In particular for "Degree of Risk", approximately 40% of participants consistent across the three groups indicated the technology is acceptable if the risk is negligible. Previous studies performed in genetic counselors and other professionals in the genetics field [5, 18] have reported significant proportions not positively accepting to genome editing expressing concerned about the safety and accuracy of the technology. Also pointed out was that even though it is an alteration of the developmental system from the genetic building blocks, 100% success cannot be guaranteed, leading to concerns. Theoretically, there is no zero-risk medical treatment in clinical settings. Thus, applying this new technique in the clinical setting would require further discussion and agreement among various stakeholders.

In general, proportions of participants who responded "Neutral" or "Unable to decide or do not want to answer" were higher in GP than PT or HCP. A study conducted in the U.S. found that those with less knowledge may have the tendency to say that they neither support nor oppose genome editing [13]. It seems that the degree of knowledge is relevant in developing clear opinions and a stance toward genome editing. A previous Japanese survey conducted in 2017 reported that 70% of the general adult population had never heard of genome editing [17]. In our survey, approximately 50% of participants in GP had never heard of genome editing and only 6.3% of them would be able to explain it. Although we provided a video describing genome editing prior to answering the questionnaire, it might have been difficult for certain participants with limited previous knowledge to develop clear thoughts regarding ethical and social issues. A study conducted in the Netherlands showed that genome editing is a topic of high interest, even among people with no previous knowledge [27]. As an implication for future efforts, it may be desirable to provide education and create opportunities for dialogue among the general population in order to better understand public opinion. We believe that, with adequate education and information provision, a proper understanding of the public's opinion on genome editing could be achieved.

The limitations of this study should be noted. First, this survey, which pursued a broad approach to sampling and recruitment through email and web-based advertising, may have resulted in a population with an over-representation of people who have interest in this topic. Although exact response rates could not be calculated, we expect that they were low for PT and HCP. However, the study population still included a mixture of people in which a large proportion showed a low level of awareness of genome editing, including those who hesitated to answer. Thus, it is possible that the level of awareness of genome editing among the GP observed in this study may have been overestimated. Second, the guestions asking for opinions on the safety, risks, and usefulness of genome editing for clinical use may have been complicated for some. Thoughts about the complex issues may have been difficult to respond to based on selection of a single answer as perceptions may differ depending on the various possible individual circumstances. Despite these limitations, this is the first study in which the same survey was conducted on three different stakeholder groups possessing different backgrounds. Our study indicated that basic knowledge and attitudes toward genome editing may vary by position and background. When considering the "public's" opinions in developing legal and regulatory framework for issues related to genome editing and its clinical use, it is necessary to pay attention to what kind of groups comprise the "public". It is expected to be a useful data source for discussing how to apply genome editing for clinical use in the future.

In conclusion, attitudes toward the clinical use of genome editing on human embryos differed among GP, PT, and HCP. In general, PT tended to be supportive of the technology, while HCP were more cautious and reluctant. People are likely to have diverse opinions on this new technology, as shown by different response patterns among the three stakeholder groups. Further efforts are needed to develop consensus among the Japanese society by accumulating opinions that are based on common understanding of the issues.

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#### COMPETING INTERESTS

The authors declare no competing interests.

## ADDITIONAL INFORMATION

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