Pediatric RESEARCH

www.nature.com/pr

CLINICAL RESEARCH ARTICLE

Using a cartoon questionnaire to improve consent process in children: a randomized controlled survey

Shanshan Qiu[1], Yang Xia[1], Feng Tian[2], Yanfang Yang[3], Jijun Song[4], Liqin Chen[5], Hao Mei[6], Fan Jiang[7], Nan Bao[1] and Shijian Liu[8]

OBJECTIVE: The aim of the study was to evaluate the effectiveness of an audio and animated cartoon questionnaire (AACQ) at improving consent process in child for biospecimen donation.

METHODS: A multi-center randomized and controlled survey was performed at two pediatric hospitals in China from 2019 to 2020. Children aged from 7 to 18 years in the pediatric surgery wards were invited to investigate the participants' willingness and attitudes for donating biospecimens. A total of 264 children, including 119 in the AACQ group and 145 in the TQ group, and 67 parents of children were analyzed. A separate knowledge test was acquired in the questionnaires.

RESULTS: Our findings showed that the response rate of the AACQ group (89.85%) was significantly higher than that of the TQ group (68.44%; $p < 0.001$). AACQ can improve the child's understanding, increase children's engagement in biospecimen donation, reduced the differences in selected characteristics affecting children understanding, and enhanced their risk awareness of donating biospecimens. We also found that increasing pain and privacy disclosure were the most popular concern among children for the refusal to donate biospecimens.

CONCLUSIONS: AACQ is an effective and standardized tool of content delivery to children from the surgical wards. Children who fully understood of biospecimen donation are suggested to participate in the consent signing.

Pediatric Research (2021) 90:411–418; https://doi.org/10.1038/s41390-020-01227-2

IMPACT:

- Using audio and animated cartoon questionnaire is a more effective and standardized tool of content delivery to children.
- This study expanded the use of an animated cartoon to a children's survey. Audio and animated cartoon questionnaire (AACQ) can improve the child's understanding, increase children's engagement in biospecimen donation compared to text questionnaire (TQ) group, and enhanced their risk awareness of donating biospecimens.
- More AACQ should be used with children in the future to effectively deliver content to children and improve children's participation in the survey.

INTRODUCTION

The usage of human biospecimens will contribute to translational research. The biobanking has raised many ethical and legal concerns, including information sharing, conflict of interest, personal privacy protection, and public trust.[1–3] Much governmental efforts worldwide have been focused on establishing appropriate laws and regulations.[4] The number of biobanks has significantly grown over the past years in China, which has also attracted the attention of Chinese regulatory authorities. A notice published in 2017[5] contributed for some progress and ameliorated the procedure for international collaborative clinical trials conducted using Chinese human genetic resources.

The biospecimens and data collected from children are essential for the research of some specific diseases, such as rare diseases. However, informed consent of children has not been addressed in detail and the appropriate age for consent lacks a legal surrounding in China. Chinese law dictates that patients aged <18 years are not regarded as autonomous, so proxies should sign informed consent for participants of legal incapacity or restricted legal capacity. Our previous study showed that 79.7% of parents in China disagreed with signing an informed consent form for donating biospecimens from their own children aged 10–18 years.[6] The appropriate age of child's assent is still under debate.[7,8] According to U.S. regulations, the children are capable of providing assent by taking into account the ages, maturity, and psychological state of the children involved (45 CFR 46.408 Electronic Code of Federal Regulations). While in most regulations, irrespective of age, assent is not required from children who are

[1]Department of Pediatric Neurosurgery, Shanghai Children's Medical Center, Shanghai Jiaotong University School of Medicine, Shanghai, China; [2]Department of Pediatric Urinary Surgery, Shanghai Children's Medical Center, Shanghai Jiaotong University School of Medicine, Shanghai, China; [3]Department of Pediatric Urinary Surgery, Henan Children's Hospital Affiliated to Zhengzhou University, Henan, China; [4]Department of Clinical Laboratory, the Sixth People's Hospital Of Zhengzhou, Henan, China; [5]Department of Pediatric General Surgery, Shanghai Children's Medical Center, Shanghai Jiaotong University School of Medicine, Shanghai, China; [6]Department of Data Science, School of Population Health, University of Mississippi Medical Center, Jackson, MS, USA; [7]Department of Developmental and Behavioral Pediatrics, Shanghai Jiaotong University School of Medicine, Shanghai, China and [8]Pediatric Health Advocacy Institute, Shanghai Children's Medical Center, Shanghai Jiaotong University School of Medicine, Shanghai, China
Correspondence: Shijian Liu (liushijian@scmc.com.cn)
These authors contributed equally: Shanshan Qiu, Yang Xia

Received: 7 August 2020 Revised: 30 September 2020 Accepted: 6 October 2020
Published online: 17 November 2020

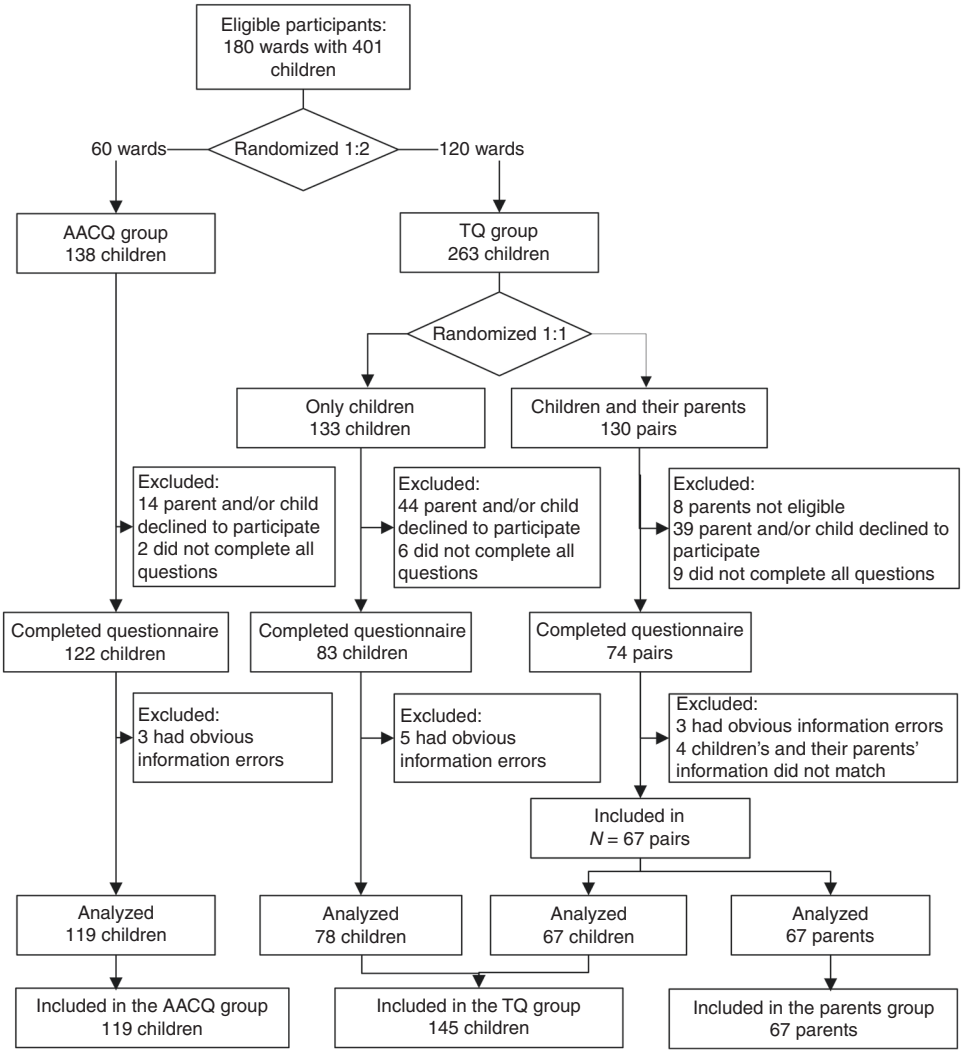

Fig. 1 Flowchart of randomization, allocation, and data collection of participants. AACQ audio and animated cartoon questionnaire, TQ text questionnaire.

deemed incapable of providing it.[9,10] But as the child grows up, the parents' choice does not always truly reflects the child's willingness, which should be respected.[11,12] According to a study, in general children aged ≥11–12 years were decision-making competent.[8] Thus children are expected to be involved in making decisions with regard to biobank participation.[13]

Although the ethics of biospecimen donation of children have attracted much attention, children understanding biospecimen donation and making an informed decision is always doubted. Animation is a novel information tool to improve comprehension, attention, recall, and adherence in health care by rendering the information about scientific research more accessible.[14] In children, Hannah reported that an internet-based educational animation had a positive impact on children with a neurodisability aged 6–11 years for magnetic resonance imaging (MRI) preparation, as it contributed to a good understanding of the MRI procedure and low anxiety levels prior to the scan.[15] Other studies in pediatric dental patients showed that even just the exposure to positive images could reduce children's dental anxiety.[16–18] An animated element has some effect on knowledge understanding and reducing anxiety, which may be helpful for children to make an appropriate decision on sample donation.

In the present study, we aimed to test whether an audio and animated cartoon questionnaire (AACQ) could help the child to understand the information about biospecimen donation, reduce differences in their understanding, and use that information to make an appropriate decision for themselves. Meanwhile, we examined factors that may influence children's willingness to donate biospecimens.

METHODS

Study design

In the preliminary study, we drafted the script and produced animations with key messages about biospecimens donation to improve the questionnaire. The pilot study was first tested on 20 children to evaluate the affinity and satisfaction of AACQ. Based on the specific feedback received from these children, such as the problem of disfluency and the use of formal words, AACQ was improved and adapted. After the preliminary research, we conducted a multi-center, cluster randomized controlled study (Fig. 1). Hospital wards were the unit of allocation to avoid the influence of different participants in the same ward using different questionnaires and make it feasible to carry out the survey. Participants were randomly clustered in an allocation ratio of 1:2 by wards (AACQ group $n = 60$; text questionnaire (TQ) group $n = 120$), one to four patients reside in each ward. In the TQ group, children were randomized in an allocation ratio of 1:1 to complete the questionnaire by himself/herself

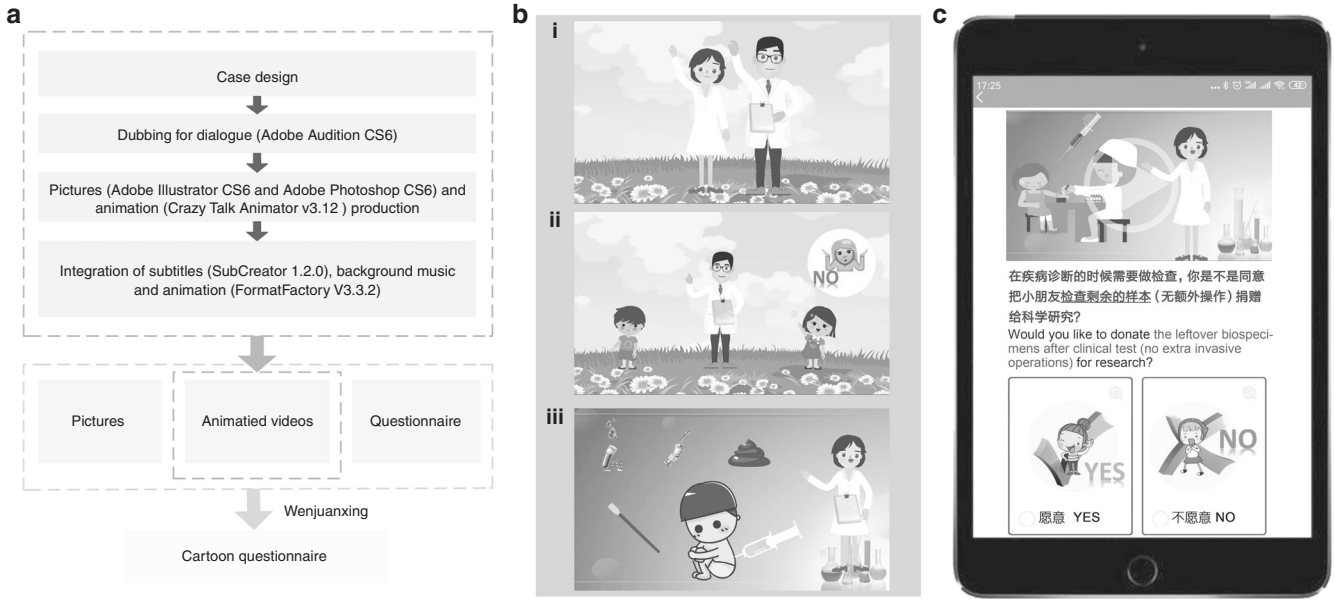

Fig. 2 The production process of cartoon questionnaire production. a Flowchart of cartoon questionnaire production. **b** Screenshot of our animated video. (i) Researches' animation image created by ourselves. (ii) The interaction between avatar children and avatar research. (iii) What kind of biospecimens can be donated for science and how they come from. **c** Display drawing of a animation of our survey on the Wenguanjing app. This animation shows children that the residual biospecimens from preoperative examination can be donated for science and no extra invasive operation is needed. The question under the animation is to ask whether they would like to donate.

or in a pair with his/her parent. A knowledge test to assess the acquired comprehension of biospecimen donation was given at the end of the questionnaire (Supplementary Table 1).

Participants

This survey was performed at two sites, Shanghai Children's Medical Center (SCMC) and Henan Children's Hospital (HCH), from July 1, 2018 to August 31, 2019. A total of 401 children were recruited. Patients aged between 7 and 18 years in the pediatric surgery wards were invited to participate in this survey. Every patient from pediatric surgery wards were supposed to leave blood samples and have examination of urine and feces regularly before surgery and they were about to have more chance to donate tissue samples than other patients. The child completed survey without parent's assistance, some parents or caregivers of the patients were also invited to complete the similar questionnaires to compare the difference of understanding between parents and their children, but parents could not disturb their child's completed questionnaire. The difference between parents' and children's questionnaires was that, when they were asked about the attitude to donate their children's biospecimens, either parent or child could decline to participate.

Data collection

After a brief introduction to our survey by one of the two trained doctors, participants were asked to complete a questionnaire on a professional platform named "Wenjuanxing app" (www.wjx.cn) before the date of surgery. The animated videos or text introduction were implanted in this platform and some cartoon pictures were made into question options to simplify the understanding and data analysis (Fig. 2), so participants could complete questionnaire as soon as the videos finished or text introduction was read. Older children who were able to read were self-administered; younger children who were not able to read were assisted by parents or investigators with only read text. Basic demographics were collected. Primary outcome measures were the answer of children's understanding of donating biospecimens. Secondary outcome measures were children's attitudes toward different kinds of biospecimens.

Sample size

We calculated the sample size of our research by the PASS (Power and Sample Size, USA) software 12.0; alpha was 0.05, beta was 0.2, tolerable bias was 0.1. Based on the preliminary research that included children of AACQ and TQ groups, the calculation was performed with average correction rates of 87.5% in the AACQ group and 75% in the TQ group. The sample size of the AACQ group was predicted to be 81 participants, and the TQ group was predicted to be 162 participants.

Animation

The animation was mainly created by ourselves using Crazy Talk Animator v3.12 (Reclusion, Taiwan, China), in which 2 adults and 4 child animated characters were created with our recorded dialog, some cartoon medical image, and Chinese subtitles (Fig. 2). The background music built a relaxed and pleasant atmosphere. The animation was an 8-min multimedia divided into different parts according to different questions for children of all ages. The first part of the animation was the introduction of biospecimens and our survey, while the other parts showed the content of the questionnaire about donating biospecimens in a vivid way. The content and language of AACQ was the same as TQ, but rich and various demonstrations were applied. We used Adobe Audition CS6 (Adobe Systems Incorporated, AK, USA) to edit voice, Adobe Illustrator CS6 (Adobe Systems Incorporated, AK, USA) and Adobe Photoshop CS6 (Adobe Systems Incorporated, AK, USA) to make images, SubCreator 1.2.0 to add Chinese-language subtitles, and Format Factory V3.3.2 to integrate subtitles, background music, and animation (Fig. 2).

Statistical methods

We summarized the participants' responses using descriptive statistics and compared the willingness to participate in biobanking by disease type, gender, age, and other basic characteristics. Data analyses were performed using the IBM SPSS software version 21.0 (IBM Corp., Armonk, NY, USA). Pearson's Chi-squared test was applied to analyze the association between categorical variables. Fisher's exact test was used to analyze associations in groups with a small sample size. A *t* test was taken to test the

significance of the mean difference between the two groups. A combined analysis of some category classifications was also performed to improve the test power and avoid the potential confounding issue of small group sizes.

Ethical consideration

The study was approved by the Institutional Review Boards of Shanghai Children's Medical Center. The clinical trial registration number is NCT04179240. Written informed consent was obtained from each patient and his/her parent.

RESULTS

Response rates and demographic characteristics

From July 1, 2019 to January 31, 2020, 401 children were randomly assigned for a survey, including 138 in the AACQ group and 263 in the TQ group, of which 124 of the 138 (89.85%) and 160 of the 263 (68.44%) participants responded and agreed to participate in this survey; the responses rate of the AACQ group (89.85%) was significantly higher than that of the TQ group (68.44%; $p < 0.001$). Finally, a total of 264 children and 67 parents were analyzed (Fig. 1). There were no significant differences between the AACQ and TQ groups across a broad array of subject characteristics unadjusted by the recruitment center, and the population of both groups were normally distributed (Table 1). After finishing the questionnaire, 113 (95.0%) of the children from the AACQ group stated that they understood all or most of the questions, while the number in the TQ group was 136 (93.8%; $p > 0.05$).

Performance of AACQ and influence factors

The understanding of eight key concepts or details was assessed (Fig. 3). Children in the AACQ group achieved higher correct rates in most questions, especially the question about voluntary donation (87.4% vs. 77.9%, $p = 0.045$). The performance of children in the TQ group was substantially lower except for questions 4 and 6, which had slightly higher correction rates. The lower scores for the last question in both groups are partly due to the fact that investigators did not explicitly tell them that both pharmaceutical companies and research institutions could accept biospecimen donation (but there were clues in the introduction). Compared to the parents' performance, children in the TQ group achieved an obviously lower correction rate in some questions (Question 1: $p < 0.001$; Question 7: $p = 0.022$). The children group (including both AACQ and TQ) had a lower correction rate than the parents' group in Question 1 ($p = 0.003$) and Question 8 ($p = 0.038$) (Supplementary Fig. 1). However, there was still a higher correction rate for Question 8 in children from the AACQ group (50.0%) than in those from the TQ group (46.2%). We also analyzed the factors that might influence the participant's correction rates in our two types of questionnaires (Table 2). None of the following factors influenced the children's correct rate ($p > 0.05$): boy or girl and only child or not. However, children in the TQ group from a different hospital (Question 1: $p < 0.001$; Question 2: $p = 0.001$; Question 8: $p = 0.001$) achieved a different understanding, while older children (Question 6: $p = 0.044$), living in urban districts (Question 1: $p = 0.007$), with a longer illness time (Question 1: $p < 0.001$), and without a family history (Questions 4 and 5: $p = 0.036$) were more likely achieve a better understanding. Meanwhile, for children in the AACQ group there were only significant differences between hospitals (Question 2: $p = 0.006$) and ages (Question 3: $p = 0.047$), but with a smaller difference in the AACQ than in the TQ group. Moreover, we analyzed whether using AACQ or TQ might have influenced the correction rates of participants with different characteristics (age, gender, residence, and illness time, among others), but none of these characteristics disclosed significant differences in correction rates between the AACQ and TQ groups (data not shown).

Table 1. Evaluation of the baseline characteristics to confirm the random assignment to the AACQ group or the TQ group.

Characteristics	AACQ ($n = 119$)	TQ ($n = 145$)	p
Age, years	10 (7–17)[a]	10 (7–17)[a]	0.074
Gender, *n* (%)			0.483
Boys	106 (89.1)	125 (86.2)	—
Girls	13 (10.9)	20 (13.8)	—
Hospital, *n* (%)			0.055
SCMC	81 (68.1)	82 (56.6)	—
HCH	38 (31.9)	63 (43.4)	—
Area of residence, *n* (%)			0.680
Urban	97 (81.5)	121 (83.4)	—
Suburban	22 (18.5)	24 (19.8)	—
Chinese ethnicity, *n* (%)			0.735
Han	114 (95.8)	141 (97.2)	—
Minority	5 (4.2)	4 (2.8)	—
Religion, *n* (%)			0.214
No religion	98 (82.4)	120 (82.8)	—
Buddhism	8 (6.7)	16 (11.0)	—
Other religions	13 (10.9)	9 (6.2)	—
Illness time, *n* (%)			0.984
<6 months	42 (35.3)	51 (35.2)	—
>6 months	77 (64.7)	94 (64.8)	—
Only child, *n* (%)			0.586
Yes	51 (42.9)	67 (46.2)	—
No	68 (57.1)	78 (53.8)	—
Family history, *n* (%)			0.840
Yes	17 (14.3)	22 (15.2)	—
No	102 (85.7)	123 (84.8)	—
Insurance, *n* (%)			0.270
Yes	90 (75.6)	119 (82.1)	—
No	15 (12.6)	10 (6.9)	—
Not sure	14 (11.8)	16 (11.0)	—

Pearson Chi-square or Fisher exact test.
AACQ audio and animated cartoon questionnaire, *TQ* text questionnaire, *SCMC* Shanghai Children's Medical Center, *HCH* Henan Children's Hospital, — not applicable.
[a]Median (minimum to maximum), calculated by *t* test.

Appropriate age for patient assent for biospecimen donation

There were 219 (83.0%) children who agreed that their own consent was necessary for biospecimen donation. In order to evaluate the children's attitudes toward biospecimen research, participants were asked to suggest an appropriate age for child assent from six age groups (Supplementary Fig. 2). Among all age groups, the most frequently suggested age was >18 years. Although we found different numbers for the age groups thought to be the most appropriate for biospecimens donation, there was no obvious difference among the TQ, AACQ, and parents' groups.

Willingness to donate biospecimens

Figure 4 shows the children's attitudes toward whether they would like to donate a particular kind of biospecimen. Of the 119 children using the AACQ, 80 (67.2%) gave their consent to donate their specific blood samples, which is a significant 13.2 perceptual points higher compared to the TQ group ($p = 0.027$). There was no difference between other groups following crossover ($p > 0.05$), but it seems that children in the AACQ group were likely to be a little more willing to give their consent to donate liquid body

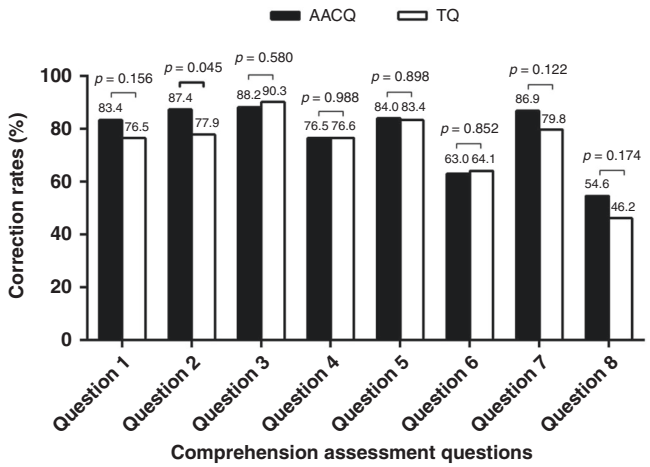

Fig. 3 Difference of correction rates between children of the AACQ group and children of the TQ group. Pearson Chi-square test; bold means $p < 0.05$. AACQ audio and animated cartoon questionnaire, TQ text questionnaire.

samples (2.7% higher), surgery samples (1.6% higher), and related clinical information (2.2% higher) than in the TQ group. In addition, children were much more reluctant to donate specific blood biospecimens ($p < 0.001$) and related clinical information ($p < 0.001$) compared to the donation of body liquid biospecimens (Supplementary Fig. 3). To evaluate whether the children's demographic condition was associated with willingness to donate biospecimens, statistical analyses were conducted. Patients from HCH were more likely to refuse to donate their specific blood biospecimens ($p = 0.036$) than those from SCMC (Supplementary Fig. 3). None of the following factors influenced consent ($p > 0.05$): children's age, gender, illness time, only child or not, and with a related family history or not (Supplementary Table 2).

Attitudes toward biospecimen research

There were some hypothetical questions. In one, it was asked whether participants gave their consent to donate their biospecimens or not. "Disclose relevant information or materials involving personal privacy" was the most popular reason among children for the refusal to donate biospecimens. In the AACQ group, 39.5% children thought it would be harmful to them or increase their pain, which was a significant 18.1 perceptual points higher than children in TQ group (21.4%, $p = 0.001$). In addition, there was no difference between the AACQ and TQ groups in other explanations for the unwillingness to donate biospecimens ($p > 0.05$; Table 3). When asked why they were not willing to donate, the participants had to choose at least one of the following options: demographic characteristics, inspection and test results, clinical treatments (i.e., surgery record, and medication administration record), genetic test results or genetic information, and none of all the above. Parents were more reluctant to donate genetic test results or genetic information than children (40.3% vs. 27.4%, $p = 0.045$). In addition, there was no difference in demographic characteristics, inspection, and test results ($p > 0.05$; Fig. 4) between children and parents except in types of biosamples. Notably, attitudes of children from different regions in China toward biospecimen donation were different. Children from SCMC were much more concerned about pain increase than children from HCH (36.2% vs. 18.8%, $p = 0.003$) but less concerned about relevant information disclose (37.4% vs. 54.5%, $p = 0.007$) (Supplementary Table 3).

DISCUSSION

Our study evaluated attitudes of donating biospecimens by two types of questionnaires; we found children from the surgical wards in a children's hospital generally responded positively to AACQ and reached higher scores in understanding biospecimen donation.

AACQ is easier to accept by children as a tool of content delivery than TQ, given that the response rate of the AACQ group was significantly higher than that of the TQ group. Most children preferred AACQ because it was funny, convenient, and environmentally friendly, but the TQ was boring and easy to understand, according to children' feedback from preliminary experiments. AACQ attracts the children's attention rapidly. Since educational videos have proven to be effective at improving children's knowledge and changing their attitudes and behavior,[19–21] we thought they could also be useful to deliver knowledge about biospecimen donation to children, and we obtained positive feedback from the AACQ. Furthermore, AACQ could also be a good chance to perform popularization of science to children. Increasing evidences demonstrated that applying animation as instructional tool can improve efficiency and effectiveness.[14] Animation can help interviewers mentally visualize the procedure, thus reducing the cognitive load compared with using static graphics or text materials.[22] In addition, it is convenient for children to repeatedly watch the animated material from mobile devices, strengthening their memory recollection and enhancing their knowledge. Thus children receiving AACQ showed better understanding compared with those children receiving TQ.

Most parents agreed that age >18 years might be more appropriate to make decisions on their own regarding biobank participation. Our findings showed that children are willing to take part in biospecimen donation, but they felt that they were not ready to be involved in medical decision-making at an earlier age. It is not supported to get children's assent until they have the ability to understand the research or until they become capable of making decisions.[10,20,21] Some studies showed that children 11–12 years and above were similarly capable of recalling, while children of 9 years and younger were not.[8,13,20] Others agreed that 15-year-old adolescents were able to fully understand all aspects of the research about biospecimens.[23] Briefly, young people aged >18 years are legally capable of signing an informed consent in China. We suggest children aged between 7 and 18 years who fully understood of biospecimens donation should be allowed to participate in the consent signing on their own willing. We have analyzed the difference according to age distribution; however, they could not sign consent on their own willing because 18 years was the recommended age from 52 to 55% pediatric patients. At the same time, we should actively listen to the voice of them, because 83% participants agreed that informed consent had to ask for their permission and actually children could achieve good understanding of biospecimen donation similar to their parents.

In our study, the AACQ group achieved higher correct rates for some questions about biospecimen donation than the TQ group. AACQ can promote the children's understanding of new information related to donating biospecimens. Furthermore, there were a lot of characteristics affecting children understanding in the TQ group, such as the hospital, age, illness time, family history, and living in an urban environment or downtown. Meanwhile, in the AACQ group, there was only a smaller significant difference between hospitals and ages compared to the text version group, suggesting that AACQ could reduce the differences in selected characteristics affecting children understanding and help to quantify or standardize the questionnaire.

Compared with the TQ group, children in the AACQ group were more willing to give their consent to donate specific blood biospecimens, although specific blood biospecimens were the most difficult to accept for children. This is different from the factors that affect the parents' willingness to donate their children's biospecimens.[24] As hypothetical questions, increasing pain and privacy disclosure were bigger concerns for children in

Table 2. Difference of children's percentage of correction of comprehension assessment questions.

Groups	Characteristics	Independent variable	Question 1		Question 2		Question 3		Question 4		Question 5		Question 6		Question 7		Question 8	
			n (%)	*p* value	*n* (%)	*p* value	*n* (%)	*p* value	*n* (%)	*p* value	*n* (%)	*p* value	*n* (%)	*p* value	*n* (%)	*p* value	*n* (%)	*p* value
TQ	Hospital	SCMC ($n = 82$)	**60 (73.2)**	**<0.001**	**72 (87.8)**	**0.001**	77 (93.9)	0.098	65 (79.3)	0.378	68 (82.9)	0.847	55 (67.1)	0.400	71 (79.0)	0.994	**50 (58.5)**	**<0.001**
		HCH ($n = 63$)	**61 (96.8)**		**41 (65.1)**		54 (85.7)		46 (73.0)		53 (84.1)		38 (60.3)		55 (78.9)		**19 (30.2)**	
	Gender	Boys ($n = 125$)	106 (84.8)	0.274	98 (78.4)	0.734	114 (91.2)	0.383	96 (76.8)	0.860	103 (82.4)	0.396	78 (62.4)	0.275	109 (78.3)	0.598	55 (44.0)	0.183
		Girls ($n = 20$)	15 (75.0)		15 (75.0)		17 (85.0)		15 (75.0)		18 (90.0)		15 (75.0)		17 (84.6)		12 (60.0)	
	Age	<10 year ($n = 72$)	58 (80.6)	0.352	52 (72.2)	0.100	66 (91.7)	0.592	56 (77.8)	0.729	58 (80.6)	0.352	**41 (56.2)**	**0.044**	62 (86.1)	0.781	29 (40.3)	0.155
		>10 years ($n = 73$)	63 (86.3)		61 (83.6)		65 (89.0)		55 (75.3)		63 (86.3)		**52 (72.2)**		64 (87.7)		38 (52.1)	
	Area of residence	Urban ($n = 95$)	79 (83.2)	0.897	77 (81.8)	0.212	87 (92.6)	0.488	71 (77.7)	0.477	**85 (84.3)**	**0.007**	63 (66.1)	0.451	84 (88.4)	0.453	44 (47.9)	0.971
		Suburban ($n = 50$)	42 (84.0)		36 (58.3)		44 (79.2)		40 (70.8)		**36 (79.2)**		30 (54.2)		42 (84.0)		23 (37.5)	
	Illness time	<6 months ($n = 51$)	**34 (66.7)**	**<0.001**	39 (76.5)	0.755	47 (92.2)	0.771	38 (74.5)	0.669	39 (76.5)	0.096	29 (56.9)	0.178	42 (73.8)	0.305	27 (52.9)	0.231
		>6 months ($n = 94$)	**87 (92.6)**		74 (78.7)		84 (89.4)		73 (77.7)		82 (87.2)		64 (68.1)		84 (81.8)		40 (42.6)	
	Only child	Yes ($n = 67$)	**50 (74.6)**	**0.008**	55 (82.1)	0.263	63 (94.0)	0.259	53 (79.1)	0.501	55 (82.1)	0.683	48 (71.6)	0.081	57 (86.3)	0.091	31 (46.3)	0.989
		No ($n = 78$)	**71 (91.0)**		58 (74.4)		68 (87.2)		58 (74.4)		66 (84.6)		45 (31.3)		69 (73.5)		36 (46.2)	
	Family history	Yes ($n = 22$)	18 (81.8)	0.762	19 (86.4)	0.408	20 (90.9)	1.000	**13 (59.1)**	**0.036**	**15 (68.2)**	**0.036**	13 (59.1)	0.592	19 (86.4)	1.000	14 (63.6)	0.075
		No ($n = 123$)	103 (83.7)		94 (76.4)		111 (90.2)		**98 (79.7)**		**106 (86.2)**		80 (65.0)		108 (87.8)		70 (43.1)	
AACQ	Hospital	SCMC ($n = 81$)	69 (85.2)	0.289	**76 (93.8)**	**0.006**	73 (90.1)	0.351	6377.8)	0.426	60 (74.1)	0.218	47 (58.0)	0.796	64 (86.6)	0.899	37 (57.8)	0.125
		HCH ($n = 38$)	35 (92.1)		**29 (76.3)**		32 (84.2)		27 (71.1)		32 (84.2)		23 (60.5)		30 (87.3)		16 (42.1)	
	Sex	Boys ($n = 106$)	92 (86.8)	1.000	95 (89.6)	0.181	93 (87.7)	1.000	82 (77.4)	0.210	82 (77.4)	1.000	64 (60.4)	0.325	83 (88.0)	0.734	54 (51.1)	0.470
		Girls ($n = 13$)	12 (92.3)		10 (76.9)		12 (92.3)		8 (61.5)		10 (76.9)		6 (46.2)		11 (84.6)		8 (60.0)	
	Age	<10 year ($n = 40$)	36 (90.0)	0.542	34 (85.0)	0.436	**32 (80.0)**	**0.047**	29 (72.5)	0.571	33 (82.5)	0.336	28 (70.0)	0.078	32 (86.1)	0.781	22 (86.6)	0.479
		>10 years ($n = 79$)	88 (86.1)		71 (89.9)		**73 (92.4)**		61 (77.2)		59 (74.7)		42 (53.2)		62 (87.7)		31 (90.9)	
	Area of residence	Urban ($n = 89$)	78 (87.6)	0.889	79 (88.8)	0.758	80 (89.9)	0.335	69 (77.5)	0.406	69 (77.5)	0.922	51 (57.3)	0.562	71 (79.8)	0.718	48 (53.9)	0.315
		Suburban ($n = 30$)	26 (86.7)		26 (86.7)		25 (83.3)		21 (70.0)		23 (76.7)		19 (63.3)		23 (76.7)		13 (43.3)	
	Illness time	<6 months ($n = 42$)	38 (90.5)	0.455	35 (83.3)	0.220	36 (85.7)	0.528	29 (69.0)	0.217	29 (69.0)	0.112	24 (57.1)	0.783	31 (82.4)	0.305	17 (53.1)	0.874
		>6 months ($n = 77$)	66 (85.7)		70 (90.9)		69 (89.6)		61 (79.2)		63 (81.8)		46 (59.7)		63 (89.4)		36 (51.4)	
	Only child	Yes ($n = 51$)	47 (92.2)	0.175	43 (84.3)	0.250	45 (88.2)	1	36 (70.6)	0.267	40 (78.4)	0.800	29 (56.9)	0.707	44 (85.1)	0.547	25 (49.0)	0.672
		No ($n = 68$)	57 (83.8)		62 (91.2)		60 (88.2)		54 (79.4)		52 (76.5)		41 (60.3)		50 (88.5)		36 (52.9)	
	Family history	Yes ($n = 17$)	14 (82.4)	0.448	16 (94.1)	0.416	16 (94.1)	0.416	14 (82.4)	0.761	13 (76.5)	1.000	13 (76.5)	0.182	15 (86.4)	0.520	10 (58.8)	0.549
		No ($n = 102$)	90 (88.2)		89 (87.3)		89 (87.3)		76 (74.5)		79 (77.5)		57 (55.9)		79 (87.0)		52 (51.0)	

Pearson Chi-square or Fisher exact test; bold means $p < 0.05$.
TQ text questionnaire, *SCMC* Shanghai Children's Medical Center, *HCH* Henan Children's Hospital, *AACQ* audio and animated cartoon questionnaire.

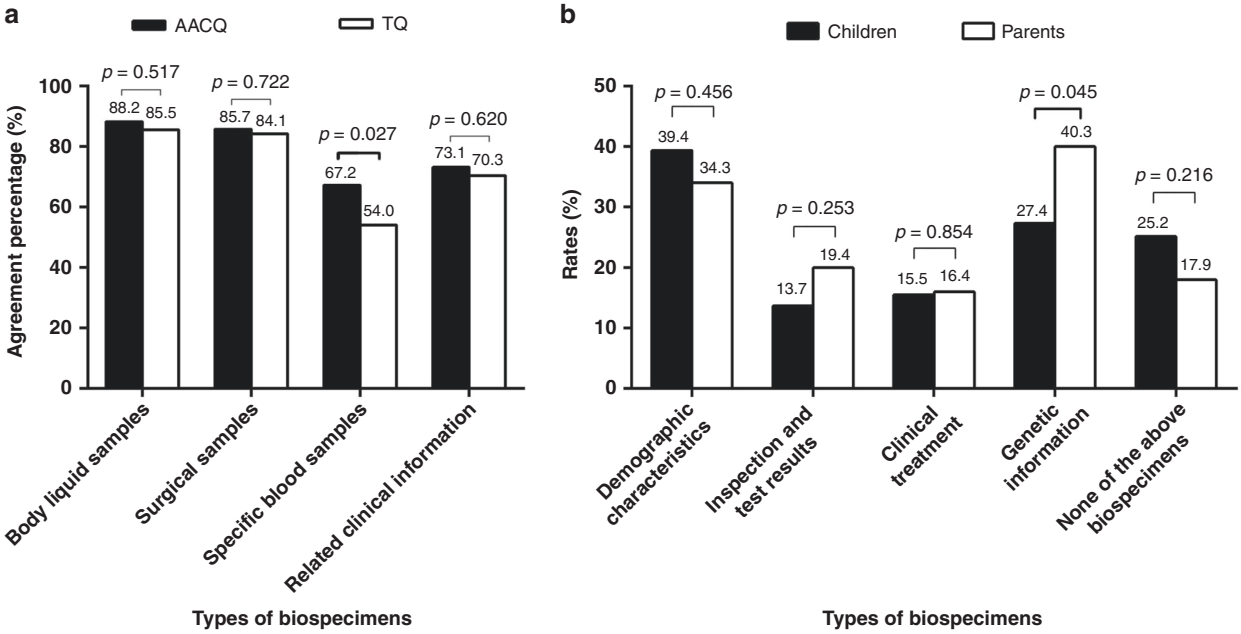

Fig. 4 Difference of attitudes toward different kinds of biospecimens. a Difference of attitudes toward different kinds of biospecimens between children of the AACQ and TQ groups. Pearson Chi-square test; bold means $p < 0.05$. **b** Comparison of the willingness to donate biospecimens between children and their parents. Pearson Chi-square test; bold means $p < 0.05$. AACQ audio and animated cartoon questionnaire, TQ text questionnaire.

Table 3. Ranking of reasons behind the decision of different groups of children to refuse donating their biospecimens.

Reason for the unwillingness to donate biospecimens	AACQ, $n = 119$ (%)	TQ, $n = 145$ (%)	p value
It would be harm to me or increase my pain	**47 (39.5)**	**31 (21.4)**	**0.001**
It would become a means of making profit for researchers	18 (15.1)	30 (20.7)	0.244
It would disclose relevant information or materials involving the personal privacy	52 (43.7)	64 (44.1)	0.943
Other reasons	31 (26.1)	53 (36.6)	0.068
It does no good to myself	16 (13.4)	19 (13.1)	0.935
Distrust of hospital and doctor	4 (3.4)	4 (2.8)	0.776

Pearson Chi-square or Fisher exact test; bold means $p < 0.05$.
AACQ audio and animated cartoon questionnaire, *TQ* text questionnaire.

the AACQ than in the TQ group, which suggests that children in the AACQ group had a stronger will to participate in biospecimen donation.

This is the first study in which AACQ has been used with the goal of improving in children the understanding of biospecimen donation. By observing audio and animated cartoons of introduction to biospecimens in a vivid way, children may become better informed. AACQ is a more effective and standardized means of content delivery in children than TQ. Other AACQ can be used in children in the future. We believe this approach is a unique and promising program for the promotion of biospecimen donation. The involvement of children enabled us to develop a feasible questionnaire, which offers ample opportunities for practical implementation in the future.

There are several limitations to our study. Our consistency evaluation on the understanding of AACQ and TQ was based on the correct rates of comprehension assessment questions. A self-controlled experiment for the feasibility was not applied in our research. Analysis of knowledge recall using this method, which has not been previously validated, opens the data to potential bias. Moreover, the participants were invited from pediatric surgery wards, but outpatients and internal inpatients were not. The majority of pediatric outpatients in China see clinic doctors not by appointment system, which makes it difficult to complete the survey in a short time during treatment procedure. While for the majority of internal inpatients who are repeatedly hospitalized and intravenous access may have already occurred, specimen collection may potentially occur with less discomfort to the child. The advantage of the choice of surgical inpatients were about to have more chance to donate different kinds of biospecimens. But the limitation was that the majority of them were boys, we could not control gender ratio, and it was hard to divide them into different age groups. For a thorough understanding of the attitude of pediatric patients and ordinary children to donating biospecimens, outpatients, internal inpatients, and school children should be employed in future studies. A further limitation was that our study only evaluated the children's knowledge regarding biospecimens after the intervention; thus the children's knowledge at baseline in both groups is unknown.

CONCLUSIONS

Compared to the TQ, AACQ is a more feasible means of content delivery to children from the surgical wards in terms of overall preference and knowledge gained during the consent process.

ACKNOWLEDGEMENTS

We are grateful to all participants. We thank LetPub (www.letpub.com) for its linguistic assistance during the preparation of this manuscript. This research was sponsored by the National Science Foundation of China [81872637, 81728017, 81974231], Shanghai Municipal Commission of Health and Family Planning [201840324, 20164Y0095], Program of National Science and Technology Commission for association of diabetes and nutrition in adolescent [2016YFC1305203], Medical and Engineering Cooperation Project of Shanghai Jiao Tong University [YG2017ZD15], The Project of Shanghai Children's Health Service Capacity Construction [GDEK201708], Science and Technology Development Program of Pudong Shanghai New District [PKJ2017-Y01], Shanghai Professional and Technical Services Platform [18DZ2294100], Shanghai Science and Technology Commission of Shanghai Municipality [17411965300, 17XD1402800, 18411962800], 2019 Science and Technology Innovation -Biomedical Supporting Program of Shanghai Science and Technology Committee [19441904400], Biological Sample Bank and Database Platform of Henan Children's Hereditary Diseases [182102310415], the Foundation of National Facility for Translational Medicine, Shanghai [TMSK-2020-124], and the Key Subject Program for Clinical Nutrition from Shanghai Municipal Health Commission [2019ZB0103].

AUTHOR CONTRIBUTIONS

S.Q. and Y.X. designed the study, participated in its implementation, analyzed, and wrote the initial draft of the manuscript; F.T., Y.Y., J.S., and L.C. collected data and carried out the initial analyses; H.M. and F.J. reviewed the study results; N.B. and S.L. conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript. All authors approved the final manuscript and agreed to be responsible for all aspects of the work.

ADDITIONAL INFORMATION

The online version of this article (https://doi.org/10.1038/s41390-020-01227-2) contains supplementary material, which is available to authorized users.

Competing interests: The authors declare no competing interests.

Patient consent: Written informed consent was obtained from each patient and his/her parent.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

REFERENCES

1. Joly, Y., Dyke, S. O. M., Knoppers, B. M. & Pastinen, T. Are data sharing and privacy protection mutually exclusive? *Cell* **167**, 1150–1154 (2016).
2. Hobbs, A., Starkbaum, J., Gottweis, U., Wichmann, H. E. & Gottweis, H. The privacy-reciprocity connection in biobanking: comparing German with UK strategies. *Public Health Genomics* **15**, 272–284 (2012).
3. Pullman, D., Etchegary, H., Gallagher, K., Hodgkinson, K. & Street, C. Personal privacy, public benefits, and biobanks: a conjoint analysis of policy priorities and public perceptions. *Genet. Med.* **14**, 229–235 (2012).
4. Sanderson, S. C. et al. Public attitudes toward consent and data sharing in biobank research: a large multi-site experimental survey in the US. *Am. J. Hum. Genet.* **100**, 414–427 (2017).
5. Yang, Y., Qin, Y., Chi, H., Li, A. H. & Li, Y. Management of data sharing of human genetic resources and its enlightenment to China. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao* **41**, 396–401 (2019).
6. Qiu, S. et al. Factors that affect Chinese parents' willingness to donate children's biospecimens in pediatric research. *Biopreserv. Biobank*. **16**, 402–410 (2018).
7. Davidson, A. J. & O'Brien, M. Ethics and medical research in children. *Paediatr. Anaesth.* **19**, 994–1004 (2009).
8. Hein, I. M. et al. Informed consent instead of assent is appropriate in children from the age of twelve: policy implications of new findings on children's competence to consent to clinical research. *BMC Med. Ethics* **16**, 76 (2015).
9. Joseph, P. D., Craig, J. C. & Caldwell, P. H. Y. Clinical trials in children. *Br. J. Clin. Pharmacol.* **79**, 357–369 (2015).
10. Rose, K. & Kummer, H. A new ethical challenge for institutional review boards (IRBs)/ethics committees (ECs) in the assessment of pediatric clinical trials. *Children* **2**, 198–210 (2015).
11. Hens, K., Lévesque, E. & Dierickx, K. Children and biobanks: a review of the ethical and legal discussion. *Hum. Genet.* **130**, 403–413 (2011).
12. Klima, J. et al. Understanding of informed consent by parents of children enrolled in a genetic biobank. *Genet. Med.* **16**, 141–148 (2014).
13. Kong, C. C., Tarling, T. E., Strahlendorf, C., Dittrick, M. & Vercauteren, S. M. Opinions of adolescents and parents about pediatric biobanking. *J. Adolesc. Health* **58**, 474–480 (2016).
14. Jia, M. *Animation as Instructional Manual: The Effects of Representational and Motivational Animation on Usability*. MSc thesis, University of Twente (2016).
15. McGlashan, H. L. et al. Evaluation of an internet-based animated preparatory video for children undergoing non-sedated MRI. *Br. J. Radiol.* **91**, 20170719 (2018).
16. Fox, C. & Newton, J. T. A controlled trial of the impact of exposure to positive images of dentistry on anticipatory dental fear in children. *Community Dent. Oral. Epidemiol.* **34**, 455–459 (2006).
17. Kamel, D. O., Wahba, N. A. & Talaat, D. M. Comparison between positive dental images and neutral images in managing anticipatory anxiety of children. *J. Clin. Pediatr. Dent.* **41**, 116–119 (2017).
18. Gangwal, R. R., Badjatia, S. R. & Dave, B. H. Effect of exposure to positive images of dentistry on dental anxiety among 7 to 12 years old children. *Int. J. Clin. Pediatr. Dent.* **7**, 176–179 (2015).
19. Myint-u, A. et al. Safe in the city: developing an effective video-based intervention for STD clinic waiting rooms. *Health Promot. Pract.* **11**, 408–417 (2010).
20. Wendler, D. S. Assent in paediatric research: theoretical and practical considerations. *J. Med. Ethics* **32**, 229–234 (2006).
21. Susman, E. J., Dorn, L. D. & Fletcher, J. C. Participation in biomedical research: the consent process as viewed by children, adolescents, young adults, and physicians. *J. Pediatr.* **121**, 547–552 (1992).
22. Mayer, R. E. Applying the science of learning: evidence-based principles for the design of multimedia instruction. *Am. Psychol.* **63**, 760–769 (2008).
23. Schachter, D., Tharmalingam, S. & Kleinman, I. Informed consent and stimulant medication: adolescents' and parents' ability to understand information about benefits and risks of stimulant medication for the treatment of attention-deficit/hyperactivity disorder. *J. Child Adolesc. Psychopharmacol.* **21**, 139–148 (2011).
24. Ondrusek, N., Abramovitch, R., Pencharz, P. & Koren, G. Empirical examination of the ability of children to consent to clinical research. *J. Med. Ethics* **24**, 158–165 (1998).