甲南経済学論集第60巻第１・２号　2019年９月

Preferences for prenatal diagnosis and ethics in Japan

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Abstract

The prevalence of Down's disease fetuses increases as late births dominate. This trend can be found anywhere in developed countries. The number of people who are interested in non-invasive preliminary testing (NIPT) is rapidly increasing around the world. This paper investigated the preferences and ethical values of unmarried Japanese men and women in their teens and early 20s about the use of new prenatal diagnosis. Contingent valuation method (CVM) was used to investigate the willing to pay (WTP) of the younger generation for NIPT. The result showed the medium WTP is 140,000 yen for NIPT. There is a view that a new prenatal diagnosis is regarded as the remarkable advances in reproductive technology. On the other hand, it is criticized as the selection of life. If the potential demands for prenatal diagnosis increase, there is not enough supply in Japan to cope with it. Previous studies on prenatal diagnosis in developed countries were reviewed and information was collected that could be used as a reference for future ethical issues.

Keyword: non-invasive prenatal testing (NIPT), Contingent Valuation Method (CVM), down syndrome, prenatal diagnosis, ethics

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1. Introduction

Non-invasive preliminary testing (NIPT) has been attracting interests worldwide in recent years (Haidar, Dupras, & Ravitsky, 2016). The background is the age at which women bear children is rising. Table 1 shows the change in the number of births by female age in Japan. The numbers in bold indicate the age class with the highest number. The table shows that the late 20's were the largest age group producing children by the year 2000, but the early 30's were the largest after 2005. This kind of elderly birth is a phenomenon that can be found anywhere in developed countries. Table 2 summarizes the fertility rates by age of women in major countries. In most developed countries, except for some countries such as Russia, the United States and France, it can now be seen that

Table 1 Trends in the number of babies born by women's age group (Japan)

year	Total numbers	15～19 years old	20～24	25～29	30～34	35～39	40～44	45～49
1950	2,337,507	56,365	624,797	**794,241**	496,240	278,781	81,953	4,524
1955	1,730,692	25,219	469,027	**691,349**	372,175	138,158	33,055	1,706
1960	1,606,041	19,739	447,097	**745,253**	300,684	78,104	14,217	942
1965	1,823,697	17,719	513,645	**854,399**	355,269	72,355	9,828	480
1970	1,934,239	20,177	513,172	**951,246**	358,375	80,581	9,860	548
1975	1,901,440	15,999	479,041	**1,014,624**	320,060	62,663	8,727	319
1980	1,576,889	14,590	296,854	**810,204**	388,935	59,127	6,911	258
1985	1,431,577	17,877	247,341	**682,885**	381,466	93,501	8,224	245
1990	1,221,585	17,496	191,859	**550,994**	356,026	92,377	12,587	224
1995	1,187,064	16,112	193,514	**492,714**	371,773	100,053	12,472	414
2000	1,190,547	19,772	161,361	**470,833**	396,901	126,409	14,848	402
2005	1,062,530	16,573	128,135	339,328	**404,700**	153,440	19,750	598
2010	1,071,304	13,546	110,956	306,910	**384,385**	220,101	34,609	792
2015	1,005,675	11,929	84,461	262,256	**364,870**	228,293	52,558	1,308
2017	946,065	9,898	79,264	240,933	**345,419**	216,938	52,101	1,512

Source: National Institute of Population and Social Security Research Latest Demographic Statistics, 'Trends in the number of babies born by women's age group'

Table 2 Fertility rate by age of women in major countries

Country / region	year	Total birth rate	Fertility rate of women by age (パーミル)						
			～19 years old	20～24	25～29	30～34	35～39	40～44	45～49
Hong Kong	2017	0.9	2.6	15.7	45.9	64.8	41.5	9.2	0.5
Korea	2017	1.04	1.1	9.6	46.9	96.6	47.1	6.1	0.2
Spain	2016	1.32	7.4	25.6	56.5	91.3	65.4	16.5	1.3
Singapore	2017	1.33	2.7	15.8	69.1	110.3	57.3	10.6	0.6
Italy	2016	1.34	4.8	27.8	66.2	91.9	59.9	15.6	1.3
Japan	2017	1.42	3.5	27.5	82.1	102.2	57.5	11.4	0.3
Canada	2016	1.54	8.4	37.6	87.6	107.6	56	11.5	0
Switzerland	2016	1.56	2.8	27.3	80	115.5	70.2	14.7	0.9
Russia	2011	1.59	25.2	85.1	101.2	68.6	31.8	6.3	0.3
Germany	2016	1.6	9.2	39.3	87	109.6	62.3	12.2	0.5
Netherlands	2016	1.67	3	28.2	100	130.6	61.9	9.9	0.4
Norway	2016	1.71	3.9	39.6	107.3	119.4	59.1	11.7	0.7
Denmark	2016	1.78	3.5	35.3	114.4	129.6	61.4	11.5	0.6
UK	2016	1.79	13.7	54.7	97.4	111.2	66.3	14.4	0.9
Australia	2016	1.79	10.4	44.6	91.9	123.4	71.9	15.3	1.2
USA	2015	1.84	22.3	76.8	104.3	101.5	51.8	11	0.8
Sweden	2016	1.86	4.4	43.1	111.6	127.4	69.3	15	0.9
France	2012	1.99	9.4	58.2	131	127.2	59.1	12.9	0.7

Source: National Institute of Population and Social Security Research Latest Demographic Statistics,' Fertility rate by age of women in major countries'

the early thirties are the largest generations for children. As late births dominate, the birth probability of Down's fetus increases.

The NIPT is a new prenatal diagnosis that examines fetal DNA to find chromosomal abnormalities that cause Down syndrome, and it has quickly spread worldwide soon after its introduction to clinical practice in Hong Kong in August 2011 and subsequently in the United States in October 2011 (Chiu & Lo, 2012). The burden on pregnant women is negligible because a prenatal diagnosis can be easily done just by collecting blood. With advances in genetic diagnostic technology and an increase in older births, the need for new prenatal diagnosis to check if the fetus has Down syndrome is now rapidly growing in every developed country (Minear, Lewis, Pradhan, & Chandrasekharan, 2015).

A number of obstetrics and gynecology societies around the world have recommended that genetic counseling be set up for new prenatal diagnosis so that families can make informed reproductive choices for diagnosis (Petersen, et al., 2014). As a new prenatal diagnosis is adopted extensively, there is a risk of life screening. Close attention must be paid to the provision of fetal gender information, especially in areas where gender abortion is taking place. However, governments will have to establish a legal framework to implement regulation and oversight. With the advancement of reproductive technology and genetic information, the United States and many other developed countries have put in place budgets and legislation to consider the ethical issues involved (Allyse, et al., 2015). On the other hand, the current situation in Japan is almost left untouched. So to speak, its national understanding and legal development have not kept pace with technological advances.

The current paper analyzes the preferences for and understandings of NIPT of the Japanese younger generation and makes use of the survey as a source for examining what matters should be considered in order to develop the ethical and legal systems.

The conventional blood test for prenatal diagnosis is a test that measures blood protein concentration by collecting a small amount of blood from a pregnant woman, such as quattro test and triple marker test. This test had poor diagnostic accuracy and a 2-7% chance of making a diagnostic error (Russo & Blakemore, 2014; Shamshirsaz, Benn, & Egan, 2010). Another conventional method of prenatal diagnosis is amniotic fluid test. The amniotic fluid is collected from the belly of a pregnant woman, and the test method to determine the shape and number of chromosomes is high in test accuracy, but it can be diagnosed only after 15 weeks of pregnancy, and there is a risk of abortion with a probability of

1～2% (Norwitz & Levy, 2013). An error in diagnosis may lead to the decision to end the life originally born to the parents based on the diagnostic information.

The new prenatal diagnosis is expanding its economic market. The global market size for prenatal diagnosis was estimated to be about 20 billion yen in 2011, but it is estimated to reach about 3,620 billion yen in 2019. As for 2011, only a few companies around the world had started offering new prenatal diagnoses, but they are now available in more than 60 countries. North America accounts for 64.5% of total revenue, followed by Europe (Allyse, et al., 2015). The diagnostic price varies from country to country: about 80,000 yen to over 300,000 yen ($795-over $3,000) in the United States, about 80,000 yen to 100,000 yen (€631-858) in Europe, about 60,000 yen to 100,000 yen (US $580-$1,000) in Hong Kong (Chandrasekharan, Minear, Hung, & Allyse, 2014). The diagnostic price is considered to play an important role when a patient decides whether to accept.

It is also important to advance cost-effectiveness analysis. According to previous reports, in spite of a decrease in the number of invasive tests in Australia, a chromosome test with 21 trisomy (Down's syndrome) alone has shown an increase of 9.7% in cost over the past two years, and the increase trend also can be found in the UK (Morris, Karlsen, Chung, Hill, & Chitty, 2014; O'leary, Maxwell, Murch, & Hendrie, 2013). However, in the United States, using NIPT as the first screening has been reported as cost effective (Ohno & Caughey, 2013). In Japan, appropriate cost-benefit analysis will be awaited as the number of new prenatal diagnosis practices increases.

2. Ethics and legal regulations

New prenatal diagnosis involves the selection of life, and ethical discussions

are essential. Currently, in developed countries around the world, expert guidelines recommend that patients undergo genetic counseling before and after new birth diagnosis (Allyse, et al., 2015). In the United States, there is much provision of NIPT, and 94% of the 278 US specialists surveyed are reported to recommend NIPT (Haymon, Simi, Moyer, Aufox, & Ouyang, 2014). It is expected to increase in Japan in the future.

Until now, medical institutions that can provide new prenatal diagnosis in Japan have been limited to facilities with obstetricians, pediatrics and experienced genetic specialists for outpatients. However, the Japan Obstetrics and Gynecology Society has accepted the plan that any obstetrician who has received training on new prenatal diagnosis can provide a prenatal diagnosis test, and clarified the policy to expand facilities that can provide new prenatal diagnosis significantly. (March 2019). If new prenatal diagnosis is to be widely used in the future, it will be necessary to deeply consider ethical issues on both the demand and supply sides of the diagnosis.

For the people who are on the demand side, the country should consider the ethical issues of the new prenatal diagnosis and analyze the people's preferences in order to ensure fair use that does not revert to eugenic concepts. Unless the patient is presented with clear guidelines for selection, they may not be given the opportunity to think about whether they should receive NIPT and how to respond to the outcome of the diagnosis (Van Schendel, et al., 2014). In the case of collecting blood from pregnant women, it is necessary to strengthen the practices of informed consent and monitoring so that new prenatal diagnosis cannot be routinely incorporated at medical institutions on the supply side.

3. Survey results on ethics

A questionnaire related to the new prenatal diagnosis was conducted from April to June 2019 for 211 unmarried men and women in their teens and 20s. The average age is 18.6 years, and the ratio of women is 41.2%.

Specifically, we asked about the extent of "accepting the examination" in some practical situations. The questionnaire contents and results will be shown sequentially.

◆◆ Questionnaire ◆◆ ～ prenatal genetic testing ～

Now genetic testing of humans is able to read all genes. As for more than 40 years old mothers, one in fifteen children is born with down's syndrome, but it can also be understood in advance only by the blood test of pregnant women ('new type prenatal (genetic)' test) for about 200,000 yen. Given this situation, answer the following questions:

Question 1: Which subsidy should be increased?

◆Program A◆ Subsidy for new type prenatal (genetic) testing

◆Program B◆ Subsidy for treatment and support for people with disabilities

Question: Which do you think should be increased one of the two programs?

1. Program A (28.0%) 2. Program B (72.0%)

As a result, more than 70% of the respondents endorsed "Program B: Grants

for treatment and support for people with disabilities." It can be interpreted that there are more than 70% of respondents who say that genetic testing does not favor preventing the birth of Down's fetus, but rather should accept and support people with disabilities in society.

In addition, the following questionnaires that include other ethical issues will be included with the results. As for the questionnaire, questions were asked with four options: "I think so", "I think so", "I do not think so", and "I do not think so". The former two options are summarized with "Yes" and the latter two options with "No".

	Questions	Yes	No
Q2	It is acceptable for the government to require the public to carry out genetic testing as a health policy.	**44.1%**	**55.9%**
Q3	Even if I pay extra money, I want to know in advance the sex of my baby.	**28.9%**	**71.1%**
Q4	It is up to the parents to decide whether to know the baby's gender in advance.	**94.3%**	**5.7%**
Q5	I think that genetic testing should be extended to all fetuses.	37.9%	62.1%
Q6	I think that it is not good that abortion after knowing that the fetus has Down syndrome because it becomes a selection of life.	**55.9%**	**44.1%**

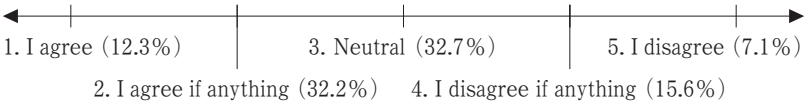
The majority is against "mandating genetic testing to the people (Q2)". It can be said that the majority is opposed to the government's health policy of intervention. Although it can be accepted that it is against "eugenic thought", 40% of respondents also accept national intervention. In addition, I think that more than 70% of young people do not want to know "sex of their baby (Q3)". Money may be the bottleneck. In addition, (Q4) "Whether the baby's gender should be known in advance" states that over 90% of respondents depend on their parents.

Furthermore, the majority opposes "should expand genetic testing to all fetuses (Q5)". This is in line with opposition to the interventions of the countries. The majority of respondents disagreed with the direction of expansion of national genetic analysis by the country.

In addition, the majority of the younger generation says that I don't think it's a right thing to do because aborting is a selection of life (Q6). If we look at the above points, it is fair to say that Japanese young people are against the intervention of national genetic analysis. However, there are many who are opposed to each other, and it can be determined that Japanese unmarried young people do not have a firm understanding or idea of prenatal diagnosis. It can be said that this is a natural result, considering that there is not enough public debate about prenatal diagnosis.

The following questions were asked about what kind of meaning the new prenatal diagnosis has to society.

Q7 There should be various people in society. NIPT testing leads to discrimination against people with disabilities. (Select one from 1 to 5).



The results are: "I think so (12.3%)", "I think so (32.2%)", "Neither (32.7%)", "I do not think so (15.6%)", " I do not think so (7.1%). About half say that "new-type prenatal (genetic) testing leads to discrimination against people with disabilities." The younger people perceive the development of medical technology as a danger rather than accept and enjoy it. It can be understood that

the spread of genetic testing is considered to lead to discrimination. However, it turns out that 30% of young people answered that "neutral", and there are many people who do not have a firm opinion.

4. Contingent Valuation Method (CVM)

For respondents, a hypothetical situation is given: "A new type of prenatal diagnosis can be received at a cost of ¥10,000. Supposing your baby will be born, would you like to use this test?" And they were asked if the respondents will use it. One of the following prices was presented to each respondent; 30,000, 50,000, 100,000, 150,000, 200,000 yen.

The results are as shown in Table 3. The median was 140,000 yen. At present, the cost of new type prenatal diagnosis in Japan is about 200,000 yen, but it was found that the medium price is about 140,000 yen, about half of the young

Table 3－1　Survey results for the use of NIPT

WTP	Yes	No
30,000 yen	38	10
50,000 yen	34	12
100,000 yen	27	14
150,000 yen	17	20
200,000 yen	14	25

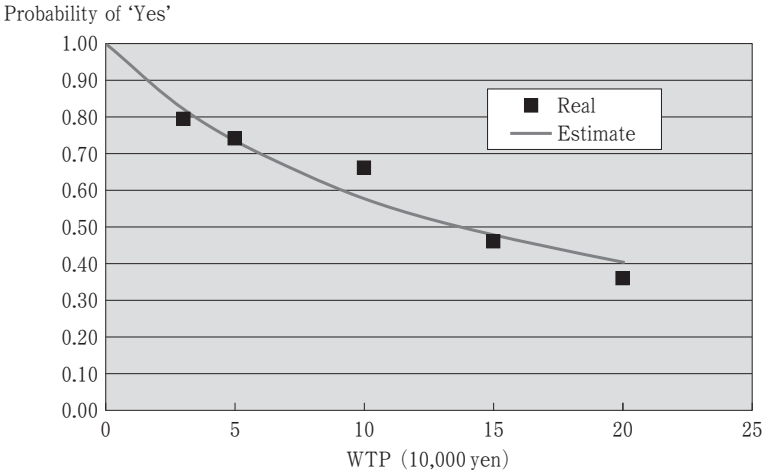
Table 3－2　Estimation results by CVM

variable	coefficient	t value	p value	
constant	2.6253	5.121	0.000	***
ln(Bid)	-1.0066	-4.519	0.000	***
n	211			
Log likelihood	-129.17			

Estimated WTP (yen)

(Medium)	140,000

Figure－1　Results by CVM



Note: I made use of the program from the site of Pro. Koichi Kuriyama 'CVM used by Excel ver 3.2'. (http://homepage1.nifty.com/kkuri/)

people are willing to use the new type of test. Figure 1 shows the estimation results by the hypothetical evaluation method. If the price is 30,000 yen, it is understood that about 80% of young people use the examination.

5. Discussions

This paper examines the preferences and ethical values of unmarried Japanese men and women in their teens and early 20s in terms of prenatal diagnosis. Despite the remarkable progress in reproductive technology, the results of this survey did not show that the younger generation enjoy it, but rather consider it as a risk. The public debates on genetic testing is not sufficiently conducted, and the understanding and insight of young people is not solid.

The majority of participants opposed to the idea of "mandating genetic testing to the public," and of "extending genetic testing to all fetuses." This can be

viewed as disliked the intervention for national genetic analysis. In addition, 70% of young people say that they do not want to know about "sex of their baby". This is a very different view from India and China.

However, opinion is divided in several points, and it can not be said that they have sufficient understanding and insight. The lowering in mothers' age limits at new prenatal diagnosis is considered premature. According to the virtual evaluation method, it was found that about half of the young people are willing to use if the new type prenatal diagnosis is 140,000 yen. However, sufficient public debate corresponding to the technology is considered essential. It will be a future task to conduct surveys to a wider audience of the people.

Appendix ～Questionnaire～

◆◆Prenatal genetic testing◆◆
Now genetic testing of humans is able to read all genes. One child with Down's syndrome is born in 15 old births older than 40 years old, but it can also be understood in advance only by the blood test of pregnant women ('new type prenatal (genetic)' test) for about 200,000 yen. Answer the following questions:

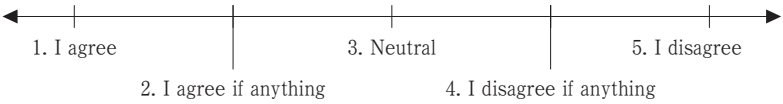
Question 1: Which subsidy should I increase?
◆Program A◆ Subsidy for new type prenatal (genetic) testing
◆Program B◆ Subsidy to treatment and support for people with disabilities

Question: Do you think you should increase one of the two programs?
1. Program A　　2. Program B

		I agree	I agree if anything,	I disagree if anything,	I disagree
Q2	It is acceptable for the government to require the public to carry out genetic testing as a health policy.	1	2	3	4
Q3	Even if I pay extra money, I want to know in advance the sex of my baby.	1	2	3	4

Q4	It is up to the parents to decide in advance whether to know the baby's gender.	1	2	3	4
Q5	I think that genetic testing should be extended to all fetuses.	1	2	3	4
Q6	I think that it is not good because it becomes a sort of life that abortion after knowing that the fetus has Down syndrome.	1	2	3	4

Q7 There should be various people in society. NIPT testing leads to discrimination against people with disabilities. (Select one from 1 to 5).



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