

Current attitudes and preconception towards expanded carrier screening in Eastern Chinese reproductive population

Fang Zhang¹, Jianxin Tan¹, Binbin Shao¹, Tao Jiang², Ran Zhou¹, Yan Wang¹, Jingjing Zhang¹, Fengchang Qiao¹, Xiuqing Ji¹, Ya Wang¹, Ping Hu¹, and Zhengfeng Xu¹

¹Nanjing Maternity and Child Health Care Hospital

²Nanjing Medical University

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Abstract

Objective To explore the Chinese reproductive-aged individual's awareness, wishes, and possible misconceptions of ECS as well as factors affecting their decision-making. **Design** Anonymous, electronic questionnaire conducted in 5 months. **Setting** Women's Hospital of Nanjing Medical University, Jiangsu, China. **Population** Chinese reproductive-aged individuals with a partner (aged 18-45 years). **Methods** Chi-square test and multivariate logistic regression to check the potential association between factors with intention of ECS. **Main outcome measures** Willingness to take ECS testing at own expenses. **Results** Only 35.0% were aware of ECS, while 93.1% of participants had the intention of ECS at their expenses, and 96.5% of participants had misconceptions of ECS and genetic diseases. Meanwhile, 53.6% would pay less than 1,000 CNY (approximately 145 US Dollars) for the test. Participants whose first reaction was of interests, who had prior awareness of the test, or who perceived the benefits were more likely to intend to use ECS ($p < 0.001$). Participants with bachelor's or above degrees or with the household income more than 150,000 CNY (approximately 21,700 US Dollars) were more likely to pay 1,000 CNY and greater ($p < 0.05$). **Conclusions** The Chinese reproductive population had an overall positive attitude towards ECS, with some misconceptions on ECS and genetic disorders. Thus, population-based implementation of ECS is clinically feasible in China, but pre- and post-test education and genetic counselling are required to raise their awareness and to reduce misconceptions. **Keywords** expanded carrier screening, attitudes, preconception, misconceptions, questionnaire.

Introduction

Expanded carrier screening (ECS) is a reproductive genetic test, which aims to identify asymptomatic carriers and assess their odds of having a serious genetic disease in their offspring before or during pregnancy. This test can screen for an extensive set of autosomal and X-linked recessive disorders simultaneously irrespective of ancestry, geographical origin, and family history.^{1, 2} The superiority of ECS over traditional carrier screening includes providing more information with a much wider array of reproductive risks in a more cost-effective way, and reduction of social discrimination.³⁻⁵ Consequently, ECS has mushroomed in the past decade, and many professional academic institutions have recommended offering ECS to all women or their partners who are already pregnant or intending to be pregnant^{4, 6-8}.

As the potential target population of ECS, a better understanding of how the reproductive population view such a test and which factors influence their decision-making is of great importance before or during its implementation in healthcare institutions despite the endorsement and recommendation of professional institutions.^{9, 10} Previous reports gauging patients' interests in ECS are either in hypothetical ECS tests or in their actual uptake of ECS, which shows their attitudes are varied and can be influenced by numerous factors.¹¹⁻¹⁵ However, the great majority of individuals in these studies are European or American, which have a relatively high socioeconomic status and high-quality medical services. Nowadays, ECS is already

in an exploratory stage in China,¹⁶⁻¹⁸ which highlights the feasibility and potential use of ECS. A growing number of Chinese reproductive individuals will be confronted with the choice to accept or refuse such a test. Their attitudes, recognition, as well as the perceived benefits of this test, will likely determine its successful implementation. Up to date, there are no studies reporting attitudes and preconceptions toward ECS in Chinese reproductive population.

The present study was performed to assess the current attitudes and cognition towards ECS in Chinese reproductive population and to know their adoption and possible misunderstandings, which have principal reference value for designing and developing ECS. Besides, we also investigated possible factors that influenced their intention. To the best of our knowledge, this is the first report regarding attitudes and preconceptions towards ECS in Chinese reproductive population.

Methods

Ethics Statement

Our study was approved by the Research Ethics Committee of Women's Hospital of Nanjing Medical University (Number: KY-037). Before responses to the questionnaires, electronic informed consent was obtained from all participants.

Study design

The questionnaire was designed based on domestic national conditions and previous literatures investigating patients' opinions on ECS^{12, 19}. We used plain language for all languages to avoid jargon. To ensure the questionnaire was accurately understood, a pre-survey was conducted in our center. Then, the final draft of the ECS questionnaire was modified by consensus of our research team, including geneticists, obstetricians, and biologists. This survey took about 10 min to complete by scanning the specific quick response code through the WeChat program on their phones. Considering that many participants may not be familiar with ECS, we provided a short informative video before the start of the questionnaire on (1) hereditary mode of recessive genetic diseases and risk in offspring; (2) what is the ECS and its benefits; and (3) a brief description of spinal muscular atrophy (SMA) as an example of these disorders. The questionnaire containing 31 questions was designed to assess the awareness, recognition and possible misconception regarding ECS, including demographics (9 questions), awareness of ECS (5 questions), perceived benefits of ECS (3 questions), misconception of ECS (5 questions), practical questions about offering ECS (6 questions), most reasons in favor of or against ECS (3 questions).

All questionnaires were filled out independently and our researchers were around to answer questions if they needed. All data were documented using a Web-based system automatically to guarantee the integrity of the data. What's more, all participants had a unique identity (ID) number to protect their confidentiality and facilitate data collection and statistical analyses.

Study population

Participants with a partner in the reproductive age (18-45 year) were recruited in our genetic counseling and prenatal diagnosis center before pursuing genetic testing (mainly cell-free fetal DNA screening and peripheral blood karyotype before pregnancy) at Women's Hospital of Nanjing Medical University from August 2019 to December 2019. Only participants who were planning a pregnancy or undergoing pregnancy, were living in China and had no mental or intellectual disabilities were qualified to our questionnaire.

The measure of intention to take an ECS test

Intention to take an ECS test was measured using the existing item " Would you undergo ECS if at your expenses? ".

Data analysis

Data management and statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS) version 22.0 for Windows (SPSS, Inc., Chicago, IL, USA). All descriptive statistics were

computed for all items. Categorical data were expressed as frequencies and percentages. Sociodemographic data, prior knowledge, and perceived benefits about the ECS program were analyzed with the chi-square test to check the association with an intention for ECS, and then a multivariate logistic regression model was used to further explore possible predictive factors. Significance was assessed at $P < 0.05$.

For multivariate logistic regression analysis, some demographics were made cutoffs. The cutoff used for education level was the Bachelor's degree. Total household income was divided into two groups: under 150,000 CNY (approximately 21,700 US Dollars) and 150,000 CNY or greater. The amount that a participant was willing to pay for ECS at their own expense was also divided into two categories: under 1,000 CNY (approximately 145 US Dollars) and 1,000 CNY or more. The average exchange rate of CNY against US Dollar in July 2020 was approximately 1 US Dollar = 6.9 CNY. The odds ratio (OR) together with the 95% confidence interval (CI) were reported for each variable.

Results

Demographics

A total of 888 reproductive individuals (aged 18-45 years) completed the electronic questionnaires. These participants were subdivided into two groups: 841 (94.7%) currently pregnant, and 47 (5.3%) considering pregnancy or receiving fertility treatment. The vast majority was female (88.9%), between the age of 24-35 years (83.5%). 873 (98.3%) respondents were Chinese Han Nationality, and 15 (2.7%) were others. Up to 718 participants (80.9%) had no religious belief, and only 170 (19.1%) reported yes. A summary of the demographics of the study population is shown in Table S1.

Awareness of ECS

Before our survey, only 35.0% of respondents expressed they had heard of ECS previously. Respondents expressed to learn more about ECS through doctors in the hospitals (66.1%), multiple ways (18.8%), and other alternative ways (15.1%). Up to 69.3% showed interests in ECS when they heard hospitals would offer ECS, while the remaining (30.7%) reported disgust or no interest. When asked about their desire for ECS if at their expense, 93.1% expressed yes, and 6.9% expressed no (Table 1).

Perceived benefits of ECS

Compared with participants against ECS, a significantly higher proportion of those desired ECS agreed with the statement 'The test will give you and your partner a better understanding of having a child with a genetic disorder' (chi-square test, $p=1.6E-06$) and the statement 'ECS will be useful for their relatives' (chi-square test, $p=0.027$, Table 3). Regarding the statement about perceived reproductive choices as a carrier couple, most participants would take measures to prevent the birth with a severe hereditary disorder, such as by in vitro fertilization (IVF) with embryo selection (19.7%), gamete donation (4.3%) and an examination of the fetus during pregnancy by chorionic villus sampling or amniocentesis (62.7%, Table 2).

Misconception of ECS

Several questions were designed to assess whether participants with intention of ECS had possible misconceptions. As shown in Table 4, when we asked whether ECS can rule out children with Down's syndrome, only 3.5% answered correctly. Regarding the statement about negative screening results, only 29.9% agreed with the statement that negative results will not exclude a severe genetic child. When questioned if they were a carrier, 17.6% would feel unhealthy and 22.0% will feel stressed or discriminated against. When asked if the cost were the same, up to 86.7% chose the bigger panel (Table S2).

Practical questions about offering ECS

When asked about the screening time, 28.1% expressed they would take the test before pregnancy, 25.3% expressed early pregnancy, while 5.9% thought it didn't matter. Regarding the statement 'What kind of diseases should be included in the ECS panel in your opinion?', the top three options were diseases that would cause intelligence or physical disability, that cause death early or shortness of life, and chronic diseases

that require lifelong care. Regarding the release form of the testing report offered to couples, 77.6% preferred the form of a couple-based report, only 12.3% preferred individual tests result privately. Finally, respondents were asked how much they would be willing to pay for this test. As a result, 53.5% would pay less than 1,000 CNY, while 46.5% would pay 1,000 CNY or greater (Table S3).

Most reasons in favor of ECS and against ECS

The most common reason in favor of ECS out of 10 reasons was that participants were not wanting a future child to suffer from a severe genetic disorder (89.4%). The second most reason was that ECS could help them make better informed reproductive decisions (73.0%). Our study showed that only 6.9% would decline the ECS test. The most frequently selected reason against ECS out of 10 reasons was that there was no hereditary disease in the family members of their participants (67.2%, 41/61), and the second most mentioned was the cost (47.6%, 29/61, Table S4).

Factors associated with the intention and cost for ECS

Unexpectedly, the chi-square test (Table S1) and multivariate logistic regression analysis (data not shown) showed that sociodemographic factors were not significantly associated with the intention of ECS ($p > 0.05$). More than a third of the participants in our survey ($n = 311$) had heard about ECS, a reflection of prior knowledge or awareness of this test. Participants whose first reaction was of interests or who had prior awareness of the test were nearly three times more likely to have intention for taking ECS, compared with those who had no interest in ECS or never heard of this test, respectively (OR=2.73, 95% CI 1.57 to 4.75, $p = 5.03E-04$; OR=2.91, 95% CI 1.34 to 6.33, $p = 0.007$). Meanwhile, those who perceived the benefits for their future offspring were five times more likely to take the test (OR=5.57, 95% CI 1.55 to 20.00, $p = 0.008$, Table 3).

Moreover, we also explored association between sociodemographic factors and the amount that participants were willing to pay. As shown in Table 4, the chi-square analysis showed that participants with bachelor's or above degrees and those with the household income more than 150,000 CNY were more willing to pay 1,000 CNY and greater for ECS ($p = 0.017$, $p = 2.10E-06$). Besides, participants with household income greater than or equal to 150,000 CNY were more likely to pay for ECS at the price of 1,000 CNY or greater (OR:1.34, 95%CI 1.40 to 2.57, $3.58E-05$, Table 4).

Discussion

Main findings

This study including 888 participants shows an overall positive attitude towards ECS among Chinese reproductive population, with some misconceptions on ECS and genetic disorders. Sociodemographic factors were not significantly associated with the intention for ECS, while awareness, highly perceived benefits of the test, and interest in the test were significantly associated with the intention for ECS.

Strengths and limitation

Our study made a detailed investigation of the attitudes and perceptions towards ECS among Chinese reproductive population. To the best of our knowledge, this is the first study to utilize a specific quick response code to conduct the research. It facilitates access to large sample sizes, lower costs, higher efficiency and greenness. The strengths of our study also include that the sample is large and all responses are anonymous. Additionally, the subjects involved in our study are the target population of ECS, including all stages of the reproductive population, such as patients who were pregnant or were trying to conceive with or without assisted reproductive technology.

However, there are still some limitations. Firstly, our participants are people who have not taken an actual uptake of ECS testing and their choices are mostly in hypothetical states. Although the results indicate a high level of willingness to test, not all will actually do so then. Therefore, further studies under actual circumstances of ECS test are needed. Secondly, our participants were mainly from Nanjing and its surrounding

areas, which had a relatively high socioeconomic level. Therefore, the population was not representative of the general Chinese population, which may limit the generalization of the results.

Interpretation

Since ECS is a new reproductive test for the Chinese population, a detailed assessment for their awareness and acceptance of this test is critical to ensure the optimization of the clinical implementation of ECS in China. Our study was performed to explore the Chinese reproductive-aged individuals' interests, needs, wishes, and possible misconceptions of ECS. As far as we know, this study presents the first glimpse of such a research subject in China.

Our survey revealed an apparent overall positive attitude towards ECS that up to 93.1% of respondents desired ECS, even though most of them had never heard of ECS or had a negative family history of monogenic disease. Consistent with prior literatures, the most common reason in favor of ECS was that participants would want to avoid their future child from a severe hereditary disorder.²⁰⁻²³ However, the level of willingness to take such a test in our study was much higher than those in the European and American countries (from one third to 76%).^{12, 20, 24, 25} This difference appears to be explained by the following aspects. Firstly, having a child with a birth defect place a heavy burden on the entire family in China because of insufficient health insurance and economic constraints. Thus, it is plausible that the top priority for most Chinese couples is having a healthy baby.²⁶ Secondly, the attitudes towards eugenics and abortion vary widely in different sociopolitical environments. Eugenics has been gradually diluted even abolished since World War II, and debate on abortion has been a major topic in Western countries for involved violations of human rights.²⁷ In contrast, the Chinese government brought eugenics into legislation, and the Chinese population are more likely to terminate an affected baby.^{26, 28} Thirdly, the Chinese government has placed a high value on implementing integrated control strategies and prevention measures to reduce birth defects, such as the Healthy China 2030 plan, which has made great efforts on health education, free pre-pregnancy medical examination, and pregnancy health care.^{29, 30}

Furthermore, we found prior knowledge, and high perceived benefits for offspring were significantly associated with the increased likelihood of intention for ECS, which agree with previous reports on the importance of awareness and knowledge in decision-making for carrier screening.³¹⁻³³ This finding is also theoretically based by Health Belief Model, which has confirmed that perceived benefits can influence individual's intention, attitudes and eventual behavior.³⁴ Taken together, the above findings suggest that propaganda work of ECS should be carried out as early as possible, ideally before marriage or pregnancy, to create a favorable social environment. On the other hand, attention should be paid to pondering educational content and strategies to get desired results.

Another significant potential factor was the cost, a common reason for decline of ECS. A previous study by Higgins and colleagues suggests that the uptake percent of ECS would increase from 3.3% to 17.5% if the cost was reduced from 350 to 99 US Dollars.³⁵ Because of imbalanced economic development in different regions in China, the average disposable income per person in Eastern China in 2015 was 30,212 CNY, compared with 18,550 CNY in the Central region and 16,546 CNY in the Western region.³⁶ This may be a reason why up to 46.4% of our participants in Eastern China would like to pay 1,000 CNY and more for ECS. In our study, if the test was priced between 500 to 999 CNY, up to 76.4% of our participants would accept it. However, China still has a significant number of people living in poverty, and the poverty line was only 2,300 CNY per person annually in 2015, despite the dramatic economic growth in the past decades.²⁷ Hence, the pricing of ECS in the future should consider this special population. Additionally, the Chinese government either at the central or local level should consider financing this screening project to ensure its success.³⁷ Moreover, we found that participants with a bachelor's and above degree or with the total household income equal to or more than 150,000 CNY were more likely to pay 1,000 CNY and greater for ECS. It is probably that participants with a higher education level seem to have a higher income than those with a lower education level.

Notably, there were some misconceptions regarding ECS among our respondents. Firstly, most participants

confused ECS with Down's syndrome screening. Surprisingly, very few of our participants could distinguish monogenic diseases from chromosome diseases. Next, most respondents also misinterpreted if they were a carrier. Only 33.97% of the participants in our study expressed clearly that they would not feel less healthy as a carrier, though being a carrier typically has no obvious symptoms. Such misconception has also been reported in previous studies on cystic fibrosis carrier screening.^{38, 39} Another misconception is neglected residual risk, which was also highlighted in other literatures.^{4, 9, 40} Most participants misinterpret their negative screening results and considered that their future child will not be susceptible to genetic conditions in our survey. Also, when the cost was the same, the vast majority of those surveyed chose the bigger panel. This is understandable because they wanted to know as much as possible about their reproductive risks. However, panels comprising many rare diseases are not recommended for routine screening^{41, 42}, because it is increasingly difficult to evaluate residual risk accurately and then will bring great trouble for genetic counseling after a positive screening result.⁴³⁻⁴⁵ In line with previous surveys on carrier screening,^{11, 23, 46} there is also a low perceived risk of being a carrier based on family history, which was the most frequently selected reason against ECS, even though most patients with recessive hereditary disorders always have a negative family history. The above misconceptions indicate that the educational video of ECS before the survey may not be truly understood. Our findings highlight the significance of providing accurate and balanced information and education to the general population. What's more, sufficient pre- and post-test genetic counseling including fully informed consent and results interpretation, especially the interpretation of negative results are crucial and has also been emphasized by American and European recommendations.^{4, 7}

We also assessed the preference for the disclosure form when offered to couples. A great majority of our participants would prefer couple-based disclosure-where a result is positive when both members are carriers of the same condition over their test results privately. This disagrees with that found by Stephanie et al, showing that the population in Dutch preferred receiving individual test results instead of a couple-based disclosure pattern¹², but is consistent with Plantinga et al in the Netherlands.²¹ As ECS aims to identify at-risk couples, not simply to identify carriers, this couple-based form is more convenient for couples to decide together for reproductive decision-making. In this society with a high divorce rate, this couple-based form can prevent carriers from discrimination and reduce anxiety if only one tests positive while the partner tests negative, for they would receive an overall negative result.

Conclusion

Taken together, our study demonstrates that Chinese reproductive population had an overall positive attitude towards ECS, with some misconceptions on ECS and genetic disorders. Thus, population-based implementation of ECS is clinically feasible in China, but pre- and post-test education and genetic counselling are required to raise their awareness and to reduce misconceptions.

Disclosure of interests

The authors declare that they have no competing interests.

Contribution to authorship

Fang Zhang and Jianxin Tan participated in the design and revision of the questionnaire, carried out the data collection and data interpretation, and drafted manuscript. Binbin Shao, Yan Wang, and Jingjing Zhang participated in the revision of the questionnaire, carried out the survey and data collection under assistance by Xiuqing Ji. Tao Jiang and Ran Zhou carried out the data analysis and statistical analysis. Fengchang Qiao and Ya Wang assisted data interpretation and revised the manuscript. Zhengfeng Xu and Ping Hu participated in the design and coordination of the study, revised the manuscript, and supervised the study. All authors read and approved the final draft of the paper.

Details of ethics approval

Our study was approved by the Research Ethics Committee of Women's Hospital of Nanjing Medical University (Number KY-037, approved on 12 July,2019). Before responses to the questionnaires, electronic informed consent was obtained from all participants.

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Table 1 Participants' knowledge and intention for ECS. Bold values indicate a statistically significant correlation.

Intention for ECS
 Yes (n=827,93.1%)

Table 1
 Intention for ECS
 Yes (n=

Table 1 Participants' knowledge and intention for ECS. Bold values indicate a statistically significant correlation. Table 1

Previously heard of ECS	Previously heard of ECS
Yes	Yes
No	No
Which way to learn more about ECS	Which way to learn more about ECS
Doctors in hospitals	Doctors in hospitals
Other alternative ways	Other alternative ways
Multiple ways	Multiple ways
What is your first reaction to ECS offered by the hospital?	What is your first reaction to ECS offered by the hospital?
Interested	Interested
Disgusted or no interest	Disgusted or no interest

Table 2 Perceived benefits of ECS and intention for ECS. Bold values indicate a statistically significant correlation.

Intention for ECS	Intention for ECS
Yes (n=827,93.1%)	Yes (n=827,93.1%)
The test will give you and your partner a better understanding of having a child with a genetic disorder	The test will give you and your partner a better understanding of having a child with a genetic disorder
Agree	820 (99.2%)
Disagree	7 (0.8%)
What is your reproductive choice if as a carrier couple?	What is your reproductive choice if as a carrier couple?
In vitro fertilization (IVF) with embryo selection	163 (19.7%)
Gamete donation	36 (4.4%)
Not take any action	106 (12.8%)
Conceive naturally and consider prenatal diagnosis during pregnancy	522 (63.1%)
If you were a carrier of a genetic disease, your relative may also be the same carrier.	If you were a carrier of a genetic disease, your relative may also be the same carrier.
Yes	344 (41.6%)
Not sure	427 (51.6%)
No	56 (6.8%)

Table 3 Multivariate logistic regression with significant associations between predictor variables and intention for ECS.

Predictor variable	Intention for ECS	Intention for ECS	Intention for ECS	Intention for ECS	Intention for ECS
	B	P values	OR	95% CI Lower bound	95% CI Upper bound
The first action to ECS		5.03E-04	2.73 -	1.57 -	4.75 -
Interested	1				
Disgusted or no interest	0				
Previous knowledge of ECS		0.007	2.91 -	1.34 -	6.33 -
Yes	1.07				
No	0				

Predictor variable	Intention for ECS				
Perceived benefits for offspring		0.008	5.57 -	1.55 -	
Agree	1.72				20
Disagree	0				-

Table 4 Education level, annual household income and the cost willing to pay (n=827).

			Chi-square test	Chi-square test	Multivariate logistic regression
	<1000 CNY	[?]1000 CNY	Value	p values	B
Educational level			5.74	0.017	0
Below Bachelor	205	146			
Bachelor and above	238	238			0.1
Annual household income			22.52	2.10E-06	0
<150,000 CNY	298	196			
150,000 CNY	145	188			0.64