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ASSISTED REPRODUCTION TECHNOLOGIES

Expanded genetic carrier screening in clinical practice: a current survey of patient impressions and attitudes

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Abstract

Purpose Expanded genetic carrier screening (ECS) is an important part of gynecological practice and preconception planning. We evaluated the awareness and attitudes among women regarding ECS and factors that may influence decision-making in a family planning context.

Methods A 32-question survey in an academic university practice was given to 521 women who were either currently pregnant ($n = 108$), undergoing gynecologic care who were considering future fertility ($n = 308$), and considering or receiving fertility treatment ($n = 105$). Data are reported descriptively.

Results Forty-seven percent ($n = 246$) of patients were aware of ECS. Though most reported feeling positive or neutral towards ECS, 51% ($n = 263$) reported no desire for testing. Fifty-eight percent ($n = 303$) felt it beneficial to know their carrier status, and 55% ($n = 257$) said it was their responsibility to undergo testing. Those considering future fertility were found to have a more positive attitude towards ECS (51.4%) than those considering or receiving fertility treatment (34%). For positive carriers of a genetic disorder, 228 (49%) of patients would proceed with having their partner screened, 58 (13%) would undergo prenatal screening only and 12 (2.6%) would continue with vitro fertilization (IVF). Related to cost for ECS, 53.5% ($n = 191$) would be willing to pay at least $50–100 for testing, while 29% ($n = 146$) would not pay anything out of pocket.

Conclusions Despite patients' beliefs that it would be beneficial and their responsibility to undergo carrier status testing, the majority reported no desire for ECS and many were unwilling to pay out of pocket. Further education is necessary to reconcile the gap between technology and patient decision-making.

Keywords Carrier screening · Expanded carrier screening · Genetic screening · Patient perceptions · Reproductive genetics

Introduction

Ethnic based carrier screening (CS) practices have been in place for more than 40 years. Such screenings have successfully reduced the incidence of severe recessive disorders prevalent in specific ethnic groups such as cystic fibrosis and Tay–Sachs disease in Ashkenazi Jews and Northern European Caucasians [1, 2] and beta-thalassemia in Mediterranean countries, as well as in Southeast Asia, India, Africa, Central America, and the Middle East [3–6].

While the American College of Obstetricians and Gynecologists (ACOG) recommends ethnic based CS to all couples [7], the increasing population of multi-ethnic individuals in the USA and high costs of polymerase chain reaction (PCR)-based single gene testing limits its use [8]. Expanded genetic carrier screening (ECS) has recently become available and offers a more cost effective and comprehensive carrier

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screen [9–13]. In one of the earliest studies of ECS, Bell et al. [9] utilized next-generation sequencing (NGS) to screen for pathogenic mutations in 437 genes associated with serious genetic disorders. The authors reported that each patient's genome contained 2.8 recessive mutations on average [9]. Advances in NGS technologies have now allowed for ECS at a laboratory cost similar to the older forms of molecular testing [14]. ECS also affords potential parents the choice to define their carrier status (or genetic-risk profile) prior to conception without regard to ethnicity. Such recent advances in screening enable patients to make highly informed decisions regarding their reproductive options and at earlier stages of family planning. Despite these advantages, ECS is not yet a common practice in most countries [15–17].

Public perception of any genetic carrier screening is multifaceted [18–23]. The support for ethnic based CS is commonly attributed to preparedness, including decisions regarding prenatal care, disease awareness, making appropriate lifestyle changes, and seeking medical and social support [23]. Reluctance towards ethnic based CS is often related to the burden involved in handling one's carrier status and the risk posed to their children followed by other factors such as time limitations and lack of interest [24, 25]. Acceptance and usage of ethnic based CS among patients seem to be dependent on the perceived usefulness of such tests [26].

There is limited data characterizing the current attitudes and opinions held by patients and prospective parents regarding ECS. We surveyed patients to characterize the current knowledge base of ECS and its expansions, their attitude(s), and whether there is a desire for increased practice of ECS in reproductive care.

Materials and methods

This prospective qualitative survey study was reviewed and approved by the Wright State Physicians, Boonshoft School of Medicine, Institutional Review Board (Dayton, Ohio) (SC-5876), and the study was in compliance with privacy act guidelines. From July 2015 to August 2016 subjects were recruited to participate in this prospective clinical study. A previously published 32-question paper survey was distributed to the patients of obstetrician/gynecology generalists and reproductive endocrinologists at Five Rivers Health Center for Women's Health at Miami Valley Hospital, Wright State Physician OB-GYN offices, and Wright-Patterson Air Force Base [27]. Patient selection criteria included those currently pregnant undergoing gynecologic care, patients who were considering future fertility, and patients considering or receiving fertility treatment. All patient participants were over 18 years old, completed a consent form, and had an adequate command of the English language. All participants reviewed and signed informed consent documents. All questionnaires were self-administered. Participants' confidentiality was protected as each participant was assigned a unique identification (ID) number that was used on all data collection forms and statistical analyses.

The questionnaire was designed to assess patient attitudes and opinions regarding medical and ethical considerations about the role of ECS and conditions that are included in ECS. Questionnaires included both closed and open-ended questions that were allowed for comments. Patient surveys inquired about patient knowledge of ECS, who the patient would desire to discuss results of screening tests with, which types of conditions patients would like to be screened for, how much patients would be willing to pay for testing, as well as how a positive test result would affect their actions.

Descriptive statistics were computed for all items. Continuous variables were expressed as mean ± standard deviation (SD). Categorical data were reported as frequencies and percentages with differences assessed by chi-square values. Statistical analysis was performed using IBM Statistical Package for the Social Sciences software (SPSS version 18.0, SPSS Inc., Chicago, IL). Significance was assessed at $P < 0.05$.

Results

Demographics

Five hundred twenty-one out of 605 patients responded to the survey (response rate 86.1%). Table 1 summarizes the demographics of the survey respondents. These patients were subdivided into three groups: 108 (21%) currently pregnant, 308 (59%) undergoing gynecologic care who were considering future fertility, and 105 (20%) considering or receiving fertility treatment. The mean age was 30 ± 7.10 years. The distribution for gender was 90% ($n = 468$) female and 10% ($n = 52$) male. Ethnicity reported by the respondents was as follows: 403 (77.5%) Caucasian, 79 (15.2%) African American ($n = 79$), 5 (1.0%) Caucasian–African American, 8 (1.5%) Asian–Hispanic, 1 (0.2%) Pacific Islander ($n = 1$), and 23 (4.6%) other. Ninety percent of respondents were patients at private practices ($n = 467$), while the remaining 9.8% were patients at a community clinic ($n = 51$). Religious affiliation was reported as 55.8% Christian denomination ($n = 274$), 0.4% Judaism ($n = 2$), 1.4% Islam ($n = 7$), 0.4% Buddhism ($n = 2$), 0.8% Hinduism ($n = 4$), 0.8% Jehovah's Witness ($n = 4$), 33.4% no religious affiliation ($n = 164$), and 6.9% reported other ($n = 34$). The highest level of education reported by patients included 102 (20.2%) high school/GED, 221 (43.8%) some college, 123 (24.4%) graduate school, 20 (4.0%) doctorate level, and 38 (7.5%) other ($n = 38$). Two hundred sixty respondents (52.5%) of respondents did not

Table 1 Patient demographics and distribution

Demographic	Proportion
Patient type	
Currently pregnant	20.7% ($n = 108$)
Considering future fertility	59.1% ($n = 308$)
Considering or receiving fertility treatment	20.2% ($n = 105$)
Gender	
Female	90% ($n = 468$)
Male	10% ($n = 52$)
Ethnicity	
Caucasian	77.5% ($n = 403$)
African American	15.2% ($n = 79$)
Caucasian–African American	1% ($n = 5$)
Asian–Hispanic	1.5% ($n = 8$)
Pacific Islander	0.2% ($n = 1$)
Other	4.6% (23)
State of residence	
Ohio	94% ($n = 489$)
Other	6% ($n = 23$)
Florida	($n = 1$)
Kentucky	($n = 3$)
New Jersey	($n = 1$)
New York	($n = 1$)
Pennsylvania	($n = 2$)
Washington D.C.	($n = 1$)
Wisconsin	($n = 1$)
Healthcare location	
Private practice	90% ($n = 467$)
Community clinic	9.8% ($n = 51$)
Religious affiliation	
Christian	55% ($n = 274$)
Judaism	0.4% ($n = 2$)
Islam	1.4% ($n = 7$)
Buddhism	0.4% ($n = 2$)
Hinduism	0.8% ($n = 4$)
Jehovah's Witness	0.8% ($n = 4$)
No religious affiliation	33.4% ($n = 164$)
Other	6.9% ($n = 34$)
Highest level of education	
High school/GED	20.2% ($n = 102$)
Some college	43.8% ($n = 221$)
Graduate school	24.4% ($n = 123$)
Doctorate level	4% ($n = 20$)
Other	7.5% ($n = 83$)
Number of living children	
None	52.5% ($n = 260$)
One or more living children	47.5% ($n = 235$)

have any living children and the remaining 235 (47.5%) reported having one or more living children.

Patient attitude towards ECS

Prior to the survey, 246 (47.9%) patients reported having previously learned about ECS, while 254 (49.4%) reported no knowledge of this testing. Only 14 (2.7%) patients were unsure of their previous knowledge of ECS. Of those who reported previous knowledge of ECS, 94 (38.1%) reported having learned from their OB/GYN, 40 (15.9%) from a fertility doctor, and 6 (2.4%) from a genetic counselor. Patients were otherwise informed of ECS through commercial media (16.7%, $n = 42$), other sources (20.6%, $n = 52$), and through multiple sources (6.4%, $n = 16$). Despite less than half of patients having prior knowledge of ECS, an overwhelming majority of patients reported having either a positive or neutral attitude towards ECS. The minority reported a negative attitude towards ECS. When asked about their desire for ECS, 176 (34.2%) indicated a desire for testing while the remaining reported being unsure (14.7%) or having no desire (51%).

Overall, the vast majority of respondents agreed that ECS should be offered to all women of reproductive age regardless of whether they are actively trying to conceive; additionally, most also agreed that all pregnant patients should be offered ECS. Many patients agreed that ECS should be available to all fertility patients (88.1%, $n = 451$); further, many also agreed that ECS offered to fertility patients should be covered by insurance.

When considering their medical and family history, patients were queried if ECS should be offered instead of ethnic based CS. A large majority of patients (63.7%, $n = 326$) felt that ECS should not be offered instead of ethnic based CS, given this scenario; only 90 (17.5%) did agree it should be offered instead of ethnic based CS, and 96 (18.7%) were unsure (Table 2).

Among those currently pregnant, those considering future fertility, and those considering or receiving fertility treatment, the desire for ECS did not significantly differ among groups ($P > 0.05$). Those considering future fertility, however, were found to have a more positive attitude towards ECS than those considering or receiving fertility treatment (51.4% ($n = 308$) vs. 34% ($n = 100$), $P < 0.05$) (Table 3).

Cost when considering ECS

Over half of respondents reported they would undergo ECS only if it was covered by insurance while 226 (46.3%) of respondents would be willing to contribute to the cost in order to undergo ECS. Of the patients who would only undergo ECS if covered by insurance, only 146 (29%) of patients reported they would not pay out of pocket. When asked about willingness to pay for ECS, 191 (53.5%) reported they would pay up to \$50–\$100, 102 (28.6%) would pay up to \$150–\$250, 47 (13.2%) would pay up to \$300–\$500, and 17 (4.7%) would be willing to pay over \$500 ($n = 17$) (Table 4).

Table 2 Patient attitude towards ECS

	No. of participants	Proportion
Previous knowledge of ECS	514	
Yes	246	47.9%
No	254	49.4%
Unsure	14	2.7%
Source of knowledge of ECS	250	
OB/GYN	94	37.6%
Fertility doctor	40	16.0%
Genetic counselor	6	2.4%
Commercial media	42	16.8%
Other sources	52	20.8%
Multiple sources	16	6.4%
Attitude towards ECS	515	
Positive	233	45.2%
Neutral	248	48.2%
Negative	9	1.7%
Unsure of feelings	25	4.9%
Desire to undergo ECS	515	
Yes	176	34.2%
No	263	51.0%
Unsure	76	14.7%
ECS should be offered to all women	511	
Yes	371	72.5%
No	140	27.5%
All pregnant patients should be offered ECS	512	
Yes	474	92.4%
No	38	7.6%
All fertility patients should be offered ECS	512	
Yes	451	88.1%
No	61	11.9%
ECS for fertility patients should be covered by insurance	510	
Yes	469	92%
No	41	8.0%
ECS should be offered as first test	512	
Yes	90	17.6%
No	326	63.7%
Unsure	96	18.7%

Carrier status and screening related to ECS

When asked to consider if patients were a carrier for a genetic disorder, 228 (49%) of patients would proceed with having their partner screened, 58 (13%) would rather undergo prenatal screening only, 12 (2.6%) would continue with vitro fertilization (IVF), and 12 (2.6%) would choose to do “other.” Approximately, one third of patients would choose to do nothing if they were a carrier for a genetic disorder (32.9%, $n = 152$). Most patients (66.9%, $n = 335$) would desire screening for both inheritable and other nonheritable disorders made possible through ECS. Some patients preferred no personal screening (17%, $n = 85$), screening for only inheritable disorders (7.8%, $n = 39$), and screening for only nonheritable disorders (8.3%, $n = 42$) (Table 5).

These trends do not seem to be related to the patient’s partner being present at the time of the survey ($P > 0.05$). If a partner was present, 52 (66.7%) of patients would still choose to screen for both inheritable and nonheritable, compared to 278 (67.3%) of patients whose partner was absent. Further, 11 (14.1%) of those with their partners present would not undergo screening, compared to 73 (17.7%) of patients whose partner was absent. Five (6.4%) patients with their partners present would undergo screening for inheritable disorders while 33 (8%) of those whose partners were absent would undergo such screening. Lastly, 10 (12.8%) patients with their partners present would choose to only screen for nonheritable disorders, while 29 (7%) of patients with their partners absent would choose the same (Table 6).

Responsibility and choice regarding ECS

Over half of patients agreed that mothers had a responsibility to prevent any and all suffering of their offspring (55%, $n = 257$). A further 207 (44.3%) patients, however, agreed that the mother’s choice was paramount, regardless of the potential outcome for the offspring (Table 7).

Attitude towards providers’ role in ECS

When questioned whether physicians have a moral obligation to support ECS, 237 (47.4%) respondents agreed that physicians do have such an obligation; however, 153 (0.6%) of patients remained uncertain and 110 (22%) did not agree physicians have such an obligation.

Discussion

ECS is increasingly used to identify patients whose children may be at high risk of inheriting recessive diseases [28] and provides couples the opportunity to make choices regarding reproductive planning and personal health [23]. Understanding patient preference is essential to enhancing autonomous reproductive choice [16, 18, 29]. Factors such as familiarity with genetic diseases, high perceived benefits of screening, perceived risk of being carriers, and low perceived social barriers have been identified among those in favor of carrier screening [17, 30]. Meanwhile, lack of knowledge, stress from testing, feelings of not being at risk, and financial limitations are the dominant concerns of those who are unsure of or are against carrier screening [20]. To optimize the clinical use of ECS, it is

Table 3 Attitude towards ECS based on patient type

Attitude towards ECS	No. of participants	Proportion	*P* value
Positive			*P* = 0.03
Currently pregnant	40 (*n* = 105)	38.1%	
Undergoing gynecologic care who were considering future fertility	159 (*n* = 308)	51.5%	
Considering or receiving fertility treatment	34 (*n* = 100)	34.0%	
Negative			NS
Gynecology patients	6 (*n* = 308)	1.9%	
Reproductive endocrinology patients	1 (*n* = 100)	1.0%	
Obstetrics patients	2 (*n* = 105)	1.9%	
Neutral			NS
Gynecology patients	132 (*n* = 308)	42.7%	
Reproductive endocrinology patients	57 (*n* = 100)	57.0%	
Obstetrics patients	60 (*n* = 105)	57.1%	
Unsure			NS
Gynecology patients	11 (*n* = 308)	3.6%	
Reproductive endocrinology patients	8 (*n* = 100)	8.0%	
Obstetrics patients	3 (*n* = 105)	2.9%	

important to understand the public perception surrounding ethnic based CS in general and how it influences the decision-making process.

Despite less than half of patients having previous knowledge of ECS, a large majority had either a positive or neutral attitude towards ECS and more than two thirds of patients expressed desire for heritable and nonheritable screening. Additionally, more than half of patients identified testing as beneficial rather than worrisome. This data echoes the findings in several studies which report patient support for CS in general [19, 21–23, 30]. Many patients have cited preparedness as the most common reason for undergoing screening [19, 21, 23]. Information regarding carrier status lends patients a sense of security and helps minimize anxiety with decision-making [22]. Patients can then exercise preventive activities and alter their approach to their health [22]. For many, ECS is not necessarily about the decision to continue pregnancy but rather the opportunity to research, to communicate with others, and to learning how to make necessary lifestyle changes [22, 23]. While ECS relieves anxiety surrounding uncertainty, patients view the impact of the information on the future of their children as more valuable [19]. Undergoing testing provides patients comfort knowing that they did everything they could for their child(ren) [23]. This is in line with our data which shows more than half of patients agreeing that mothers had the responsibility to prevent any and all suffering. Furthermore, almost half of patients would have their partners screened if they were a carrier themselves.

Although very few couples held negative views relating to ECS, more than half of patients had no desire for ECS.

Table 4 Cost when considering ECS

	No. of participants	Proportion
Would undergo ECS if covered by insurance	262	53.7%
Would pay for ECS	226	46.3%
Would pay out of pocket if ECS was covered by insurance	503	
Yes	357	71.0%
No	146	29.0%
How much patients would pay for ECS	357	
\$50–\$100	191	53.5%
\$150–\$250	102	28.6%
\$300–\$500	47	13.2%
Over \$500	17	4.7%

Table 5 Desire for ECS if carrier status was known

	No. of participants	Proportion
Action patient would take if carrier for genetic disorder	462	
Screen their partner	228	49.3%
Prenatal care only	58	12.6%
Proceed with IVF	12	2.6%
Other	12	2.6%
Nothing	152	32.9%
Desire for screening	501	
Screen for heritable and nonheritable	335	66.9%
No screening	85	17.0%
Inheritable only	39	7.8%
Nonheritable only	42	8.3%

Table 6 Desire for types of screening in presence or absence of partner

	No. of Participants	Proportion	*P* value
Screen for heritable and nonheritable			NS
Partner present	52 (*n* = 78)	66.7%	
Partner absent	278 (*n* = 413)	67.3%	
No screening			NS
Partner present	11 (*n* = 78)	14.1%	
Partner absent	73 (*n* = 413)	17.7%	
Inheritable only			NS
Partner present	5 (*n* = 78)	6.4%	
Partner absent	33 (*n* = 413)	8.0%	
Nonheritable only			NS
Partner present	10 (*n* = 78)	12.8%	
Partner absent	29 (*n* = 413)	7.0%	

Such hesitation for testing seems to be shared by many couples [15, 22–25]. While CS can improve reproductive autonomy, it also complicates the decision-making process surrounding family planning [18]. The burden in managing knowledge given one's genetic status and the risk that it may pose on their future child(ren) has led to some patient support for the "right to not know" [24, 25]. Reluctance for testing also exists due to opposition of child selection [15]. Couples commonly shy away from CS due to the fear and anticipated negative feelings related to carrier screening [22, 31]. Couples have cited time limitation, lack of interest, travel limitations, health insurance discrimination, and long-term care as additional reasons for not undergoing CS [25, 32, 33]. A higher decline rate has been found among unaffected populations as well with healthy patients perceiving the results of testing as less valuable or were less willing to put in the effort required to participate [25, 34].

The utilization of ECS is highly influenced by its perceived usefulness [26]. If ECS was offered, almost one third of couples stated they would do nothing if testing revealed a carrier status. Some couples are reluctant to invest time and money into hypothetical situations [22], stating that the unpredictable outcomes and adult onset diseases were not worth the worry [23]. Others find no use in CS as it would not change their decision to start a family [22, 23]. Kraft et al. [23] report couples placing little value in testing serious diseases stating that if nothing could be done about it, the results would only yield more stress. Patients also viewed mild diseases as more manageable and were confident in their ability to navigate the necessary lifestyle changes. Lastly, patients emphasized the inconclusive nature of CS as reasons for declining screening [23].

Table 7 Mothers' responsibility and choice

	No. of participants	Proportion
Mother is responsible for preventing suffering of offspring	467	
Yes	257	55.0%
No	210	45.0%
Mother's choice is paramount.	467	
Yes	207	44.3%
No	260	55.7%

While more than half of couples would undergo ECS if covered by insurance, a majority were only willing to spend $50–$100 out of pocket for such tests. Such interventions can be costly to couples; however, the potential costs of lifelong care and medical intervention can match and exceed the costs of carrier screening [24]. This speaks to the gap in patient support for CS and their willingness to undergo testing.

Although ECS was not preferred as the first test to be offered by clinicians, most patients agreed that ECS should be offered regardless of whether it was to all women, pregnant patients, or fertility patients. Furthermore, 37.6% patients were informed about ECS via commercial media or other sources, which is equivalent to the percentage of patients informed by clinicians. Regardless of a couple's decision to undergo ECS or not, the opportunity to make that choice is important. Choice lends patients a sense of security and control over their results and aids them in accepting possibly difficult information [22, 23]. The freedom to choose is significant as patients' unique experiences and expectations deeply impact their decision-making process [23]. This includes the choice to seek out information, type and quantity or results, how results are received, and through whom the results would be discussed with [23]. Patients desire numerous options and clear communication with their providers to cater to their unique needs, and by addressing these concerns, barriers to screening may be reduced, and reproductive autonomy is preserved [22, 23]. The role of the physician in offering ECS assumes prime importance. Yet, a recent study by our group has reported that the lack of comfort with ECS counseling and varying beliefs surrounding ECS continue to hinder its utilization [27]. Thus, further education and training programs are warranted [27].

The strengths of this study include anonymous responses to the survey that increases the likelihood for truthful responses. Lastly, our sample includes patients who were not actively trying to conceive, those patients who were pregnant at the time of the survey, and those who were actively trying to conceive through medically assisted means. The limitations of our study include lack of population distribution. Being that most respondents identified as Caucasian women of the Christian faith and living in Ohio, these results may not accurately reflect the predominant opinions and attitudes of patients, nationwide. Other limitations may include errors common to survey-based research such as sampling, coverage, and nonresponse.

Conclusion

The recent availability of ECS allows patients access to carrier screening at lower costs and provides expanded results. Despite its positive reception by patients, ECS remains underutilized in the healthcare setting. The implementation of new reproductive technology increasingly complicates decisions regarding family planning made by patients. Understanding patients' attitudes, preferences, and how they would proceed with such information is important in reconciling the gap between availability of ECS and patient use.

Compliance with ethical standards

This prospective qualitative survey study was reviewed and approved by the Wright State Physicians, Boonshoft School of Medicine, Institutional Review Board (Dayton, Ohio) (SC-5876), and the study was in compliance with privacy act guidelines. From July 2015 to August 2016 subjects were recruited to participate in this prospective clinical study.

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