Evaluating the efficacy of three carrier screening workflows designed to identify at-risk carrier couples

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Abstract

Objective: To evaluate the efficacy of three different carrier screening workflows designed to identify couples at risk for having offspring with autosomal recessive conditions.

Methods: Partner testing compliance, unnecessary testing, turnaround time, and ability to identify at-risk couples (ARCs) were measured across all three screening strategies (sequential, tandem, or tandem reflex).

Results: A total of 314,100 individuals who underwent carrier screening were analyzed. Sequential, tandem, and tandem reflex screening yielded compliance frequencies of 25.8%, 100%, and 95.9%, respectively. Among 14,595 couples tested in tandem, 42.2% of females were screen-negative, resulting in unnecessary testing of the male partner. In contrast, less than 1% of tandem reflex couples included unnecessary male testing. The median turnaround times were 29.2 days (sequential), 8 days (tandem), and 13.3 days (tandem reflex). The proportion of ARCs detected per total number of individual screens were 0.5% for sequential testing and 1.3% for both tandem and tandem reflex testing.

Conclusion: The tandem reflex strategy simplifies a potentially complex clinical scenario by providing a mechanism by which providers can maximize partner compliance and the detection of at-risk couples while minimizing workflow burden and unnecessary testing and is more efficacious than both sequential and tandem screening strategies.

Highlights

What's already known about this topic?
• Studies have explored barriers to carrier screening and follow up partner testing to identify at-risk couples. However, to date, no one has explored the efficacy of different carrier screening workflows.
1 | INTRODUCTION

Carrier screening is offered to individuals and couples to identify those at risk of having children with certain recessive and X-linked genetic conditions. Over the last decade, more than a million individuals have undergone pan-ethnic expanded carrier screening (ECS), that is, screening for a large number of conditions regardless of one’s ethnic background or family history.\(^1,2\) ECS is one of the carrier screening strategies supported by the American College of Obstetricians and Gynecologists (ACOG),\(^3\) and has been shown to more effectively identify carriers and affected pregnancies across all ethnicities than currently recommended ethnicity-based screening.\(^4\)

Approximately 1 in 300 pregnancies in the United States is expected to be affected with a serious genetic condition and 1 in 22 couples is at risk of having an affected child.\(^5\)

To provide comprehensive risk information to patients pursuing ECS and identify at-risk couples (ARCs), it is critical to obtain results from both partners. Results enable couples to make reproductive decisions based on their personal values and preferences.\(^6,7\) ARCs can pursue options, such as in-vitro fertilization with preimplantation genetic testing, use of an egg or sperm donor, prenatal diagnostic testing, adoption, and/or pregnancy termination.\(^8\) Advanced knowledge can also help individuals and providers develop a pregnancy management plan, decrease time to diagnose an affected child, improve perinatal outcomes, and facilitate education about special care needs after birth.\(^9\)

The most common way to identify ARCs is via “sequential screening,” in which the female partner is screened first and, if found to be a carrier,\(^6,7\) the partner is screened for the condition(s) for which the female was found to be a carrier (Figure 1). In current practice, this commonly necessitates a subsequent visit to a provider for collection of the partner’s sample, such that the time to receive a combined couple report is often more than double the time it takes to receive an individual report.\(^3,7,8\)

The need for a secondary sample submission has been found to significantly reduce subsequent partner screening, and ultimately ARC detection, primarily due to workflow challenges and lack of follow-up of male partners.\(^7\) In one study, only 38% of male partners followed-up with screening.\(^7\) Lack of male partner follow-up diminishes the ability of ECS to provide clinically actionable results, underscoring the need for mechanisms to efficiently gather the male partner’s sample and decrease provider workload.

Alternatively, both partners’ samples can be collected and tested simultaneously with “tandem screening” (Figure 1). This strategy is recommended if there are time constraints for decisions about prenatal diagnostic evaluation.\(^8\) Tandem screening addresses the inherent time delays of sequential screening and the challenge of arranging for a second clinic visit to collect the partner’s sample. However, it results in needless testing of partner samples for which no reproductive risk was identified in the partner.\(^7\)

“Tandem reflex” screening is a novel strategy to limit unnecessary partner testing by collecting both partners’ samples in tandem, but testing the second partner’s sample only if the first partner was found to be a carrier of an autosomal recessive condition (Figure 1). In this study, we evaluated the overall efficacy of a pilot tandem reflex screening program in comparison to traditional sequential and tandem screening strategies by examining partner compliance, unnecessary testing, turnaround time, and ARC detection, as well as the efficiency of healthcare utilization, associated with each strategy. We anticipated that tandem reflex screening would be the most efficient screening solution.

2 | METHODS

2.1 | Patient population and carrier screening

We retrospectively analyzed deidentified data from samples tested using the Foresight® Carrier Screen (Myriad Women’s Health), which included up to 176 genes,\(^5,9\) over a 25-month period. The methodology of the Foresight Carrier Screen has been previously described in Hogan et al.\(^5\) The panel prioritizes prevalent diseases that are profound and severe as described in Beauchamp et al.\(^9\) and Arjunan et al.\(^10\) Patients and couples considered to be “at risk” were those with variants that were interpreted as being likely pathogenic or pathogenic via the American College of Medical Genetics and Genomics Criteria.\(^11\) The at-risk calculations accounted for known disease-specific variant combinations that influence pathogenicity (e.g., a couple in which both partners were silent carriers for alpha thalassemia and therefore not at risk of an affected child were not counted as an ARC). Patients were excluded if they were under age 18 years, opted out of being involved in research at Myriad Women’s Health, were from New York state, or indicated that they were egg/sperm donors. After exclusions, a total of 314,100 patients were included in analysis, including 35,899 total couples. For those screened sequentially, a couple-based report was issued when a provider indicated that the patient’s partner had been screened. Patients and providers could also request a couple-based report after both partners had been screened. Couple-based reports were automatically generated following tandem and tandem reflex screening. Clinical and demographic data were obtained from the provider-completed test requisition form and included date of birth, ethnicity, and pregnancy status. This study was designated as exempt from institutional review board (IRB) oversight by Advarra IRB (Pro00042075).
**2.2 Efficacy of screening strategies**

The primary outcome of this study was to determine the efficacy of the sequential, tandem, and tandem reflex strategies. This outcome was evaluated by measuring impact on partner testing compliance, unnecessary male testing, turnaround time, and ability to identify ARCs across all screening strategies.

Partner compliance was defined as the testing of the male partner when the female was identified as a carrier (screen-positive) for one or more autosomal recessive conditions (Figure 2). To calculate the frequency of compliance, the total number of compliant couples was divided by the total number of females screening positive for an autosomal recessive condition, irrespective of whether they had an identified male partner (Figure 2). For sequential screening, we could not verify partner identity for some screened males because not all males were linked to a female screen. Therefore, we calculated an upper bound of compliance by assuming that all males were screened as a result of having a screen-positive female partner. For such patients, we included a 20-day lag time between females and males to allow sufficient time for sequential screening to take place so that both partners would be captured (i.e., both males and females were sampled over 24 months, but respective start and end dates were staggered by 20 days).

Unnecessary male testing for each screening strategy was defined as a male receiving testing after his female partner initially screened negative for all autosomal recessive conditions screened (Figure 2). For testing to qualify as unnecessary, three conditions had to be met: (1) the female partner screened negative for all autosomal recessive conditions; (2) the female partner had an identified male partner that was also screened; and (3) the female partner had to receive her screening either before or tandemly with her male partner (females who were screened following a completed male partner screen were excluded). To calculate the frequency of unnecessary testing, the total number of females meeting the three conditions above was divided by all males that were tested following (or in tandem with) a female screen.

Turnaround time for couples was defined as the time difference (in days) between start of laboratory processing of the first partner (irrespective of sex) and the reporting of couple-based report results to the provider.

**2.3 Impact of screening strategy on ARC detection**

Couples were counted as ARCs if both partners were carriers for the same autosomal recessive disease (i.e., excluding X-linked conditions). To control for biases that panel size could have on disease-wide carrier frequency, we limited ARC analyses to individuals screened for all autosomal conditions on the Foresight 176-gene panel and couples in which the first partner screened was female (or tandemly tested with a male partner). We calculated the number of observed ARCs divided by the total patients screened rather than the total number of couples screened to incorporate both the impact of compliance and unnecessary testing on ARC detection. Additionally, provider burden was calculated as percentage of expected provider follow-up coordination as a function of number of female screens (assumes one provider
consultation for follow-up per carrier identification and per ARC identification).

### 2.4 | Modeling the impact of screening strategies on healthcare utilization

The secondary outcome of this study was to determine the impact of the three partner screening strategies on healthcare utilization. For this outcome, a simulation modeling approach was used to compare the impact of the different screening strategies on healthcare utilization (see Methods in Supporting Information Material).

### 2.5 | Data analysis

All pairwise comparisons of partner screening strategies, including turnaround times, were analyzed via a two-sided Mann–Whitney U test. Differences in proportion of ethnicities screened by each strategy were analyzed using a $\chi^2$ test. For assessing significance, an $\alpha$ of 0.05 was used for all statistical tests. All calculations were performed using Python version 3.6.8.

## 3 | RESULTS

### 3.1 | Patient population

After exclusion criteria were applied, a total of 314,100 individuals (including 35,899 total couples) who underwent sequential ($N = 280,090$), tandem ($N = 29,190$), or tandem reflex ($N = 4820$) carrier screening workflows were analyzed. Demographics of patients that underwent each screening strategy are summarized in Tables 1 and S1. The ethnicity distributions across all screening strategies were significantly different from one another ($p < 0.05$, Table 1). Between 26% and 57% of the females across the screening strategies were pregnant when they received screening (Table 1).

### 3.2 | Efficacy of screening strategies

#### 3.2.1 | Compliance

Partner compliance refers to screening of the male partner when the female partner is identified as a carrier (screen-positive) for one or
more autosomal recessive condition(s). Out of 70,429 females who screened positive via the sequential screening strategy, 18,166 had a male partner screened, yielding a compliance frequency of 25.8% (Figure 3A). Because we cannot assess partner status for some screened males (i.e., 32,498 total males outside of tandem and tandem reflex were unpartnered), we calculated an upper bound of compliance by assuming that these unpartnered males were screened following a screen-positive female. This yielded an upper bound compliance estimate of 71.9% for sequential screening. Out of 1762 total females who screened positive using tandem reflex, 1690 (95.9%) had a male partner screened, as some males opted out of continuing screening. This represented a fourfold increase in compliance for tandem reflex relative to sequential screening (Figure 3A) and a 1.3-fold increase when comparing to the upper bound estimate for sequential screening. As expected for tandem screening, compliance was 100%—all 8432 females who screened positive using tandem had a male partner screened (Figure 3A).

### 3.2.2 Unnecessary testing

Unnecessary testing refers to screening of the male partner after the female partner has already screened negative. Among females screened using the tandem strategy, 42.2% (6163/14,595) were found not to be carriers for any autosomal recessive conditions. Because the tandem strategy tests all male partners regardless of the female’s result, the 6163 male partners screened by the tandem strategy represented unnecessary tests (Figure 3B). The frequency of unnecessary male testing for the sequential and tandem reflex strategies was 3.2% and 0.6%, respectively, as some male partners

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**Table 1** Characteristics of patients who underwent expanded carrier screening (n = 314,100)

| Characteristic                  | Sequential (n = 280,090) | Tandem (n = 29,190) | Tandem reflex (n = 4820) |
|--------------------------------|--------------------------|---------------------|-------------------------|
| **Age, n (%)**                  |                          |                     |                         |
| 18–24                          | 32,162 (11%)             | 598 (2%)            | 151 (3%)                |
| 25–29                          | 55,546 (19%)             | 3,054 (10%)         | 601 (12%)               |
| 30–34                          | 93,649 (33%)             | 9,802 (33%)         | 1,912 (39%)             |
| 35–39                          | 69,220 (24%)             | 9,969 (34%)         | 1,504 (31%)             |
| 40 and above                   | 29,513 (10%)             | 5,767 (19%)         | 652 (13%)               |
| **Self-reported ethnicity, n (%)** |                          |                     |                         |
| Mixed/other Caucasian          | 71,652* (25%)            | 5,456* (18%)        | 1,063 (22%)             |
| Unknown                        | 60,382* (21%)            | 6,825* (23%)        | 1,449 (30%)             |
| Northern European              | 40,238* (14%)            | 7,377* (25%)        | 945 (19%)               |
| Hispanic                       | 31,726* (11%)            | 1,326* (4%)         | 257 (5%)                |
| African or African American    | 29,953* (10%)            | 1,456* (4%)         | 249 (5%)                |
| Ashkenazi Jewish               | 13,004* (4%)             | 1,490* (5%)         | 185 (3%)                |
| East Asian                     | 10,163* (3%)             | 2,201* (7%)         | 266 (5%)                |
| South Asian                    | 8,465 (3%)               | 1,266* (4%)         | 159 (3%)                |
| Southern European              | 4,590* (1%)              | 572* (1%)           | 129 (2%)                |
| Southeast Asian                | 3,996 (1%)               | 408 (1%)            | 59 (1%)                 |
| Middle Eastern                 | 3,754* (1%)              | 621* (2%)           | 42 (0%)                 |
| French Canadian or Cajun       | 1,068 (0%)               | 105 (0%)            | 14 (0%)                 |
| Native American                | 646* (0%)                | 49 (0%)             | 1 (0%)                  |
| Pacific Islander               | 398 (0%)                 | 34 (0%)             | 2 (0%)                  |
| Finnish                        | 55 (0%)                  | 4 (0%)              | 0 (0%)                  |
| **Pregnancy status, n (%)**    |                          |                     |                         |
| Pregnant                       | 129,508 (56.8%)          | 3,865 (26.5%)       | 1,016 (32.9%)           |

*Includes females/males without a testing partner.  
*Significant difference (p < 0.05) when compared to the tandem reflex screening strategy.
partner number was screened around time (Figure screened time screened p strategy after days representing to turnaround it refers a the compared p 3C median 8.0 screening. sequential 3C Couples in significant 13.3 tandem). had time Turnaround 54.5% screening days 3C to of Couples reduction via couple reduction 0.05) has time median turnaround (had turnaround turnaround based tandem of representing 0.05). been 29.2 < time median compared reflex in (Figure Couples for a takes 72.6% statistically a to in sequential 3.2.3 to their continue screening their elected negative (Figure 3B).

3.2.3 | Turnaround time

Turnaround time refers to the time it takes for a couple to receive results after screening has been ordered. Couples screened via the sequential strategy had a median turnaround time of 29.2 days for a couple-based report (Figure 3C). Couples screened in tandem had a median turnaround time of 8.0 days (Figure 3C), representing a significant 72.6% reduction in turnaround time (p < 0.05) compared to sequential screening. Couples screened via the tandem reflex strategy had a median turnaround time of 13.3 days (Figure 3C), representing a statistically significant 54.5% reduction in turnaround time compared to sequential screening (p < 0.05).

3.2.4 | Carrier and ARC identification

As cystic fibrosis (CF) and spinal muscular atrophy (SMA) are the only conditions recommended by ACOG for pan-ethnic screening, we assessed the frequency of patients identified as carriers and ARCs when screening for CF and SMA only by each screening strategy, and compared such frequencies to those identified by a 176-gene ECS panel (Table 2). The carrier frequencies for CF and SMA were 6.9%, 8.3%, and 7.1% for the sequential, tandem, and tandem reflex strategies, respectively. In contrast, the panel-wide carrier frequencies were 57.4%, 60.6%, and 59.0%, respectively, for patients that underwent ECS (Table 2). The percentage of CF and SMA ARCs identified per total number of individual screens were 0.1%, 0.2%, and 0.2% for sequential, tandem, and tandem reflex, respectively. In contrast, the percentage of ARCs identified were 0.5%, 1.3%, and 1.3% respectively for patients that underwent ECS (Table 2; Figure 3D). Taken together, ECS detected more than
We used a modeling approach to demonstrate the impact of noneffective tests for different partner screening implementation scenarios. Simulation of widespread partner screening of 50,000 total screens resulted in 21,551 (43.1%) and 21,066 (42.1%) noneffective tests for the sequential and tandem screening strategies, respectively (Figure 4A). In contrast, tandem reflex screening resulted in only 1,359 (2.7%) noneffective tests, a more than 15-fold reduction when compared to both the sequential and tandem strategies.

### 3.3 | Efficiency of healthcare utilization

To compare the efficiency of healthcare utilization for each screening strategy, we examined the number of noneffective tests (due to either partner noncompliance or unnecessary screens) for each screening strategy. We used a modeling approach to demonstrate the impact of noneffective tests for different partner screening implementation scenarios. Simulation of widespread partner screening of 50,000 total screens resulted in 21,551 (43.1%) and 21,066 (42.1%) noneffective tests for the sequential and tandem screening strategies, respectively (Figure 4A). In contrast, tandem reflex screening resulted in only 1,359 (2.7%) noneffective tests, a more than 15-fold reduction when compared to both the sequential and tandem strategies.

We also modeled the number of autosomal recessive ARCs identified using the 176-gene ECS panel, while also controlling for known differences in the ethnicity distribution of patients tested across each strategy. Simulations showed that ARC detection by the tandem reflex strategy was 1.3-fold higher compared to the tandem strategy (1.5% vs. 1.2%, p < 0.05) and threefold higher compared to the sequential strategy (1.5% vs. 0.5%, p < 0.05; Figure 4B). Simulation of 50,000 female screens resulted in over 100 additional ARCs captured by tandem reflex screening compared to tandem screening (tandem reflex: 749 ARCs, tandem: 607 ARCs, p < 0.05) and nearly 500 additional ARCs compared to sequential screening (sequential: 273 ARCs, p < 0.05; Figure 4C).

### 4 | DISCUSSION

Efficient strategies for enabling partner carrier screening are needed to maximize ARC detection and clinical utility. In this study, we demonstrated that a tandem reflex screening strategy was the most effective of those evaluated for identifying ARCs, as it resulted in high partner compliance, low unnecessary testing, and a short turnaround time.

The sequential screening strategy had a frequency of compliance that was nearly fourfold lower than the tandem and tandem reflex strategies (25.8% vs. 100% and 95.9%, respectively). Although the reasons for noncompliance in the sequential screening group were not collected here, we can surmise several. Partner samples can be difficult to obtain, often requiring the partner to visit a laboratory/clinic that may be outside of their insurer.7 Male partners have also reported the belief that results would not impact pregnancy management, not wanting to know their carrier status, and concern about the cost and insurance coverage of screening.12,13 A recent study's comparatively high frequency of compliance (77%) was attributed to the center's
protocol for arranging posttest counseling appointments, drawing
the partner’s blood on the day of the follow-up visit, and offering
free or reduced-cost testing in many cases. In our study, high
compliance in the tandem and tandem reflex groups translated
into a higher percentage of identified ARCs compared to the
sequential group, a result additionally demonstrated by modeling
data.

This study also demonstrated the ability of the tandem reflex
approach to reduce unnecessary screening. In contrast to the more
than 40% of males screened by the tandem strategy whose partners
had already screened negative, almost no males were screened un-
necessarily using the tandem reflex strategy. When evaluating
the strategies as a function of noneffective screens—which combines
the effects of both noncompliant and unnecessary testing—the tandem
reflex strategy resulted in a 15-fold reduction in noneffective tests.
This illustrates that tandem reflex is a more efficient screening
strategy overall than sequential or tandem screening, thereby maxi-
mizing efficient healthcare utilization. Cost-effectiveness analyses
that characterize the extent of efficiency will be important as large-
scale partner screening programs are implemented.

A short turnaround time is critical when a couple is pregnant and
at a gestational age at which decisions about diagnostic testing or
other interventions must be made without delay. ACOG, therefore,
recommends concurrent screening of both partners if such time
constraints exist. The tandem reflex strategy is consistent with this
recommendation, with a median turnaround time more than half that
of sequential screening (13.3 days compared to 29.2 days). These
results for sequential screening are similar to those observed in other
studies; in a study in which partners had to return to the clinic for
sample collection, the time to generate a couple-based report was
over a month (33.9 days). Patients have reported anxiety waiting for
partner screening results and a reduction in turnaround time
could reduce such anxiety, though additional research may be needed
to test this hypothesis.

Pan-ethnic carrier screening has traditionally been limited to CF
and, more recently, SMA. However, ECS identifies ARCs for many
conditions that are equally as or more severe than CF and
SMA. An additional consideration is the time commitment
required for provider follow-up for both partner testing and results
disclosure, particularly for ECS panels that may result in a higher
number of positive results than screening for only CF or SMA. For
sequential screening, providers must coordinate follow-up for indi-
vidual carriers to discuss partner screening and for ARCs to
communicate results, whereas for tandem and tandem reflex
screening, providers need only coordinate follow-up with ARCs. The
tandem reflex strategy reduced the number of patients with whom
providers must follow up by 3.3-fold, even when dozens of conditions
are included in the panel, versus sequential screening for only CF and
SMA. This reduction in provider burden could additionally contribute
to the potential healthcare cost reductions realized by the increased
compliance and reduced unnecessary testing seen with tandem reflex
screening, though additional studies are needed to explore this
hypothesis.

4.1 Limitations

This study was primarily based on female/male couples pursuing a
pregnancy and is not generalizable to situations in which couples
use donor gametes or females pursue a pregnancy without a male
partner. We could not account for all partners in the sequential
strategy because some reports did not reflect results of both
members of the reproductive couple. It is also possible that some
of these individuals were utilizing gamete donors, which would not
result in a couple-based report. Reasons for noncompliance were
not collected, as all data were obtained in the course of routine
clinical testing. It is possible that partner compliance is dependent
on certain patient demographics that were different across the
three screening strategies; for example, those in the sequential
screening group tended to be younger and were more likely to be
pregnant when screened compared to those in the tandem and
tandem reflex groups. Further research is needed to determine

FIGURE 4 Modeled impact of screening strategies on healthcare utilization. (A) Simulated number of noneffective tests as a function of
the number of females screened. (B) The simulated frequency of at-risk couples (ARCs) detected per total patients screened for autosomal
recessive conditions on the 176-gene panel for each screening strategy, while also correcting for differences in ethnicitv distribution in patient
cohort across screening strategies. (C) The simulated number of ARCs detected by each screening strategy as a function of total patients
screened on the 176-gene panel [Colour figure can be viewed at wileyonlinelibrary.com]
whether these factors appreciably impact partner compliance. Additionally, due to data deidentification, we could not identify the exact reasons for the small number of unnecessary tests in the tandem reflex group, although we speculate this number reflected the ability of partners to request screening even when their partner had already screened negative.

5 | CONCLUSIONS

Our study demonstrates that the tandem reflex screening strategy has the ability of partners to request screening even when their partner had already screened negative. The tandem reflex group, although we speculate this number reflected whether these factors appreciably impact partner compliance. Additionally, due to data deidentification, we could not identify the exact reasons for the small number of unnecessary tests in the tandem reflex group, although we speculate this number reflected the ability of partners to request screening even when their partner had already screened negative.

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CONFLICT OF INTERESTS

All authors were employees of Myriad Women’s Health or Myriad Genetics, Inc., at the time the research for this study was conducted and received salary and stock options.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study have been completely reported in this manuscript and shared in the tables, figures, and supplementary material.

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REFERENCES

1. Haque IS, Lazarin GA, Kang HP, Evans EA, Goldberg JD, Wapner RJ. Modeled fetal risk of genetic diseases identified by expanded carrier screening. J Am Med Assoc. 2016;316(7):734-742.
2. Westemeyer M, Saucier J, Wallace J, et al. Clinical experience with carrier screening in a general population: for a comprehensive pan-ethnic approach. Genet Med. 2020;22:1320–1328.
3. ACOG Committee on Genetics. Committee Opinion No. 690: carrier screening in the age of genomic medicine. Obstet Gynecol. 2017;129(3):595-596.
4. Ben-Shachar R, Svenson A, Goldberg JD, Muzzey D. A data-driven evaluation of the size and content of expanded carrier screening panels. Genet Med. 2019;21(9):1931-1939.
5. Hogan GJ, Vysotskaia VS, Beauchamp KA, et al. Validation of an expanded carrier screen that optimizes sensitivity via full-exon sequencing and panel-wide copy number variant identification. Clin Chem. 2018;64(7):1063-107.
6. Edwards JG, Feldman G, Goldberg J, et al. Expanded carrier screening in reproductive medicine-points to consider: a joint statement of the American College of Medical Genetics and Genomics, American College of Obstetricians and Gynecologists, National Society of Genetic Counselors, Perinatal Quality Foundation, and Society for Maternal-Fetal Medicine. Obstet Gynecol. 2015;125(3):653-662.
7. Giles Choates M, Stevens BK, Wagner C, Murphy L, Singletary CN, Wittman AT. It takes two: uptake of carrier screening among male reproductive partners. Prenat Diagn. 2020;40:311-316.
8. ACOG Committee on Genetics. ACOG Committee Opinion No. 691: carrier screening for genetics conditions. Obstet Gynecol. 2017;129(3):e41-e55.
9. Beauchamp KA, Muzzey D, Wong KK, et al. Systematic design and comparison of expanded carrier screening panels. Genet Med. 2018;20(1):55-63.
10. Arjunan A, Bellerose H, Torres R, et al. Evaluation and classification of severity for 176 genes on an expanded carrier screening panel. Prenat Diagn. 2020;40(10):1246–1257.
11. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015;17(5):405-424.
12. Simone L, Khan S, Ciariariello M, et al. Reproductive male partner testing when the female is identified to be a genetic disease carrier. Prenat Diagn. 2020.
13. Carlotti K, Hines K, Weida J, Lah M, Schwantes-An TH. Perceived barriers to paternal expanded carrier screening following a positive maternal result: to screen or not to screen. J Genet Counsel. 2020.
14. Rothwell E, Johnson E, Mathiesen A, et al. Experiences among women with positive prenatal expanded carrier screening results. J Genet Counsel. 2017;26(4):690-696.
15. Beard CA, Amor DJ, Di Pietro L, Archibald AD. “I’m Healthy, It’s Not Going to Be Me”: exploring experiences of carriers identified through a population reproductive genetic carrier screening panel in Australia. Am J Med Genet. 2016;170(8):2052-2059.
16. Lazarin GA, Haque IS. Expanded carrier screening: a review of early implementation and literature. Semin Perinatol. 2016;40(1):29-34.
17. Briggs A, Nouri PK, Galloway M, O’Leary K, Pereira N, Lindheim SR. Expanded carrier screening: a current survey of physician utilization and attitudes. J Assist Reprod Genet. 2018;35(9):1631-1640.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.