Hull LE, Cheng D, Hallman MH, Rieu-Werden ML, Haas JS. Association of patient and site-of-care characteristics with reproductive carrier screening timing in a large integrated health system. *JAMA Netw Open*. 2022;5(11):e2240829. doi:10.1001/jamanetworkopen.2022.40829

**eAppendix.** Supplementary Materials

**eFigure 1.** Cohort Creation

**eTable 1.** Comparing Characteristics of Patients by Data Types Available

**eFigure 2.** Predicted Probability of Pre-Conception Screening Across Providers Based on Model 1 by Site-Clinic

**eFigure 3.** Number of Conditions Tested for on Carrier Screening Panel by Timing and Provider Specialty

**eTable 3.** Frequencies of Positive and Negative Carrier Screen Results by Timing of Carrier Screening

**eTable 4.** Characteristics of Ordering Providers Who Participated in Interviews (N=9)

This supplemental material has been provided by the authors to give readers additional information about their work.
Supplementary Qualitative Methods for Explanatory Interviews

Explanatory Interviews: Overview

To better understand variability in carrier screening, we conducted semi-structured telephone interviews of ordering providers.

Recruitment

Providers were recruited directly via email between 9/22/20 and 1/15/2021. We purposively focused on outreach to providers who had either ordered little to no preconception screening in FY2019, ordered both prenatal and preconception screens in the same year, or ordered carrier screens testing for different numbers of recessive conditions to identify providers who could speak to variability in practice, who could serve as cases helping to explain and explore the observed variability in our quantitative data. 47 invitations were sent; 9 providers agreed to participate. Reasons for non-participation were not ascertained. No remuneration was provided. Providers received information about the study as part of email recruitment and during the verbal consent process using procedures approved by the MGB Institutional Review Board.

Interview Guide Development

We used the Consolidated Framework for Implementation Research (CFIR), an implementation science framework used widely to elucidate the barriers to implementation of evidence-based healthcare practices, to direct interview guide design. The full copy of the interview guide is available in this supplement. Given our interest in providers’ beliefs about preconception carrier screening, questions were developed using the assistance of the CFIR interview guide tool (https://cfirguide.org/guide/app/#/), with a specific focus on developing questions related to the following Constructs: Intervention Characteristics, Characteristics of Individuals, and Outer Setting. The interview guide was piloted amongst the research team, as well as a group of volunteer genetic counselors, prior to use.

Data Collection

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Phone interviews were scheduled for 30 minutes and were conducted either from the investigator’s private home office or research office. They were conducted by LEH, a junior faculty physician-investigator with training in qualitative methods. MH was present on the phone interviews and took field notes. A transcription service (Transcribe Me, https://www.transcribeme.com/) was used to transcribe telephone interview transcripts. Transcripts were reviewed to ensure no personal identifiers were contained. If so they were removed. Field notes and the original recordings were consulted as needed if there were gaps in transcription during the cleaning process (performed by MH).

Data Analysis

A rapid qualitative matrix approach was used for data analysis.\textsuperscript{30,31} First, the transcripts were broken up by question and the responses were organized into cells in Microsoft Excel notebooks based upon the CFIR construct each question was designed to address. LEH and MHH independently reviewed and coded each cell and then met to compare codes by CFIR construct, reconcile any differences, and discuss resulting themes. Results were organized for presentation by CFIR domain.
## STROBE Checklist

**STROBE Statement**—Checklist of items that should be included in reports of *cross-sectional studies*

| Item No | Recommendation | Page No |
|---------|----------------|---------|
| **Title and abstract**<br>1 | *(a)* Indicate the study’s design with a commonly used term in the title or the abstract<br>*<br>*(b)* Provide in the abstract an informative and balanced summary of what was done and what was found | 3<br>3-4 |
| **Introduction**<br>2 | Explain the scientific background and rationale for the investigation being reported | 5 |
| **Objectives**<br>3 | State specific objectives, including any prespecified hypotheses | 5-6 |
| **Methods**<br>4 | Present key elements of study design early in the paper | 6 |
| **Setting**<br>5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6-8 |
| **Participants**<br>6 | *(a)* Give the eligibility criteria, and the sources and methods of selection of participants | 6-7 |
| **Variables**<br>7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 7-8 |
| **Data sources/ measurement**<br>8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 6-8 |
| **Bias**<br>9 | Describe any efforts to address potential sources of bias | 6-8, Supplement |
| **Study size**<br>10 | Explain how the study size was arrived at | 6-8, SFig 1 |
| **Quantitative variables**<br>11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 7-8 |
| **Statistical methods**<br>12 | *(a)* Describe all statistical methods, including those used to control for confounding<br>*<br>*(b)* Describe any methods used to examine subgroups and interactions<br>*<br>*(c)* Explain how missing data were addressed<br>*<br>*(d)* If applicable, describe analytical methods taking account of sampling strategy<br>*<br>*(e)* Describe any sensitivity analyses | 8-9, Supplement<br>n/a |
| **Results**<br>13* | *(a)* Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed<br>*<br>*(b)* Give reasons for non-participation at each stage<br>*<br>*(c)* Consider use of a flow diagram | SFig 1, 10<br>SFig1, Stable 1<br>SFig 1 |
| **Descriptive data**<br>14* | *(a)* Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders<br>*<br>*(b)* Indicate number of participants with missing data for each variable of interest | Table 1<br>Table 1 |
| **Outcome data**<br>15* | Report numbers of outcome events or summary measures | Table 1<br>Table 1 |
| **Main results**<br>16 | *(a)* Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included<br>*<br>*(b)* Report category boundaries when continuous variables were categorized<br>*<br>*(c)* If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | Table 2<br>Table 2<br>n/a |

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| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | n/a |
|----------------|----|-----------------------------------------------------------------------------|-----|
| **Discussion** |    |                                                                             |     |
| Key results    | 18 | Summarise key results with reference to study objectives                     | 13  |
| Limitations    | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 14-15 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 14-15 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results         | 14-15 |
| **Other information** |    |                                                                             |     |
| Funding        | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 15  |
COREQ Checklist

COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

| Topic                                      | Item No. | Guide Questions/Description                                                                 | Reported on Page No. |
|--------------------------------------------|----------|---------------------------------------------------------------------------------------------|----------------------|
| **Domain 1: Research team and reflexivity**|          |                                                                                             |                      |
| **Personal characteristics**               |          |                                                                                             |                      |
| Interviewer/facilitator                    | 1        | Which author/s conducted the interview or focus group?                                       | Supplement           |
| Credentials                                | 2        | What were the researcher’s credentials? E.g. PhD, MD                                         | Supplement           |
| Occupation                                 | 3        | What was their occupation at the time of the study?                                          | Supplement           |
| Gender                                     | 4        | Was the researcher male or female?                                                           | Supplement           |
| Experience and training                    | 5        | What experience or training did the researcher have?                                         | Supplement           |
| **Relationship with participants**         |          |                                                                                             |                      |
| Relationship established                   | 6        | Was a relationship established prior to study commencement?                                 | Supplement           |
| Participant knowledge of the interviewer  | 7        | What did the participants know about the researcher? E.g. personal goals, reasons for doing the research | Supplement           |
| Interviewer characteristics                | 8        | What characteristics were reported about the interviewer/facilitator? E.g. Bias, assumptions, reasons and interests in the research topic | Supplement           |
| **Domain 2: Study design**                 |          |                                                                                             |                      |
| **Theoretical framework**                  |          |                                                                                             |                      |
| Methodological orientation and Theory      | 9        | What methodological orientation was stated to underpin the study? E.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis | Supplement           |
| **Participant selection**                  |          |                                                                                             |                      |
| Sampling                                   | 10       | How were participants selected? E.g. purposive, convenience, consecutive, snowball           | Supplement           |
| Method of approach                         | 11       | How were participants approached? E.g. face-to-face, telephone, mail, email                 | Supplement           |
| Sample size                                | 12       | How many participants were in the study?                                                     | Methods/Supplement    |
| Non-participation                          | 13       | How many people refused to participate or dropped out? Reasons?                              | Methods/Supplement    |
| **Setting**                                |          |                                                                                             |                      |
| Setting of data collection                 | 14       | Where was the data collected? E.g. home, clinic, workplace                                   | Supplement           |
| Presence of non-participants               | 15       | Was anyone else present besides the participants and researchers?                           | Supplement           |
| Description of sample                      | 16       | What are the important characteristics of the sample? E.g. demographic data, date            | Supplement           |
| **Data collection**                        |          |                                                                                             |                      |
| Interview guide                            | 17       | Were questions, prompts, guides provided by the authors? Was it pilot tested?                | Supplement           |
| Repeat interviews                          | 18       | Were repeat interviews carried out? If yes, how many?                                        | Supplement           |

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| Audio/visual recording | 19 | Did the research use audio or visual recording to collect the data? | Supplement |
|------------------------|----|---------------------------------------------------------------|------------|
| Field notes            | 20 | Were field notes made during and/or after the interview or focus group? | Supplement |
| Duration               | 21 | What was the duration of the interview or focus group? | Supplement |
| Data saturation        | 22 | Was data saturation discussed? | Supplement |
| Transcripts returned   | 23 | Were transcripts returned to participants for comment and/or | Supplement |
| Topic | Item No. | Guide Questions/Description | Reported on Page No. |
|-------|----------|------------------------------|---------------------|
| correction? | | | |
| **Domain 3: analysis and findings** | | | |
| **Data analysis** | | | |
| Number of data coders | 24 | How many data coders coded the data? | Supplement |
| Description of the coding tree | 25 | Did authors provide a description of the coding tree? | Supplement |
| Derivation of themes | 26 | Were themes identified in advance or derived from the data? | Supplement |
| Software | 27 | What software, if applicable, was used to manage the data? | Supplement |
| Participant checking | 28 | Did participants provide feedback on the findings? | Supplement |
| **Reporting** | | | |
| Quotations presented | 29 | Were participant quotations presented to illustrate the themes/findings? | Supplement |
| | | Was each quotation identified? e.g. participant number | |
| Data and findings consistent | 30 | Was there consistency between the data presented and the findings? | Supplement |
| Clarity of major themes | 31 | Were major themes clearly presented in the findings? | Supplement |
| Clarity of minor themes | 32 | Is there a description of diverse cases or discussion of minor themes? | Supplement |

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

Once you have completed this checklist, please save a copy and upload it as part of your submission. **DO NOT** include this checklist as part of the main manuscript document. It must be uploaded as a separate file.
### Section 1. Assessment of understanding of genetic carrier screening and preferences.

[Interviewer]: *Thank you again for taking part in this interview. I am interested in learning more about your perceptions of genetic carrier screening.*

| Questions                                                                                                                                                                                                 | CFIR Constructs                                                                 |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|
| I’d like to start off by having you describe for me what genetic carrier screening means to you.                                                                                                           | Characteristics of Individuals: Knowledge & Beliefs about the Intervention       |
| ![image](https://via.placeholder.com/150) When is it used?                                                                                                                                             |                                                                                 |
| ![image](https://via.placeholder.com/150) What does it test for?                                                                                                                                          |                                                                                 |
| Please describe your process for ordering genetic carrier screening. Please take me through what you tell the patient and how you order the test step-by-step.                                                | Individual’s current practices – Not from a CFIR Construct                       |
| ![image](https://via.placeholder.com/150) How do you decide when to order carrier screening for a patient?                                                                                           |                                                                                 |
| ![image](https://via.placeholder.com/150) How to you decide what conditions to screen for?                                                                                                            |                                                                                 |
| Please describe your process for sharing the results of carrier screening with your patients.                                                                                                           | Individual’s current practices – Not from a CFIR Construct                       |
| ![image](https://via.placeholder.com/150) For example, do you or a member of your team let the patient know about the results, and if so, how (e.g. by phone, secure messaging, or other means)? |                                                                                 |
| ![image](https://via.placeholder.com/150) Are there any cases when you wouldn’t share the results with your patient(s)?                                                                                 |                                                                                 |
| Have you heard of expanded carrier screening?                                                                                                                                                           | Characteristics of Individuals: Knowledge & Beliefs about the Intervention       |
| ![image](https://via.placeholder.com/150) If so, could you describe it for me?                                                                                                                         |                                                                                 |
| If you could choose when and how to order genetic carrier screening for your patients, what do you think would be your ideal way to offer this type of test?                                                 | Perception of best practices for carrier screening – Not from a CFIR construct   |
| ![image](https://via.placeholder.com/150) For example, who would order the test, what testing would you order, in what clinical setting would testing be done, and how would the results be followed-up? If you need a minute to think about this, please feel free to do so. |                                                                                 |
| Are you aware of any other clinics, practices, or health care systems that you think are doing a particularly good job providing patients with carrier screening?                                         | Outer Setting: Peer Pressure                                                      |
How else could you imagine someone using information about their carrier status outside of pregnancy? Take a moment to think about this, if you'd like.

- Tell me a story about a patient who used their carrier screen information outside of pregnancy….

| Characteristics of Individuals: Knowledge & Beliefs about the Intervention |
|---|
| Section 2. Barriers and facilitators to implementing preconception carrier screening. |

[Interviewer:] Thank you for your responses. We are interested in learning about ways to expand access to preconception carrier screening, or carrier screening performed prior to pregnancy. We’d like to learn more about your perspectives on if and how to expand offering this service to patients, and the barriers that we would need to address to do so.

| Questions | CFIR Constructs |
|---|---|
| How do you feel about offering preconception carrier screening in your clinical practice? | Characteristics of Individuals: Knowledge & Beliefs about the Intervention |
| • What advantages does preconception carrier screening have compared to prenatal carrier screening?  
• What disadvantages? | Intervention characteristics: Relative advantage |
| What barriers will your patients face to participating in preconception carrier screening?  
• Tell me a story about a barrier you or your patient faced when pursuing preconception carrier screening. | Outer Setting: Patient Needs & Resources |

| Questions | CFIR Constructs |
|---|---|
| How do you feel about offering expanded carrier screening as the default type of carrier screening performed in your clinical practice? | Characteristics of Individuals: Knowledge & |

Section 3. Barriers and facilitators to implementing expanded carrier screening.

[Interviewer:] We are also interested in barriers you may face to offering expanded carrier screening in your practice, as well as things that can be done to make using expanded carrier screening more accessible. For the purposes of these questions, we will define expanded carrier screening as genetic carrier screening for multiple autosomal and X-linked recessive disorders, beyond a set of core disorders included in current guidelines, that is not based on a patient’s self-reported race or ethnicity. The screening tests generally include hundreds of genes. Examples of expanded carrier screens you may have heard of include the Myriad Foresight® Expanded Carrier Screen and the Invitae Comprehensive Carrier Screen, among others.
| Beliefs about the Intervention | Intervention characteristics: Relative advantage |
|--------------------------------|--------------------------------------------------|
| • What advantages do expanded carrier screens have compared to more targeted or limited screening? | |
| • What disadvantages? | |

| Outer Setting: Patient Needs & Resources |
|-----------------------------------------|
| What barriers will your patients face to participating expanded carrier screening? |
| • Have you heard stories about the experiences of participants with expanded carrier screening? Can you describe a specific story? |

Section 4. Conclusion

[Interviewer:] Thank you for answering our questions. Before we finish, is there anything else that you’d like share with me about genetic carrier screening?

Thank you again for your participation.
eFigure 1. Cohort Creation

Myriad Identified 6663 Completed Carrier Screening Tests at MGB Locations

69 Tests Excluded From Analysis
Unable to Link to EHR Data or Did Not Meet Inclusion Criteria

6594 Tests with Linked EHR Data for 6509 distinct Patients

For 84 patients with >1 test, duplicates were dropped and first test performed in FY2019 was retained

Final Cohort
6509 Tests for 6509 Distinct Patients

*61 out of the 84 patients with >1 test had the same pregnancy status for both screens

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### eTable 1. Comparing Characteristics of Patients by Data Types Available*

| Characteristics | Myriad Data and EHR Order | Myriad Data but No EHR Order Found (EHR Data Available for Linkage) | EHR Order Only but No Myriad Data | p-value** |
|-----------------|---------------------------|----------------------------------------------------------------|----------------------------------|-----------|
| **Pregnancy Status** | 6716 | 5709 (85%) | 800 (12%) | 207 (3%) | <0.001 |
| Pregnant        | 4333 | 3600 | 587 | 146 | |
| Not Pregnant    | 2383 | 2109 | 213 | 61 | |
| **Age Group**   |   |   |   |   | <0.001 |
| 18-25           | 611 | 472 | 125 | 14 | |
| 26-30           | 1795 | 1503 | 240 | 52 | |
| 31-35           | 2696 | 2313 | 298 | 85 | |
| 36-40           | 1327 | 1166 | 117 | 44 | |
| 41 or Greater   | 287 | 255 | 20 | 12 | |
| **Race/Ethnicity** |   |   |   |   | <0.001 |
| White NH        | 4115 | 3400 | 586 | 129 | |
| Black NH        | 757 | 664 | 72 | 21 | |
| Hispanic        | 8 | 1 | 0 | 7 | |
| Asian           | 832 | 745 | 64 | 23 | |
| Other           | 783 | 710 | 53 | 20 | |
| Unknown         | 221 | 189 | 25 | 7 | |
| **Insurance Type*** |   |   |   |   | <0.001 |
| Public          | 1436 | 1235 | 170 | 31 | |
| Private         | 3566 | 3012 | 458 | 96 | |
| None            | 1712 | 1462 | 170 | 80 | |
| **# Comorbidities*** |   |   |   |   | <0.001 |
| No Comorbidities | 5440 | 4637 | 631 | 172 | |
| 1 Comorbidity   | 1077 | 915 | 134 | 28 | |
| 2 or More Comorbidities | 175 | 156 | 17 | 2 | |

Abbreviations: EHR=electronic health record; NH = Non-Hispanic
*Could not compare cohorts by ordering location, ordering provider ID, clinic location on order requisition, or provider specialty as these data were not available for those with an EHR order only
**p-value based on Person’s Chi-square test except in case of low cell counts (<5 in any cell) where Fisher’s exact test was used
***Missing: Insurance (2); Number of comorbidities (24)
eFigure 2: Predicted Probability of Pre-Conception Screening Across Providers Based on Model 1 by Site-Clinic

Abbreviations: BWH=Brigham & Women's Hospital; MGH=Massachusetts General Hospital; NWH=Newton Wellesley Hospital; NSMC = North Shore Medical Center; OB/Gyn=Obstetrics & Gynecology; REI=Reproductive Endocrinology and Infertility; MFM=Maternal Fetal Medicine; PA=Physician's Assistant; NP=Nurse Practitioner

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eFigure 3. Number of Conditions Tested for on Carrier Screening Panel By Timing and Provider Specialty

Figure 3A: Number of Conditions Tested for on Carrier Screen Panel by Pregnancy Status
eFigure 3B: Number of Conditions Tested for on Carrier Screen Panel by Pregnancy Status & Ordering Provider Specialty

Number of Conditions Tested for On Carrier Screen By Pregnancy Status & Provider Specialty
Preconception (0) versus Prenatal (1)

eTable 3. Frequencies of Positive and Negative Carrier Screen Results by Timing of Carrier Screening*

| Result    | Prenatal | Preconception |
|-----------|----------|---------------|
| Positive  | 478      | 745           |
| Negative  | 3593     | 1693          |

*These are raw frequencies and have not been adjusted for panel size or carrier frequency by ancestry. Differences in positive and negative results are likely associated with the size of the carrier screening panels in both groups. No formal analysis has been performed at this time.
eTable 4. Characteristics of Ordering Providers who Participated in Interviews (N=9)

| Provider Specialty | Total Carrier Screens Ordered In FY2019 by Provider | % of Tests Ordered Preconception |
|--------------------|-----------------------------------------------------|---------------------------------|
| REI                | 108                                                 | 100%                            |
| REI                | 77                                                  | 99%                             |
| REI                | 116                                                 | 91%                             |
| MFM                | 54                                                  | 69%                             |
| MFM                | 11                                                  | 45%                             |
| OB/Gyn             | 18                                                  | 39%                             |
| MFM                | 43                                                  | 12%                             |
| PA-C               | 144                                                 | 2%                              |
| OB/Gyn             | 79                                                  | 0%                              |