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Implementation Of Genetic Carrier Screening In The Ob Population: Healthcare Cost Impact And Recommendation Adherence

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IMPLEMENTATION OF GENETIC CARRIER SCREENING IN THE OB POPULATION:

HEALTHCARE COST IMPACT AND RECOMMENDATION ADHERENCE.

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A

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Background. The recent increases in availability of and demand for genetic testing have been observed alongside concerns regarding the appropriate ordering of such tests by providers, and subsequent unnecessary costs to the healthcare system. Professional organizations, such as ACOG and ACMG, develop guidelines to aid providers in ordering appropriate genetic testing. In this study, the ordering of carrier screening by obstetricians and genetic counselors was used to determine if duplicate genetic testing was taking place at a large academic institution along with adherence to ACOG and ACMG carrier screening guidelines.

Methods. A retrospective chart review of primigravida and multigravida women seen in January 2019 at a large academic institution in Houston, Texas was conducted. The study sample was obtained by reviewing ultrasound and genetic counseling schedules during the study period. A total of 503 charts were reviewed. Three patients were excluded from the duplicate screening analysis since they were nulliparous. Out of the remaining 500 patients, two did not have their ethnicities recorded in the medical record; therefore, they could not be included in the ethnicity demographics. Furthermore, one of these patients had carrier screening done with an obstetrician but she was excluded from the secondary analysis since her ethnicity could not be determined. Descriptive statistics were used to characterize data.

Results. The percentage of patients who underwent duplicate carrier screening in January 2019 was 16.2% (51/314). Out of these 51 duplicate carrier screening tests, 24 of them were determined

to be inappropriate. The estimated cost of inappropriate duplicate carrier screening, derived from the CMS' Clinical Diagnostic Laboratory Fee Schedule, was $6,382.12. Provider adherence to ACOG/ACMG recommended carrier screening guidelines was 31.4% (86/274).

Conclusions. This study found that duplicate carrier screening was ordered at a large academic institution by both genetic counselors and obstetricians, resulting in unnecessary cost burden to the healthcare system. This study also concluded that ACMG/ACOG carrier guidelines are not routinely followed by ordering providers at this academic institution.

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Definitions

Carrier screening: type of genetic test that looks for pathogenic variants within known genes that give rise to autosomal recessive or x-linked conditions.

Targeted carrier screening: type of carrier screening that is ordered based on guidelines and/or personal and family history.

Expanded carrier screening: type of carrier screening performed when there is no clinical indication or is not guideline-driven.

Duplicate carrier screening: repeat carrier screening in the same or subsequent pregnancies.

Appropriate duplicate carrier screening: carrier screening that provides new genetic information about the patient.

Inappropriate duplicate carrier screening: carrier screening that does not provide new genetic information about the patient.

Introduction

Completion of the Human Genome Project in 2003 has led to an improved understanding of genetic variants and their contributions to disease (1). This knowledge has contributed to the creation and application of genetic testing in the clinical setting. As of May 2018, Phillips et al. estimated that there are approximately 75,000 genetic tests on the market, with about ten new tests entering the market daily (2). However, the increased availability of genetic testing has yet to match the availability of genetic specialists, trained specifically in ordering and interpreting these types of tests. As of 2019, the American Board of Medical Genetics and Genomics reported 1,687 clinical medical geneticists practicing in the United States (3), leading to an estimate of one clinical geneticist per 200,000 people. The recent explosion of and demand for clinical genetic testing services has placed non-genetic healthcare providers in the position of ordering and interpreting genetic tests. This has led to an increase in inappropriate ordering of genetic tests, as noted by genetic testing laboratories (4). The largest source of mistakes, within the pre-analytic phase of molecular genetic testing, is inappropriate selection of laboratory tests (1). This practice not only delays patient diagnosis and treatment, but also increases healthcare costs (1).

A reported type of inappropriate genetic test is duplicate genetic testing. Duplicate genetic testing not only results in redundant information, but also increases the cost to patients, institutions, and insurers. This practice is addressed by two medical organizations: The American College of Medical Genetics (ACMG) and the American College of Obstetricians and Gynecologists (ACOG). In the context of duplicate genetic testing, ACMG states that genetic testing for an inherited condition should not be reordered, unless there is uncertainty regarding the validity of the existing test result that requires confirmation (5). ACOG states that carrier screening for a particular condition should be performed only once in that person's lifetime (6).

Duplicate genetic testing has been studied and its cost assessed previously. In 2008, Riegert-Johnson et al. recorded duplicate genetic testing over the course of a year within their institution's laboratory. They concluded that duplicate genetic testing was common, occurring between 0.3% to 3.3% per particular gene they tested, costing their institution an additional, unnecessary $76,728 for that year (7). Another study performed in 2014 by Associated Regional University Pathologists Laboratories examined the impact of duplicate genetic testing and its estimated cost. Genetic testing orders were reviewed by laboratory genetic counselors and duplicated testing orders were canceled resulting in a savings of $2,400 per month (4). These two studies demonstrate that the incidence of duplicate genetic testing may be common within an academic and clinical laboratory, and canceling these duplicate orders has the potential of saving healthcare dollars.

Not only do professional guidelines address inappropriate genetic testing, they also provide recommendations related to specific genetic tests. These recommendations, when followed, ensure optimal care is provided to patients. In the realm of prenatal genetic testing, both ACOG and ACMG provide recommended guidelines for carrier screening. This type of screening has traditionally been offered to individuals who are pregnant or considering pregnancy with a family history of an autosomal recessive condition, or those considered to be of a high-risk ethnicity for certain conditions. However, as society has become increasingly multiethnic, guideline recommendations have shifted to offer carrier screening for certain genetic conditions in all individuals. This was addressed by both ACOG and ACMG, and lead to the implementation of universal carrier screening for cystic fibrosis in 2001 (8). In 2008, ACMG released a practice guideline recommending universal carrier screening for spinal muscular atrophy (SMA). Nine years later this recommendation was echoed by ACOG's committee opinion number 691 which recommends that carrier screening for SMA should be offered to all patients considering

pregnancy or currently pregnant (6). In addition to pan ethnic carrier screening for CF and SMA, ACOG recommends hemoglobinopathy screening of all individuals of African, Southeast Asian, and Mediterranean descent (9).

This study aimed to determine the incidence and theoretical cost of duplicate carrier screening and to assess if providers at a large academic institution were following ACOG/ACMG guideline recommendations for this type of testing. The population studied was pregnant women receiving prenatal care at Maternal Fetal Medicine clinics at UTHealth McGovern Medical School located in Houston, Texas. As evidenced by previous studies, determining if duplicate carrier screening is taking place and mitigating this practice can have a positive impact on the overall cost to the healthcare system, while assessing provider's adherence to professional guidelines is a way of measuring whether the standard of care is truly standardized across all patients.

Materials and Methods

This study was reviewed and approved by UT Health's Committee for the Protection of Human Subjects on June 12th, 2019 (HSC-GEN-19-0459).

A retrospective chart review was performed for three UT Health Maternal Fetal Medicine clinics in the city of Houston, Texas. Ultrasound and genetic counseling schedules were reviewed for the month of January 2019 from each clinic to obtain the sample. Patients were referred to UT Physicians for maternal-fetal-medicine services and/or genetic counseling by internal obstetrician referrals or community-based physician referrals for a wide range of indications.

Data extraction

Data extracted from the electronic medical record included the following: the service date of the patient's genetic counseling appointment or ultrasound, their age, ethnicity, insurance type, number of pregnancies, parity, and any current or past genetic counseling visits. Additionally, it was noted whether the patient underwent any carrier screening, the type of carrier screening that was performed, and whether this testing was ordered by an obstetrician or genetic counselor. If the patient had duplicate carrier screening, the type and date were recorded. Duplicate carrier screening was defined as repeat carrier screening in the same or subsequent pregnancies. Duplicate carrier screening, either in a patient's first or subsequent pregnancy, was furthered defined as inappropriate or appropriate. Inappropriate carrier screening was defined as carrier screening that does not provide new genetic information about the patient. In contrast, appropriate carrier screening was defined as carrier screening that provides new genetic information about the patient. Guideline adherence was defined as carrier screening that follows ACOG/ACMG recommendations for CF, SMA, and hemoglobinopathies.

Excluded patient charts

Five hundred and three (503) patient charts were reviewed during the study period. To be included in the chart review, patients had to be either primigravida or multigravida and seen at one of three UT Physician MFM clinics during the study period for genetic counseling and/or ultrasound services. Three patients were excluded from analysis since they were nulliparous. Out of the remaining 500 patients, the ethnicities of two patients were not recorded in the medical record; therefore, they could not be included in the ethnicity demographics. Furthermore, one of these patients had carrier screening done with an obstetrician but she was excluded from our secondary analysis since ethnicity data was not available. One patient with duplicate carrier screening from the primigravida group was excluded from cost analysis since the patient had sickle cell anemia and thus had multiple hemoglobin electrophoresis in her medical record due to her underlying condition.

Data completeness

In order to determine the completeness of the data being studied, the records were separated into two categories: incomplete vs complete. This was only applied to multigravida pregnancies to determine if all records from past pregnancies were available. Patients that were classified as multigravida, but experienced loss of pregnancy before 11 weeks were treated as primigravida. For a multigravida record to be considered a complete record, it had to meet three out of four categories: availability of ultrasound reports (either viability, anatomy, or growth) for all pregnancies, availability of aneuploidy testing for all pregnancies (including first trimester screening, maternal serum screening, or non-invasive prenatal testing), availability of obstetric panels for all pregnancies, and availability of carrier screening reports.

Cost analysis

To quantify the cost of duplicate carrier screening, the 2019 Clinical Diagnostic Laboratory Fee Schedule (CDLFS) from Centers for Medicare and Medicaid Services (CMS) was utilized. The cost was calculated by determining the amount and type of duplicate carrier screening for each patient multiplied by their 2019 CDLFS rate. Ultimately, the excess amount per patient was added to calculate the total cost for the month of January 2019. The CPT codes, 2019 rates, and type of screens ordered by providers are found in the supplementary section.

Guideline adherence

To evaluate obstetrician ACMG/ACOG adherence, the type of carrier screening ordered for each patient and the patient's ethnicity were assessed. The total number of patients who underwent guideline-recommended carrier screening was obtained by adding up all patients with recommended screening by ethnicity (Table 3).

Outcome measures

The outcome measures in this study were duplicate testing and obstetrician adherence to ACMG/ACOG recommended carrier screening guidelines.

Results

Demographics

Five hundred charts (500) were included in the primary data analysis and one chart with an unrecorded ethnicity was excluded from secondary data analysis. Out of the 500 charts reviewed, the age range was 16 to 45 years old, with the largest percentage (32.4%) of women between the ages of 30 to 34 years old. Of the 498 charts reviewed with ethnicity data available, Hispanic (33.3%), African American (28.9%), and Caucasian individuals (25.5%) made up the largest ethnic groups. Refer to Table 1 to review the complete list of demographic information for this study.

Table 1. Demographics

	Frequency %, (n)
Insurance	
Private	46.4%, (232/500)
Medicaid	53.6%, (268/500)
Pregnancy status	
Primigravida	26%, (130/500)
Multigravida	74%, (370/500)
Ethnicity	
Hispanic	33.3%, (166/498)
African/African-American/Black	28.9%, (144/498)
Caucasian	25.5%, (127/498)
Asian	9.2%, (46/498)
Indian	0.4%, (2/498)
Mediterranean/Greek/Italian	0.4%, (2/498)
Middle Eastern	0.6%, (3/498)
Mixed	1.6%, (8/498)

Three hundred and fourteen women (314/500; 62.8%) underwent carrier screening. The type of carrier screening varied by ordering provider and laboratory that performed the analysis. Carrier screening from this population was ordered either by a genetic counselor or an obstetrician. Out of the women who underwent carrier screening, 39 (39/314; 12.4%) had carrier screening only through a genetic counselor, 26 (26/314; 8.3%) had carrier screening through a genetic counselor and an obstetrician, and 249 (249/314; 79.3%) had carrier screening only through their obstetrician (Figure 1).

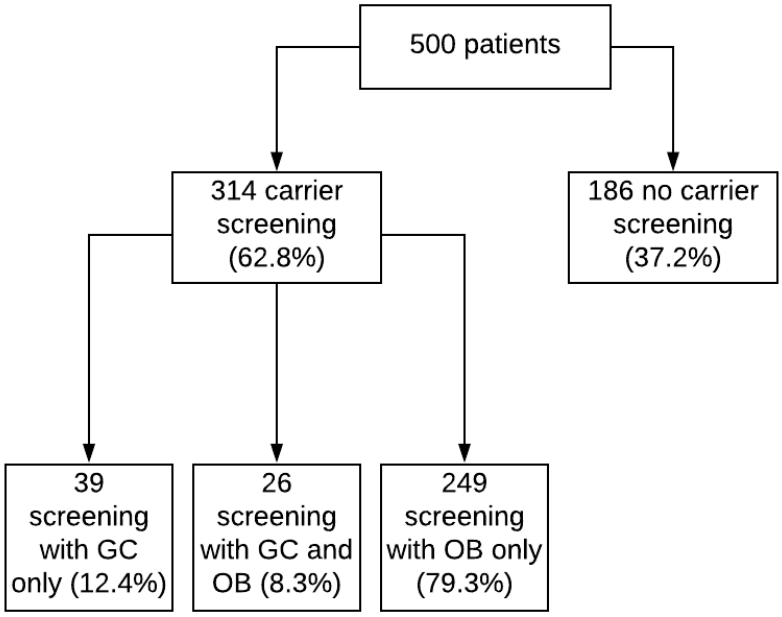


Figure 1. Carrier screening diagram

Duplicate carrier screening

Fifty-one patients (16.2%) had duplicate carrier screening offered by either an obstetrician or genetic counselor. Eight patients (15.7%) were primigravida and 43 patients (84.3%) were multigravida. One patient from the primigravida group was excluded from the cost analysis since she had sickle cell anemia. All the remaining seven primigravida patients had testing with a genetic counselor after screening had already been ordered by an obstetrician. Fifteen patients from the multigravida group had duplicate carrier screening with a genetic counselor and an

obstetrician. Duplicate carrier screening within the multigravida group took place between both provider types and there was no difference in the amount of duplicate carrier screening recommended between obstetricians and genetic counselors (p= 0.21). For a breakdown of duplicate carrier screening offered through genetic counselors and obstetricians please refer to Figures 2 and 3.

Figure 2. Duplicate carrier screening ordered by genetic counselors

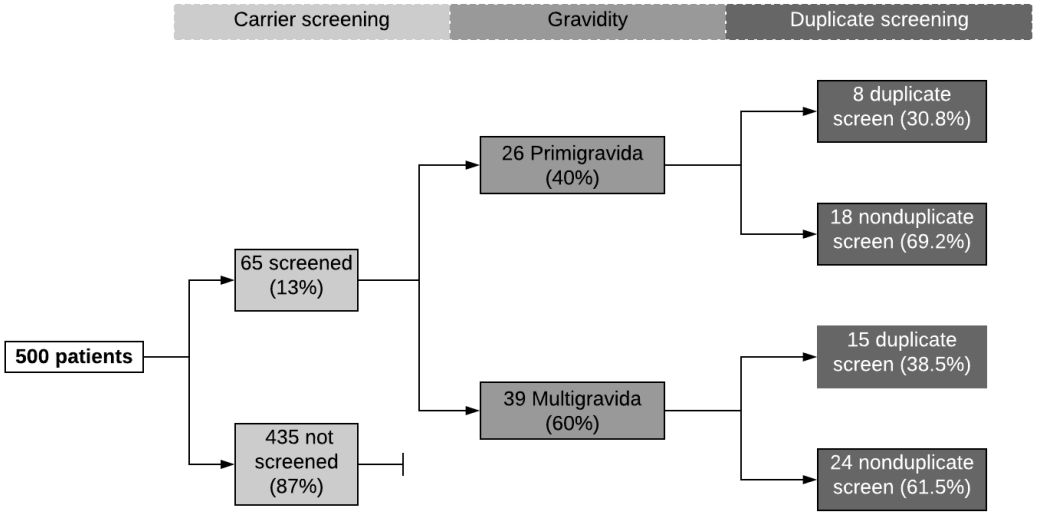
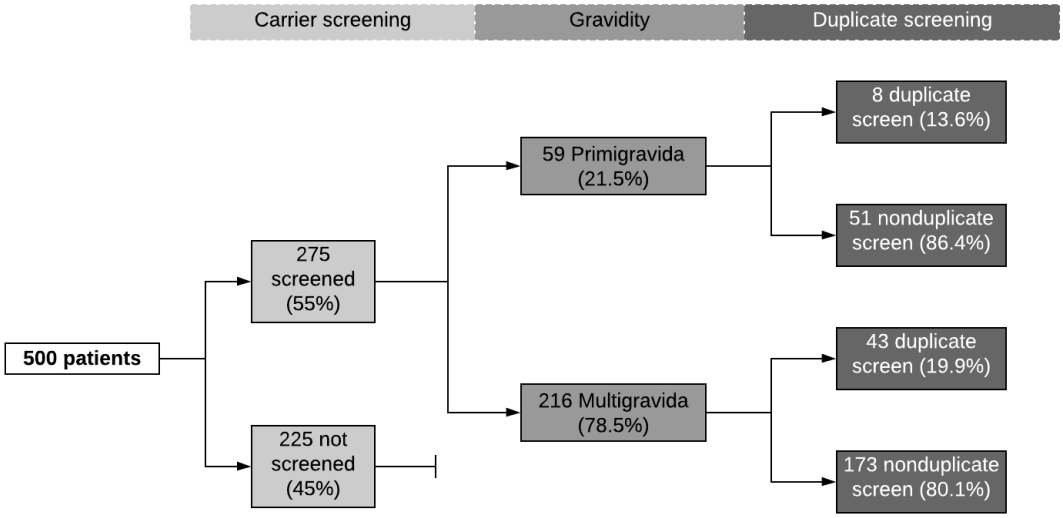


Figure 3. Duplicate carrier screening ordered by obstetricians



Data analysis

Chi-square analysis was done in ordered to assess the relationship between duplicate carrier screening and the following variables: ethnicity, pregnancy status, insurance, and completeness of records. Patients with Medicaid were significantly more likely to undergo duplicate carrier screening than patients with private insurance. The total amount of patients with Medicaid that underwent duplicate carrier screening was 19% compared to 11.3% of patients with private insurance ($p<0.000$). Patients with complete records were also significantly more likely to undergo duplicate carrier screening than patients with incomplete records. The total amount of patients with complete records that underwent duplicate carrier screening was 31 (60.8%) compared to 20 (39.2%) in the incomplete record category ($p<0.000$). There were no significant associations identified between duplicate carrier screening and ethnicity ($p=0.49$) or pregnancy status ($p=0.07$).

Cost analysis of duplicate carrier screening

The total cost of inappropriate duplicate carrier screening, utilizing the test pricing from the Clinical Diagnostic Laboratory Fee Schedule (CDLFS) from CMS, was $6,382.12. The CDLFS was used to standardize the cost of genetic testing since carrier screening in this study was performed by various laboratories and through different insurances. Furthermore, the prices represented on the CDLFS are equal to the median of private payor rates (10) giving an approximate cost that includes both private payors and Medicaid. Table 2 lists each repeated test, its cost, and the sum of inappropriate cost for this study.

Table 2. Cost analysis of inappropriate duplicate carrier screening

Repeated Test	Cost/repeated test
HEF	$ 14.30
HEF	$ 14.30
HEF	$ 14.30
HEF	$ 14.30
HEF	$ 14.30
HEF	$ 14.30
HEF	$ 14.30
HEF	$ 14.30
2 HEF	$ 28.60
HEF, CF 155 mutation panel, ECS	$ 3,019.46
2 HEF	$ 28.60
HEF	$ 14.30
2 HEF	$ 28.60
HEF	$ 14.30
HEF	$ 14.30
HEF	$ 14.30
HEF	$ 14.30
ECS	$ 2,448.56
HEF	$ 14.30
HEF	$ 14.30
CF 32 mutation panel	$ 556.60
HEF	$ 14.30
HEF	$ 14.30
2 HEF	$ 28.60
Total	$ 6,382.12

HEF: hemoglobin electrophoresis
ECS: expanded carrier screening

ACOG/ACMG carrier screening recommendation adherence by obstetricians

Two hundred and seventy-five patients underwent carrier screening with an obstetrician. Out of these 275 patients, one was excluded from the ACOG/ACMG analysis as their ethnicity could not be determined. From the remaining 274, 31.4%, (86/274) had carrier screening that included conditions recommended by ACOG/ACMG guidelines. Seventy-three of these women (73/86; 84.9%) underwent expanded carrier screening, defined in this study as a type of carrier screening performed when there is no clinical indication or is not guideline-driven. Thirteen patients (13/86; 15.1%) of patients had screening for ACOG/ACMG recommended conditions only. A breakdown of patient ethnicity and screening type can be visualized in Table 3.

Table 3. Patient ethnicity and screening type ordered by obstetricians

	CF	HEF	CF & SMA	CF & HEF	CF, SMA, & HEF	ECS	SMA	Guideline adherence (n)	Total (n)	Percentage/ethnicity
Hispanic	4	31	3	21	6	29	1	38	95	40%
African/African-American/Black	4	44	0	34	2	22	0	24	106	23%
Caucasian	2	11	1	12	1	15	1	17	43	40%
Asian	2	7	0	5	0	5	1	5	20	25%
Indian	0	2	0	0	0	0	0	0	2	0%
Mediterranean/Greek/Italian	0	1	0	0	0	0	0	0	1	40%
Middle Eastern	0	0	0	0	0	1	0	1	1	100%
Mixed	0	3	0	2	0	1	0	1	6	17%
Total	**12**	**99**	**4**	**74**	**9**	**73**	**3**	**86 (86/274) = 31.4%**	**274**	

CF: Cystic fibrosis
HEF: Hemoglobin electrophoresis
SMA: Spinal muscular atrophy
ECS: expanded carrier screening

Discussion

This study found that duplicate carrier screening accounts for a measurable percentage of the total testing ordered by both obstetricians and genetic counselors. Duplicate carrier screening occurred regardless of pregnancy status or ethnicity. However, patients with Medicaid and complete charts were significantly more likely to undergo duplicate testing. This study also found that only 31.4% of obstetricians in our cohort followed the recommended carrier screening guidelines delineated by ACOG and ACMG.

Duplicate carrier screening and cost

Our study focused on a clinical setting and found that the cost of inappropriate duplicate testing for the month of January 2019 was $6,382.12. For this study, inappropriate duplicate testing was defined as testing that did not provide new genetic information about the patient. Extrapolating this cost to the year 2019, the cost comes to $76,585.44. Most of the inappropriate duplicate testing was done by repeating hemoglobin electrophoresis either in the same or subsequent pregnancies. The cost of repeated expanded carrier screening in two patients contributed the most to the final sum of inappropriate duplicate testing.

The price estimated by this study was compared to duplicate testing in another health care setting. Stewart et al. focused on inpatient cardiac duplicate testing, including imaging and blood sample panels, and determined that in their cohort of 85 patients, 17 had non-clinically indicated duplicate testing. This study also used CDLFS from CMS and estimated the cost of duplicate testing to be $1,255 for the entire population. By utilizing an inflation calculator that uses official records from the U.S. Department of Labor, the price they derived in 2008 is equivalent to $1,490.23 in 2019. The cost of duplicate carrier screening in this study ($6,382.12) was found to be over $4,000 more than the cost of inpatient duplicate cardiac testing.

Duplicate carrier screening in the same pregnancy

Primigravida patients

All the primigravida patients (n=7) in this study that underwent duplicate carrier screening met with a genetic counselor after carrier screening was performed by their obstetrician. The reasons for meeting with a genetic counselor varied. In four of these cases, the patient was referred for genetic counseling to discuss first trimester aneuploidy screening options. In these sessions, options for further carrier screening were discussed and then elected by the patient. One patient was referred for a personal history of Alport syndrome. This patient had Medicaid and it did not cover complete testing for all genes related to Alport syndrome. Therefore, she elected expanded carrier screening, which evaluated three genes related to Alport syndrome. A second patient was referred for an abnormal hemoglobin electrophoresis consistent with beta thalassemia trait. This patient underwent HBB sequencing for molecular confirmation. Another patient was referred for an ultrasound finding of echogenic bowel. This patient had previously undergone hemoglobin electrophoresis only and the genetic counselor ordered expanded carrier screening to include cystic fibrosis. All duplicate genetic testing for this cohort was deemed appropriate since it provided new genetic information about these patients.

Multigravida patients

Among multigravida patients (n=43), thirteen patients underwent duplicate carrier screening in the same pregnancy. Ten of these patients met with a genetic counselor after having screening done with their obstetrician. Initially, nine of these patients had incomplete carrier screening ordered through their obstetrician, which is defined as either having only hemoglobin electrophoresis or both hemoglobin electrophoresis and cystic fibrosis screening, but no testing for spinal muscular atrophy. As with the primigravida patients, this type of duplicate carrier

screening was deemed appropriate as it contributed new genetic information for these patients. The remaining patient had targeted carrier screening with their obstetrician and was subsequently referred to genetic counseling for discordant sex between NIPT and ultrasound. The genetic counselor ordered expanded carrier screening to rule out congenital adrenal hyperplasia.

The remaining three multigravida patients that underwent duplicate carrier screening in the same pregnancy had duplicate screening through their ordering obstetricians. All patients had both CF genotyping and hemoglobin electrophoresis, and then underwent expanded carrier screening. A breakdown of duplicate carrier screening in multigravida patients within the same pregnancy in shown in Table 4.

Table 4. Duplicate carrier screening in multigravida patients during the same pregnancy

1st Test	2nd Test	Ordering providers
HEF	ECS	OB and GC
HEF	ECS	OB and GC
HEF	ECS	OB and GC
HEF	ECS	OB and GC
HEF	ECS	OB and GC
HEF	ECS	OB and GC
CF 32 mutation panel + HEF	ECS	OB and GC
CF 32 mutation panel + HEF	ECS	OB
CF 70 mutation panel + HEF	ECS	OB
HEF	ECS	OB and GC
CF 99 mutation panel + HEF + SMA	ECS	OB and GC
CF 155 mutation panel + HEF	ECS	OB
CF 32 mutation panel	ECS	OB and GC

HEF: hemoglobin electrophoresis
ECS: expanded carrier screening
OB: obstetrician
GC: genetic counselor

Duplicate carrier screening across multiple pregnancies

Twenty-nine multigravida patients had duplicate carrier screening across different pregnancies. Five of these patients had duplicate carrier screening because this testing was done by both genetic counselors and obstetricians. The remaining 24 patients had duplicate genetic testing ordered by different obstetricians. One possible explanation of the repeat carrier screening by different obstetricians is the difficulty in accessing testing records through the electronic

medical record, particularly external records. Electronic medical records are often difficult to navigate, especially given time constraints and patient volumes in obstetrical clinics. Therefore, it may be reasonable to assume that a thorough chart review of all testing in previous pregnancies may not necessarily be completed before a routine OB visit, which could ultimately lead to duplicate testing. Another reason for duplicate carrier screening across multiple pregnancies could be incomplete records in transferred patients. Although this could not be assessed in this retrospective study, loss of records from transferred patients has been documented in the literature. Stewart et al. published a case report looking at the incidence of duplicate testing in a cardiac setting between transferred patients. They determined that duplicate testing was seen when patients transferred between care facilities with incompatible medical records, leading to incomplete records transfer (11). In the OB setting, providers may not obtain carrier screening records from past pregnancies, leading to duplicate testing.

Guideline adherence

Practice-developed clinical guidelines by governing organizations, such as ACOG or ACMG, have two main purposes. First, they are constructed to aid in decision making by describing the current state of knowledge and provide evidence-based recommendations for health care practitioners (12). Their second purpose is to serve as a means to external control, allowing for the translation of key indicators which can be used to review healthcare professional's performance (12). In this study it was observed that the majority of obstetricians (68.6%) did not follow the carrier screening recommendations set by ACOG/ACMG. This was largely due to the fact that copy number SMA testing was not routinely ordered in our population. Out of 274 patients that had screening with an obstetrician, only three had SMA testing, four had SMA testing in conjunction with CF testing, and nine had SMA, CF, and HEF testing. Therefore, a total of 16 patients (6% of the cohort) had SMA testing performed by their obstetricians during

this time period. Most obstetricians, when ordering carrier screening for their patients, ordered cystic fibrosis and/or hemoglobin electrophoresis. Dyr et al. previously analyzed this trend in a study done in 2019 by LabCorp. This study looked at SMA ordering trends by healthcare practices after implementation of ACOG's committee opinion 691. It concluded that there was an increase in ordering SMA carrier screening after adoption of the committee opinion but that it had yet to reach the level of CF carrier testing (13). One potential explanation for the lag in SMA ordering by healthcare providers is that according to the National Institute for Health and Clinical Excellence, it can take up to three years for clinical guidelines to be implemented into practice (14). As ACOG's committee opinion was released in March 2017, it could be that full incorporation of this practice by clinicians may not occur until later in 2020. However, it should be noted that panethnic carrier screening for SMA was first recommended by ACMG in 2008. The study by Dyr et al did not note what type of healthcare providers were ordering SMA testing but if we assume these were only obstetricians, like our cohort, it could be theorized that obstetricians may base their clinical practice on recommendations from their foremost professional organization, ACOG, and not ACMG. Therefore, the practice of SMA ordering could be thought as newly recommended with ACOG's 2017 guidelines and its implementation is being actively incorporated into obstetrical practice.

An important limitation to the study done by Dyr et al. is that it did not look at expanded carrier screening to assess the ordering trends pre and post ACOG's committee opinion 691; rather it only looked at single gene testing orders for SMA. Our study took expanded carrier screening into account for guideline adherence. In our study populations, most obstetricians that followed carrier screening guidelines did so by ordering this type of testing. The offering of expanded carrier screening to all women brings up the issue of whether or not this is appropriate practice, an issue that has been discussed by various medical organizations including ACOG, ACMG, and

the National Society of Genetic Counselors (NSGC). One of the reasons for this growing discussion is the variety and size of expanded carrier screening panels offered by different laboratories. These panels can include multiple genetic conditions that may be incredibly rare or mild. Based on ACOG's recommendations, rare conditions are defined as those having a carrier frequency of less than 1% and mild conditions are defined as those that do not have a detrimental effect on quality of life, cause cognitive or physical impairment, and require medical or surgical intervention. According to Stevens et al., undergoing screening for such rare and mild conditions not only increases undue patient anxiety (15), but also leads to higher cost via unnecessary follow-up testing.

To further address the role of expanded carrier screening in the prenatal and preconception setting, the Society for Maternal-Fetal Medicine (SMFM), ACOG, and ACMG held a "Prenatal Genetic Testing" workshop in January of 2017. The consensus of this working group was that ethnicity based screening should not be abandoned in favor of panethnic expanded carrier screening (16). Later that year, ACOG released a committee opinion stating that ethnic-specific, panethnic, and expanded carrier screening are all acceptable approaches to carrier screening, emphasizing that if expanded carrier screening is offered to patients, it should be accompanied by pretest and posttest counseling (9). ACOG furthered provided guidance on criteria that should be considered when adding genetic conditions to expanded screening panels. This criterion includes conditions that:

> have a carrier frequency of 1 in 100 or greater, have a well-defined phenotype, or have an onset early in life (9).

In addition, these conditions should be able to be tested for prenatally. Therefore, if expanded carrier screening is the preferred method of testing by obstetricians, as represented by this study, these providers should select clinically useful panels that have been modeled to include criteria set forth by ACOG.

Conclusion

The main outcomes of this study were to quantify duplicate carrier screening across the same or subsequent pregnancies and to assess adherence to ACOG/ACMG recommended carrier screening guidelines. This study achieved both outcomes, determining that duplicate carrier screening is taking place in our cohort and that the majority of obstetricians are not following the recommended carrier screening guidelines. In particular, the vast majority of patients did not receive Spinal Muscular Atrophy (SMA) screening. The lack of SMA ordering, was the major driving force for why providers did not meet the recommended guidelines. When obstetricians are adhering to guidelines, it is through ordering expanded screening panels. In addition to determining if duplicate carrier screening was taking place, this study looked at the theoretical cost of inappropriate duplicate testing. This cost was determined to be $6,382.12 for the month of January 2019.

Limitations

We recognize that this study is a retrospective chart review and as such is limited by various factors, the most important of which being missing documentation within patient charts. Therefore, it is possible that patients with duplicate carrier screening were missed and that our cost analysis is under representative of the actual total cost of inappropriate duplicate carrier screening. Another limitation for this study is that this data only represents one healthcare system in an urban setting; therefore, it may not be generalizable to other healthcare systems. Additionally, our study determined the cost of duplicate carrier screening by looking at the prices set out by Medicare and Medicaid and we were unable to determine the actual cost billed to patient who utilized private health insurance, which is routinely higher than the cost billed to Medicaid.

Future Research/Practice Implications

Inappropriate duplicate genetic testing was estimated to cost $6,382.12. This should be a focus of attention for medical practices in order to avoid overspending resources in redundant information. This is an important behavior to mitigate since it can lead to unmet health needs and disparities (17).

As evidenced by our study, expanded carrier screening is the most commonly ordered panel used by providers that meets ACOG/ACMG guidelines, as individual providers have been slow to implement SMA screening following updated guidelines. Future research should assess healthcare provider knowledge of recommended carrier screening guidelines and attitudes regarding the variety of expanded carrier screening panels offered.

Supplementary tables

Table 5. 2019 Clinical Diagnostic Laboratory Fee Schedule

CPT Code	2019 Rate	Type of Screen
81220	$556.60	CFTR gene com variants
81222	$435.07	CFTR gene duplication/deletion variants
81223	$499.00	CFTR gene full sequence
81329	$137.00	SMN1 gene dosage analysis
81443	$2,448.56	Genetic testing severe inherited conditions
83020	$14.30	Hemoglobin electrophoresis

Table 6. Type of carrier screening ordered with a genetic counselor

Test Type	Frequency	Percent
CF & SMA	1	2%
ECS	55	85%
HEF	1	2%
HBB	1	2%
CF, SMA & HBB	4	6%
CF, SMA, HBA & HBB	3	5%
Total	65	100%

CF: cystic fibrosis
SMA: spinal muscular atrophy
ECS: expanded carrier screening
HEF: hemoglobin electrophoresis
HBB: hemoglobin subunit beta gene
HBA: hemoglobin subunit alpha gene

Table 7. Type of carrier screening ordered with an obstetrician

Test Type	Frequency	Percent
CF	12	4%
HEF	100	36%
CF & SMA	4	1%
CF & HEF	74	27%
CF, SMA & HEF	9	3%
ECS	73	27%
SMA	3	1%
Total	275	100%

CF: cystic fibrosis
HEF: hemoglobin electrophoresis
SMA: spinal muscular atrophy
ECS: expanded carrier screening

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