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Cases in Precision Medicine: When Patients Present With Direct-to-Consumer Genetic Test Results

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A couple is planning to start a family, and they decide to order a 23andMe test after reading about the company's carrier screening test and the new *BRCA1/BRCA2* test. They bring the results to their internist for advice on how to proceed. Given the rise in public interest in human genetics and precision medicine, direct-to-consumer genetic testing is becoming increasingly popular, and clinicians should expect patients to present the results of these tests more frequently. This article uses a case scenario to provide information about what the results of these tests mean, and what they do not mean.

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A couple is planning to start a family. The husband is aged 25 years and Ashkenazi Jewish and has heard that he could pass on "Jewish diseases," such as Tay–Sachs disease, to his children. His wife, who is also 25 years old and Latina, is worried because her mother and grandmother both developed breast cancer in their early 40s. They decide to order a 23andMe test after reading about the company's carrier screening test and the new *BRCA1/BRCA2* test. After receiving the results, the wife is relieved to learn that she tested negative for *BRCA1/BRCA2* (Table 1). However, they are concerned to find that the husband is a carrier for Gaucher disease type 1 and the wife is a carrier for cystic fibrosis, although they know of nobody in their families with either condition. The husband is also shocked to discover that he has 2 copies of the ε4 variant in the *APOE* gene and is now worried about his risk for Alzheimer disease. They take the test results to their internist for advice on how to proceed.

Given the rise in public interest in human genetics and precision medicine, direct-to-consumer (DTC) genetic testing is becoming increasingly popular, and clinicians should expect patients to present the results of these tests, such as the one in the composite case just described, more frequently. Direct-to-consumer genetic tests are advertised and sold directly to the public. In addition to ancestry and nondisease traits (such as eye and hair color, preferred wake-up time, aversion to cilantro, caffeine consumption, or ability to smell urine odor after eating asparagus), these tests may offer information on risks for certain diseases, carrier status for autosomal recessive diseases that have reproductive implications, and pathogenic variants (the preferred term for what are colloquially called "mutations"). Although DTC tests can provide genetic information to a much broader audience than might otherwise be reached because of difficulties accessing clinical genetic testing, high costs, or poor insurance coverage, they are not diagnostic and offer information on a limited number of genes and diseases. In addition, concerns have been raised about the accuracy and technical validity of the analysis underlying the risk profiles given to consumers and the clinical utility of providing consumers with health information that can easily be interpreted as medical advice (1).

What Information Do DTC Genetic Tests Provide?

Companies vary in the DTC services they provide. Some, such as AncestryDNA and National Geographic, provide only genetic ancestry information. Others provide more extensive information, but only with physician approval. For example, Genos offers full-exome sequencing, whereas Veritas provides detailed genetic health risk information. 23andMe, one of the most prominent DTC companies and one of the first to offer genetic testing to the general public, is notable for providing genetic health risk information without physician approval or involvement.

After an investigation by the U.S. Government Accountability Office in 2006 concluded that DTC companies were involved in deceptive advertising and after congressional hearings in 2013 that warned that DTC testing could threaten individual health and safety, the U.S. Food and Drug Administration (FDA) issued a cease-and-desist order in 2013 to 23andMe and several other companies requiring immediate discontinuation of DTC testing (2). However, in 2015, the FDA partially reversed its position and approved 23andMe's carrier screen for hereditary Bloom syndrome (a rare autosomal recessive disorder characterized by short stature, a wide variety of cancer types, and chromosome instability), indicating that 23andMe had provided sufficient evidence that the public was capable of understanding the results. In April 2017, the FDA authorized 23andMe to market genetic health risk tests for 10 conditions (Parkinson disease, late-onset Alzheimer disease, celiac disease, α_1-antitrypsin deficiency, early-onset primary dystonia, factor XI deficiency, Gaucher disease type 1, glucose-6-phosphate dehydrogenase deficiency, hereditary hemochromatosis, and hereditary thrombophilia) (3). The following month, 23andMe began offering reports for Parkinson disease, late-onset Alzheimer disease,

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Key Summary Points

Direct-to-consumer (DTC) genetic testing is becoming increasingly popular, and clinicians should be prepared to provide guidance to their patients when presented with results from these tests.

23andMe does not perform comprehensive testing of known pathogenic variants and may have limited value and sensitivity for patients who are not of European or Ashkenazi Jewish descent.

The positive predictive value of many 23andMe genetic tests is limited because risk is often modified by interacting genes, environment, lifestyle, and family history, which are not included in the risk predictions.

Clinicians should refer patients with concerns about genetic test results or genetic concerns not addressed by DTC testing to a genetic counselor or another qualified provider.

α_1-antitrypsin deficiency, and hereditary thrombophilia. Over the next year, the company added hereditary hemochromatosis, age-related macular degeneration, celiac disease, and glucose-6-phosphate dehydrogenase deficiency to its reports. In March 2018, the FDA authorized 23andMe to test for 3 specific pathogenic variants in the *BRCA1/BRCA2* hereditary breast and ovarian cancer genes that are observed largely in persons of Ashkenazi Jewish descent (4). Although the FDA's decisions were based on the difference between "genetic health risk" tests (those providing information about genetic risk for a disease) and "diagnostic" tests (those providing information to diagnose a disease once symptoms are present), the general public does not necessarily understand this distinction (5).

What Are the Limitations of DTC Genetic Tests?

Many of the conditions tested by 23andMe are rare, and the clinical utility of such information for the general public is limited (6). Although the small panel of variants included in the test may increase risk, they typically account for only a fraction of the variants contributing to a particular disease, and none of the genes that are analyzed are comprehensively sequenced or assessed. The predictive value of a positive result for many of the conditions is low because many of the variants are modified by additional factors, such as other interacting genes, environment, and lifestyle.

Analysis of a few variants without the context of medical and family history can lead to misinterpretation of test results and inaccurate assessment of disease risk. The likelihood of misinterpretation is particularly high for persons of non-European ancestry because, for many of the conditions screened, the test does not include common variants found in minority populations. However, for persons of Ashkenazi Jewish descent, many 23andMe tests are more informative for variants found specifically in that community (6).

How Can Clinicians Help Patients Understand the Meaning and Limitations of DTC Genetic Test Results?

In the 2017 order permitting 23andMe to offer its DTC testing for genetic health risk, the FDA identified 3 risks related to the tests and means of mitigating them. The risks included lack of understanding of the test by the consumer, incorrect results (false-positives or false-negatives), and erroneous interpretation of the results. The mitigating factors included "limiting statements" explaining how the tests work, how to interpret the results, and the limitations of the results; requirements for the statistical basis for the accuracy of the information with respect to the variants reported; and consumer education (7). However, questions remain about how "protective" these mitigating steps are for the average consumer and how a clinician should advise his or her patient about a 23andMe report. We believe that there are several ways clinicians can help patients understand the meaning and limitations of DTC test results. The following have been suggested by the American College of Medical Genetics and Genomics (1).

Appropriate Clinical Data Generation and Analysis

Data generation and analysis in genetic testing may be performed by a single entity (a DTC company) or may be split between 2 entities (a DTC company and a third-party interpretation company). All clinical data should be generated and analyzed in a Clinical Laboratory Improvement Amendments (CLIA)–certified laboratory (the laboratory's certification can be checked at the Genetic Testing Registry [www.ncbi.nlm.nih.gov/gtr]). If any part of the process does not meet CLIA requirements, the full test and interpretation should be confirmed in a CLIA-certified laboratory. Although 23andMe tests are analyzed at CLIA-certified laboratories, patients may send the data they receive to third-party interpretation companies that provide risk estimates that may not be accurate for clinical diagnostic interpretation. If the 23andMe result is negative but clinical suspicion is high, further testing covering all of the genes and variants associated with the condition of concern may be warranted, with comprehensive analysis for those genes. The results should be interpreted and delivered by a provider who is knowledgeable in genetics or a board-certified genetics professional.

Availability of Genetics Expertise

A certified medical geneticist or genetic counselor is often helpful in interpreting test results in the context of personal and family history. If the practitioner has insufficient knowledge of genetics, input from a genetics professional may alleviate risks for misinterpretation of results, inappropriate disease management or prevention, or inadequate follow-up.

Table 1. Typical 23andMe Results and Suggested Clinician Responses

Disease	Reported Results	Suggested Clinician Response
Breast cancer	"You do not have the 3 genetic variants we tested; 0 variants detected in the *BRCA1* and *BRCA2* genes"	Only 3 out of >1000 variants are tested by 23andMe Many other genes can increase breast cancer risk Most breast cancer cases are explained by factors other than these 3 variants Patient's family history suggests increased risk for breast cancer, regardless of test result
Gaucher disease type 1	"You have 1 of the variants we tested; 1 variant detected in the *GBA* gene"	Does not screen for all disease-causing variants Residual risk for carrying another variant 25% chance of having child with disease if both parents are carriers Genetic counselors can advise about increased risk for Parkinson disease in carriers
Cystic fibrosis	"You have 1 of the variants we tested; 1 variant detected in the *CFTR* gene"	Does not screen for all disease-causing variants Residual risk for carrying another variant 25% chance of having child with disease if both parents are carriers
Alzheimer disease	"You have 2 copies of the ε4 variant we tested; variant detected in the *APOE* gene"	The test result is associated with increased risk for the disease No proven interventions for eliminating risk Lifestyle changes may reduce risk

More Nuanced Disclosure

The patient should be told that DTC tests are not diagnostic and provide limited information on disease risk. Medical interpretation of results is often complex and includes additional patient-specific information, such as family and personal medical history and inclusion of other risk factors. This information must be incorporated and communicated to the patient in the appropriate context and in an understandable and culturally appropriate manner.

Information About Privacy Concerns

To have the genetic testing offered by 23andMe, the consumer is required to agree to a 25-page terms of service and a 29-page privacy statement. Each of these is a legal agreement that permits the company to use various types of personal information, some by virtue of use of 23andMe's services and some (such as identifiable genetic or self-reported information) pursuant to what the company considers to be explicit consent for research. 23andMe has sold deidentified information to pharmaceutical companies trying to develop new medical treatments.

All of this may leave the average consumer bewildered. Patients should carefully read the agreements they sign and should contact the testing laboratory with questions about data privacy. The internist has no responsibility to address privacy issues and should refer the patient to the testing laboratory.

How Should the Internist Advise the Patients in This Case?

Given all of this information, what should the internist tell the couple in the example at the beginning of the article?

He or she should tell the couple that the 23andMe test targets specific variants and does not screen for all disease-causing variants of Gaucher disease or cystic fibrosis; thus, the spouse who tested negative for each of these recessive conditions could still be carrying a disease-causing variant. An important factor to consider is the couple's residual risk for being carriers given their ancestry (Table 2). Gaucher disease and cystic fibrosis are more common in certain ethnic groups, but disease-causing variants have been found in all ethnicities (10). Therefore, they still have a small possibility of having a child with either disease, and additional testing is available if the residual risk level concerns them. For example, although the husband tested negative as a cystic fibrosis carrier, 23andMe reports that a person of Ashkenazi Jewish ancestry has a residual risk of 1 in 390 of being a carrier for cystic fibrosis even with a negative result (Table 2). For Gaucher disease, 23andMe does not provide a residual risk estimate for Latina women, so consultation with a genetic professional would be necessary to determine the wife's residual risk for being a carrier. If the husband and wife are both carriers for the same recessive condition, they have a 25% chance of having a child with the condition. They could speak with a genetic counselor about their options for more comprehensive genetic testing as well as details about Gaucher disease and cystic fibrosis, including the natural history of the conditions; treatment options, such as enzyme replacement therapy, medication, nutritional support, and lung transplant (Table 2); the efficacy and effect of these treatments; and reproductive options, including prenatal testing and in vitro fertilization with preimplantation genetic diagnosis if they are both found to be carriers. A genetic counselor or another qualified provider can also supply additional information, such as that Ashkenazi Jewish persons who are carriers for Gaucher disease have a 7.7% higher lifetime risk for Parkinson disease (10).

The internist should explain to the wife that the 23andMe test includes only 3 pathogenic variants in *BRCA1/BRCA2* that are common in Ashkenazi Jewish persons and does not comprehensively evaluate the genes to assess more than 1000 other known disease-causing variants in *BRCA1/BRCA2* (Table 3). It also does not include any of the other genes that can increase risk for

Table 2. Selected Carrier Status Tests Offered by 23andMe*

Disease (Reference)	Gene Tested	Number of Pathogenic Variants Tested and Proportion of Recommended Variants Tested†	Ethnicities at Highest Risk‡
β-Thalassemia and related hemoglobinopathies (8, 9)	*HBB*	Total: 10 ACOG: Screening is recommended for African, Southeast Asian, Mediterranean, Middle Eastern, and West Indian persons by complete blood count and hemoglobin electrophoresis before genetic testing	Cypriot, Greek, Italian/Sicilian, Sardinian, African, Southeast Asian, Middle Eastern, and West Indian
Bloom syndrome (8, 9)	*BLM*	Total: 1 ACMG: 1/1 (for Ashkenazi Jewish)	Ashkenazi Jewish
Canavan disease (8, 9)	*ASPA*	Total: 3 ACMG: 2/2 (for Ashkenazi Jewish)	Ashkenazi Jewish
Cystic fibrosis (8, 9)	*CFTR*	Total: 29 ACMG: 22/23 (for all ethnicities)	Ashkenazi Jewish, European, Hispanic
Familial dysautonomia (8, 9)	*IKBKAP*	Total: 1 ACMG: 1/2 (Ashkenazi Jewish)	Ashkenazi Jewish
Fanconi anemia group C (8, 9)	*FANCC*	Total: 3 ACMG: 1/1 (for Ashkenazi Jewish)	Ashkenazi Jewish
Gaucher disease type 1 (8, 9)	*GBA*	Total: 3 ACMG: 2/4 (for Ashkenazi Jewish)	Ashkenazi Jewish
Mucolipidosis type IV (8, 9)	*MCOLN1*	Total: 1 ACMG: 1/2 (for Ashkenazi Jewish)	Ashkenazi Jewish
Niemann-Pick disease type A (8, 9)	*SMPD1*	Total: 3 ACMG: 3/3 (for Ashkenazi Jewish)	Ashkenazi Jewish
Sickle cell anemia (8, 9)	*HBB*	Total: 1 ACOG: Screening is recommended for African, Southeast Asian, Mediterranean, Middle Eastern, and West Indian persons by complete blood count and hemoglobin electrophoresis before genetic testing	African
Tay-Sachs disease (8, 9)	*HEXA*	Total: 4 ACMG: 3/3 (for Ashkenazi Jewish)	Ashkenazi Jewish, Cajun (French Canadian variants not tested)

ACMG = American College of Medical Genetics and Genomics; ACOG = American College of Obstetricians and Gynecologists.
* 23andMe offers 43 carrier status tests. The 11 listed are those for which screening is currently recommended by ACMG.
† Total number of pathogenic variants in the gene tested by 23andMe and the number of pathogenic variants tested by 23andMe relative to the total number of pathogenic variants recommended for testing by ACMG or ACOG.
‡ Ethnicities in which the tested pathogenic variants are known to be most frequent.
§ Percentage of all pathogenic variant carriers of a given ethnicity that the test is expected to detect given the specific pathogenic variants tested by 23andMe.
‖ Risk for carrying a pathogenic variant with a negative result on the targeted 23andMe test.

hereditary breast cancer, such as *TP53*, *PTEN*, or *PALB2* (Table 3). Because the test is most accurate for Ashkenazi Jewish persons and given the wife's Latina ancestry, the test provides little information about whether she carries a pathogenic variant in *BRCA1/BRCA2*. In addition, the test result is positive in only about 10% of women who develop breast cancer (16), meaning that most Ashkenazi Jewish women who develop breast cancer do so for other reasons, including other genetic variants beyond *BRCA1/BRCA2* and nongenetic factors. On the basis of her family history, the wife has increased risk for breast cancer, and it is recommended that she meet with a genetic counselor to discuss her risk for breast cancer, her risk for carrying a pathogenic variant in one of the hereditary breast cancer genes, and the more comprehensive genetic tests available (17). She has options for managing her breast cancer risk, such as enhanced screening, chemoprevention, and risk-reducing surgery (Table 3).

The internist should advise the husband that carrying 2 copies of the ε4 *APOE* variant increases his risk for Alzheimer disease, even if he has no known family history of it. The lifetime risk for a male with 2 copies of the ε4 *APOE* variant is estimated to be 51%, regardless of family history (Table 3). Although no specific interventions have been proven to eliminate risk, data suggest that regular exercise, a healthy diet, and good cardiovascular health may reduce risk (Table 3). However, the effectiveness of lifestyle modifications in preventing Alzheimer disease has not been definitively demonstrated.

In conclusion, the clinical value of 23andMe testing is currently limited because the number of genes and variants included is small and the test does not comprehensively assess risk for most persons and most conditions. The result that most often has clinical utility is identification of a pathogenic variant in *BRCA1/BRCA2* in a person of Ashkenazi Jewish ancestry. However, re-

Table 2–Continued

Pathogenic Variant Detection Sensitivity, by Ethnicity§	Residual Risk, by Ethnicity‖	Available Interventions for Treatment or Management
Cypriot: 90% Greek: 75% Italian/Sicilian: 82% Sardinian: 97% North African: 50%–61% Turkish: 66% Balkan: 41%–80% South Asian: 20%–70% Southeast Asian: 11%–73% Middle Eastern: 29%–64%	Cypriot: 1/71 Greek: 1/37 Italian/Sicilian: 1/61 Sardinian: 1/250 Turkish: 1/65 Balkan, South Asian, Southeast Asian, North African, Middle Eastern: Unknown	Symptom management, blood transfusion, bone marrow transplant
Ashkenazi Jewish: 99%	Ashkenazi Jewish: 1/11 000 Other ethnicities: Unknown	No cure; symptom management to prevent infections/cancer
Ashkenazi Jewish: 98%	Ashkenazi Jewish: 1/2000 Other ethnicities: Unknown	No cure; symptom management
Ashkenazi Jewish: 94% European: 89% Latina: 73% African American: 65% Asian: 55%	Ashkenazi Jewish: 1/390 European: 1/230 Hispanic: 1/210 African American: 1/170 Asian: 1/210 Other ethnicities: Unknown	Some mutation-specific medications, treatment of pulmonary and gastrointestinal symptoms, lung transplant, assisted reproductive technologies for male infertility
Ashkenazi Jewish: 99%	Ashkenazi Jewish: 1/2300 Other ethnicities: Unknown	No cure; symptom management only
Ashkenazi Jewish: 99%	Ashkenazi Jewish: 1/88 000 Other ethnicities: Unknown	Hematopoietic stem cell transplant
Ashkenazi Jewish: 92%	Ashkenazi Jewish: 1/200 Other ethnicities: Unknown	Enzyme replacement or substrate reduction therapy
Ashkenazi Jewish: 77%	Ashkenazi Jewish: 1/550 Other ethnicities: Unknown	No cure; symptom management only
Ashkenazi Jewish: 97%	Ashkenazi Jewish: 1/3000 Other ethnicities: Unknown	No cure; symptom management only
All ethnicities: 99%	None	Symptom management, blood transfusion, bone marrow transplant
Ashkenazi Jewish and Cajun: 99%	Ashkenazi Jewish: 1/2700 Cajun: 1/29 000 000 French Canadian and other ethnicities: Unknown	No cure; symptom management only

gardless of ancestry, anyone with an identified pathogenic variant requires management based on National Comprehensive Cancer Network guidelines. Before acting on DTC test results, patients should have them confirmed by a clinical diagnostic laboratory and should discuss them with a knowledgeable medical professional. Clinicians should be prepared to address patients' concerns about genetic test results. If the volume of patients bringing DTC test results to their internists increases significantly, scalable solutions to educate patients and address common questions will need to be developed by the testing laboratories.

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Table 3. Diseases Included in the Genetic Health Risk Test Offered by 23andMe

Disease (Reference)	Gene Tested	Variants Tested/Total Known Pathogenic Variants, *n/N*	Ethnicities at Highest Risk*
Age-related macular degeneration (8, 11, 12)	*CFH*, *ARMS2* (not tested: ≥34 additional known risk genes)	2/52	White, followed by Hispanic and Asian; least common in African American
α_1-Antitrypsin deficiency (8, 9)	*SERPINA1*	2/>35	White
Breast cancer (8, 9)	*BRCA1*, *BRCA2* (not tested: *TP53*, *PTEN*, *CDH1*, *CHEK2*, *ATM*, *PALB2*, *STK11*, *BLM*, *WRN*, *RAD51C*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, *EPCAM*)	3/>1000	Ashkenazi Jewish, but observed in all ethnicities
Celiac disease (8, 9)	*HLA-DQA1*, *HLA-DQB1* (not tested: 39 other genetic risk loci that contribute about 5% of the genetic risk for celiac disease)	2/2	White (rarely diagnosed in persons of sub-Saharan African descent)
G6PD deficiency (8, 13)	*G6PD*	1/>160	African (variants common to Italian, Mediterranean, and Middle Eastern ethnicities not tested)
Hereditary hemochromatosis (HFE-related) (8, 9)	*HFE*	2/~28	White (these variants are most common in Northern Europeans but are also found in Hispanics, African Americans, and Asians)
Hereditary thrombophilia (prothrombin-related and factor V Leiden thrombophilia) (8, 9)	*F2*, *F5*	2/2	White (both variants most common in Europeans; extremely rare in African and Asian populations)
Late-onset Alzheimer disease (8, 9, 14)	*APOE* (not tested: *APP*, *PSEN1*, *PSEN2*)	1/1 (for late-onset Alzheimer disease)	All ethnicities
Parkinson disease (8, 9, 15)	*LRRK2*, *GBA* (not tested: *SNCA*, *VPS35*, *PRKN/PARK2*, *PINK1*, *PARK7*, *ATP13A2*, *FBX07*, *SLC6A3*, *TAF1*)	2/≥28	White, Ashkenazi Jewish, North African Berber

COPD = chronic obstructive pulmonary disease; G6PD = glucose-6-phosphate dehydrogenase; HFE = human factors engineering.
* Ethnicities in which the tested pathogenic variants are known to be most frequent.
† Percentage of all pathogenic variant carriers of a given ethnicity that the test is expected to detect given the specific pathogenic variants tested by 23andMe. The test may not detect any pathogenic variant carriers among other ethnicities not listed. There may be other disease-causing genes that are not tested by 23andMe.
‡ Percentage of persons with a positive test result who will develop the disease at some point in their lifetime. Estimates are often available only for well-studied ethnicities/populations.

Table 3–Continued

Pathogenic Variant Detection Sensitivity, by Ethnicity†	Penetrance‡	Available Interventions to Prevent or Delay Disease Onset	Available Interventions for Treatment or Management
Uncertain	0-1 copies: 1.4% 2 copies: 5.2% 3-4 copies: 15.3%	Smoking cessation	No cure
Northern European: 95%	Risk estimates available for Europeans: *MZ genotype: Nonsmokers unlikely to develop COPD; smokers at slightly increased risk; insufficient data for cirrhosis *SZ genotype: 20%–50% lifetime risk for COPD among smokers; insufficient data for cirrhosis *ZZ genotype: >80% risk for COPD, 30%–40% risk for cirrhosis after age 50 y	Smoking cessation and limitation of alcohol intake	Enzyme replacement, bronchodilators, antibiotics, lung transplant
Ashkenazi Jewish: >95%	*BRCA1* female (by age 70 y): 45%–85% breast, 39%–46% ovarian *BRCA2* female (by age 70 y): 45%–85% breast, 10%–27% ovarian *BRCA2* male (lifetime): 7%–8% breast	Increased screening, chemoprevention, prophylactic surgery	Surgery, chemotherapy
White: 100%	≥1 copy of HLA-DQ2.5 or HLA-DQ8 haplotypes: about 3%	Gluten-free diet	Gluten-free diet
African descent: 90%	Dependent on exposure to triggering medication Males: about 71% (X-linked) Females with 2 copies: about 48% Females with 1 copy: about 7.5%	Avoidance of triggers (fava beans, certain drugs)	Elimination of triggers, blood transfusion
White: 91%	Males with 2 copies of C282Y: 24%–36% Females with 2 copies of C282Y: 4%–14% Males with 1 copy of C282Y and 1 copy of H63D: 3% Females with 1 copy of C282Y and 1 copy of H63D: 2% Other genotypes: Not likely to be at risk	Phlebotomy	Phlebotomy
White: >95%	1 copy of F5: 2/1000 2 copies of F5: 15/1000 (1-y risk for blood clot)	Avoidance of estrogen-containing contraception and hormone replacement therapy	May include anticoagulation
All ethnicities: 100%	Lifetime risk: Males with 1 copy of ε4: 20%–23% Females with 1 copy of ε4: 27%–30% Males with 2 copies of ε4: 51% Females with 2 copies of ε4: 60%	Healthy diet, exercise, and improved cardiovascular health	No specific treatment, supportive care
White: 100% for *GBA*; uncertain for *LRRK2*	1 copy of G2019S: 24%–91% 2 copies of N370S: 9.1% 1 copy of N370S: 5.9%	None	Dopaminergic therapy

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