PBL in Bioinformatics: Genetic epidemiology

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Case:

Your friend Sasha is adopted, and since her 25th birthday, she has become increasingly worried about her inherited disease risk. She has no contact with her birth family and is completely oblivious to her family history of disease. Sasha is especially worried about developing Alzheimer's disease, after watching her adopted grandmother suffer from dementia for the last five years. Sasha also wants to learn about how her genes influence her BMI.

Sasha approaches you, her expert friend in bioinformatics, and asks whether she should buy a 23andMe genetic testing kit ("Health + Ancestry Service"). She says that 23andMe will analyze her genetic data and return health predisposition reports for 10+ diseases (e.g., Alzheimer's disease) and 5+ wellness traits (e.g., BMI), as well as her risk of carrying rare genetic variants like mutations in the *BRCA1* and *BRCA2* breast/ovarian cancer genes. Sasha also sees on the 23andMe website that she can request her raw genetic information from the company, and she asks if you'll analyze it to provide even more answers about her inherited disease risk.

What do you advise Sasha to consider before pursuing direct-to-consumer (DTC) genetic testing? If she proceeds with testing, when she receives the 23andMe-generated reports, how will you help her put these into context? What will you do with her raw genome sequence results?

Learning objectives:

1. Develop intuition about the relative role of genes vs. "environment" in different human traits and diseases (i.e., **heritability**).
2. Compare **polygenic** traits to monogenetic/oligogenic/omnigenic traits. Give examples of traits that are more and less polygenic.
3. Describe **polygenic risk scores**, and interpret results of association tests between polygenic risk scores and other outcomes.
4. Identify **threats to validity** at all stages of assessing the relationship between a consumer's genetic material and their future risk of developing a trait or disease.
5. Describe **ethical, legal, and social implications** of direct-to-consumer genetic testing and other forms of genetic testing.

Guiding Discussion Questions	Learning Objectives
1. What is the relative contribution of genetic and non-genetic factors in different human traits and diseases?	1
2. How many genes contribute to the risk of Alzheimer's disease? BMI?	2
3. How are genetic variants used for risk prediction and how does this prediction vary depending on the underlying genetic architecture (i.e., monogenic vs. polygenic)?	3
4. What is Sasha's ethnicity and how does this affect genetic risk prediction?	4
5. What types of genetic variants are captured by the genotyping array used by 23andMe?	2, 4
6. If Sasha screens positive for a tested mutation in *BRCA1*, what should she do next?	4, 5
7. What are the properties of a good screening test? What components of 23andMe genetic testing fit those properties?	4, 5
8. What are some of the ethical, legal, social and social implications of direct-to-consumer genetic testing?	5