Hereditary Cancer and Hereditary High Cholesterol – Disorders Where Early Knowledge Can Make a Difference
Disclosures

• I am a paid employee of Color and have equity in Color.
• I am very passionate about increasing access to genetic testing/information.
Agenda

Genetic testing: a tool for prevention

Genetic testing in everyday practice

Research that illustrates importance of broad access to genetic testing
Heart disease and cancer are the leading causes of death.
In the US alone, cancer and heart disease cost >$1.1 trillion per year

Estimates of 2016 national expenditure by disease

Source: National Cancer Institute, Milken Institute, Department of Health & Human Services
US health expenditures are expected to continue to rise

More than any other country with similar life expectancy

Source: Department of Health and Human Services, NPR
“US healthcare spending is wildly uneven. About 5 percent of the population - those most frail and ill - accounts for nearly half the spending in a given year.”

PBS Newshour citing Department of Health and Human Services study
What if our higher-risk population could understand their risk earlier and manage it better?
Earlier detection improves survival rates and reduces treatment costs

Average 5-yr survival rate by stage

- Breast: 90%
- Colon: 95%
- Melanoma: 98%
- Ovarian: 85%

Estimated treatment cost by stage

- Breast (2 yrs): $250K, -54%
- Colon (1 yr): $125K, -50%
- Melanoma (annual): $50K, -89%
- Ovarian (5 yrs): $500K, -65%

Early stage cancers have much higher survival rates...

...and lower average treatment costs than advanced stage cases
Early detection of all 2017 new breast cancer cases would **save 22K lives** and reduce treatment costs by **$4.5B**

Prevention = more effective than any drug

Source: SEER cancer.gov, National Cancer Institute, American Health & Drug Benefits, Journal of the National Cancer Institute and Health Care Financing Review, JAMA Dermatology, Current Women's Health Reviews and Cancer Research UK
Genetic information is the key to prevention
Personalized medicine has used genetic testing for ~20 years

- Classic PGx (pharmacological genetics)
- Molecular Oncology
- Inherited Disease Testing
Inherited disease testing allows for personalized preventive health

- Genetic analysis
- Cancer-predisposing mutation identified
- Tailored risk management plan
- High survival rates, low treatment costs
However, >90% of people with genetic mutations are still not aware of their elevated risk
Scientific breakthroughs in gene sequencing are enabling access to vast amounts of genetic information.

Cost to sequence a human genome (USD)

- **$100 M**
- **$10 M**
- **$1 M**
- **$100 K**
- **$10 K**
- **$1 K**
- **$100**

- **Moore’s Law**
- **Illumina launched HiSeq X Ten Sequencing System**

Next generation sequencers entered the market.

Source: National Human Genome Institute
Translating this information to identify actionable disease risk requires board-certified genetic experts combined with software and data science.

“...the complexities of genetic data management clearly will require improved computerized clinical decision support tools, as opposed to continued reliance on traditional rote, memory-based medicine.”

Agenda

Genetic testing: a tool for prevention

Genetic testing in everyday practice

Research that illustrates importance of broad access to genetic testing
Providers can responsibly identify one’s risk for hereditary cancer and hereditary high cholesterol

Cancer Prevention

Tests for increased risk for 8 hereditary cancers

Heart Health

Beginning with testing for hereditary high cholesterol
10-15% of cancers in women and men are due to inherited genetic mutations

- **Hereditary cancer** is caused by an inherited genetic mutation. It is typical to see a recurring pattern of cancer across two to three generations—like multiple individuals diagnosed with the same type of cancer.

- **Familial cancer** refers to cancer that appears to occur more frequently in families than is expected from chance alone. While no specific mutation has been linked to these cancers, familial cancer may have a hereditary component that has not yet been identified.

- **Sporadic cancer** refers to cancer that occurs due to spontaneous mutations that accumulate over a person’s life. Sporadic cancer cannot be explained by a single cause. There are several factors, such as aging, lifestyle, or environmental exposure, that may contribute to the development of sporadic cancer.
Mutations may tremendously increase the risk of cancer
Genetic testing for hereditary cancer risk

BRCA1+
JAMA Oncology confirms genetic testing can be more cost-effective than a pap smear

**Cost-effectiveness of testing strategies in the US**

<table>
<thead>
<tr>
<th>Screening</th>
<th>Cost-effective ratio ($/QALY)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>$250 BRCA1/2</td>
<td>$50,000</td>
<td></td>
</tr>
<tr>
<td>Pap smear every 3 years</td>
<td>$75,000</td>
<td></td>
</tr>
<tr>
<td>Annual mammography</td>
<td>$100,000</td>
<td></td>
</tr>
</tbody>
</table>

Note: QALY = quality-adjusted life year. Source: JAMA Oncology, JAMA Internal Medicine
What is FH
(familial hypercholesterolemia)

A hereditary disorder that causes very high cholesterol levels from an early age

About 1 in 50 people with high cholesterol are born with Familial Hypercholesterolemia (FH)
What happens when you have FH?

- Your liver is unable to remove enough LDL (bad cholesterol) from your blood.

- This means your LDL level remains high, despite positive lifestyle choices.

- You are 22x more likely to develop coronary heart disease than are those with normal cholesterol and no FH.
Knowledge of inherited high cholesterol can also lead to improved compliance and reduced risk of heart disease.

- Genetic testing reveals FH+
- Known higher risk of heart disease
- Personalized risk management plan
- Greater compliance
- Meaningful benefits

**Familial Hypercholesterolemia (FH)**

- Risk of heart disease vs. general population:
  - No FH + High Cholesterol: 6x
  - FH + High Cholesterol: 22x

- Effective medication available for pennies a day:
  - No FH + High Cholesterol: <50%
  - FH + High Cholesterol: 93%

- Medication adherence after 1 year:
  - No FH + High Cholesterol: 80%
  - FH + High Cholesterol: 20-25%

Source: American Journal of Managed Care, Journal of Managed Care Pharmacy, Archives of Internal Medicine, Journal of the American College of Cardiology
Agenda

Genetic testing: a tool for prevention

Genetic testing in everyday practice

Research that illustrates importance of broad access to genetic testing
BRCA1 and BRCA2

- >90% of people with BRCA mutations are unaware they have a mutation
- In some populations as much as 50% of people with a BRCA1 or BRCA2 mutation do not have a significant personal or family history of cancer

Familial Hypercholesterolemia

- More than 90% of people with FH don’t know they have the disorder
- Most people (though not all) with FH have high cholesterol.

“There is no reason now that any woman with BRCA1 or BRCA2 should ever die of breast or ovarian cancer.” – Dr. Mary-Claire King
Population-level testing underway with medical and academic collaborations

WISDOM

Chosen as exclusive genetic testing platform for 100,000 women WISDOM trial

FLOSSIES

Helped develop and publish a 10,000 women database of germline genetic variation in older, healthy women

MAGENTA

Providing testing and genetic counseling services for this study focused on understanding the efficacy of genetic counseling
Hereditary cancer risk testing of 14,055 individuals with a multi-gene panel
Key Takeaways

• *BRCA1* and *BRCA2* accounted for 31.6% of pathogenic variants identified.
• An overall positive rate of 11.7% was identified.
• Genetic testing is likely to be more useful in individuals under the age of 40, when preventative care is more relevant.
• Taken together, these data reinforce the continued need to increase awareness and broaden access to genetic testing within the general population.
We analyzed 14,055 individuals to determine what proportion of mutations may have been identified in individuals who do not meet current NCCN criteria for test eligibility.
Positive Rate

- Met criteria: 16%
- Did not meet criteria: 12%
- Incomplete: 8%

Qualification of positives

- Met criteria: 68%
- Did not meet criteria: 17%
- Incomplete: 15%
Mutation spectrum of not qualified/incomplete

- BRCA1/2: 22%
- Lynch: 7%
- All Others: 71%
Key Takeaways

• 25% of those who took the Color Test for hereditary cancer did not meet NCCN guideline qualification.
• The positive rate for those who did not qualify was 8.1%.
• Of those who tested positive, 17% did not meet criteria.
• These data suggest that in order to increase mutation detection rate, the current gene-specific and multi-gene panel guidelines may need to be revisited and broadened.
• Testing may be considered in individuals who do not strictly meet current criteria depending on their priorities.
Questions?

lily@color.com

(and we are right outside the door today)