CIBC 2019

Chicago International Breast Course
The Westin Chicago River North
November 1-3, 2019

Breast Cancer Genetic Screening

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Disclosure

- No real or apparent relationships to report.

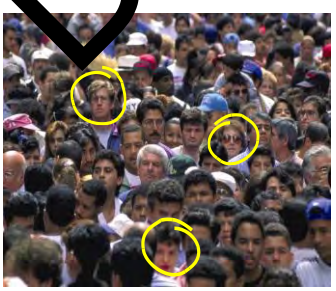
Personalized Medicine … *the why*

- Better risk assessment
- Better screening strategies
- Better and more targeted treatment
- Better care and outcomes for patients

Health and disease risk

- Environmental
- Lifestyle choices
- Genetic factors
- Other "omics"

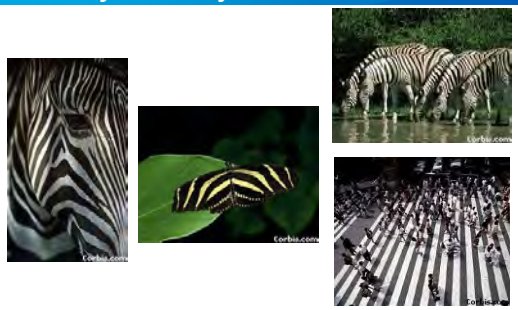
Who Is at High Risk?



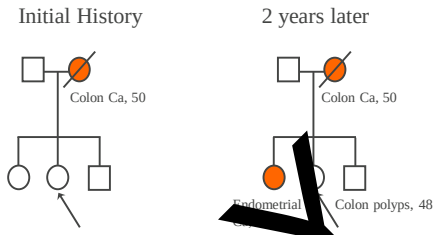
"Traditional" Personalized Medicine: Hereditary Cancer

- Cancer in 2 or more close relatives (on same side of family)
- Early age at diagnosis
- Multiple primary tumors
- Bilateral or multiple rare cancers
- Pattern of cancers suggestive of a specific cancer syndrome
- Evidence of autosomal dominant transmission

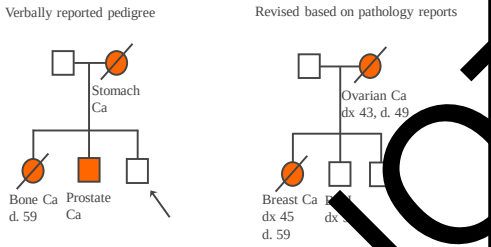
Recognition of Hereditary Cancer Syndromes



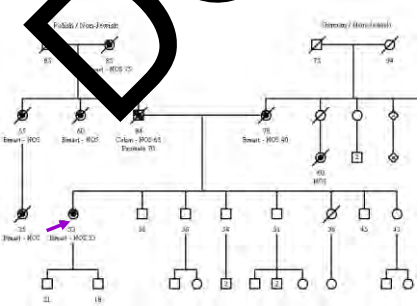
Family Cancer Histories Are Dynamic



Verify Family History



Information Gathering – Not always as easy as it seems

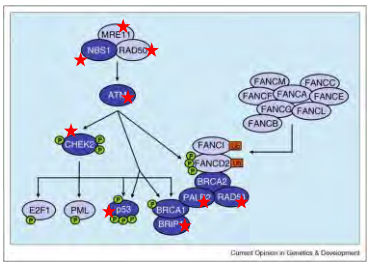


BRCA2 886delGT mutation

What if BRCA testing in a family with significant breast/ovarian cancer history is negative?

- Many genes linked to breast cancer risk
- How to go "beyond" BRCA1/2?

DNA Repair Pathway



Shift in Cancer Genetic Testing

- From single gene testing …
  - e.g. BRCA1/2 then consider other individual genes based on pattern of cancers
- To panel approach
  - Assess many genes linked to specific cancer risk, including BRCA1/2, at same time
- Bridge to whole exome and genome analysis
  - Polygenic Risk Scores

Background … *the why*

- 2001 "Completion"
- Lots of promise, hype
- Reality
  - Starting blueprint
  - Costs high
  - GINA not enacted
  - *What is normal?*

The time is right … *the why*

GINA

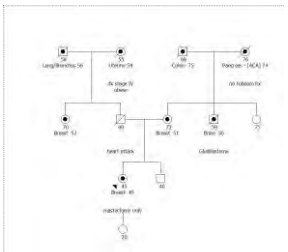
- The Genetic Information Nondiscrimination Act of 2008 (GINA) is a federal law that protects individuals from genetic discrimination in health insurance and employment
  - Separate from Affordable Care Act
  - http://ginahelp.org/

Single Gene Approach

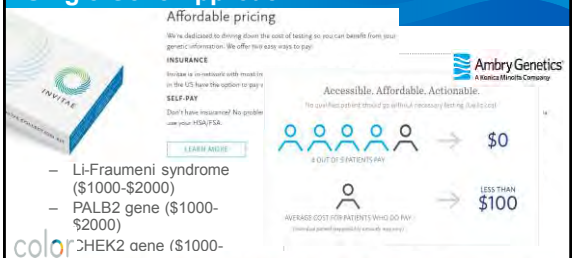
Historically

BRCA testing - $4000

- Costs coming down with competition
- Risk on both sides of the family
- If results are normal …



Single Gene Approach



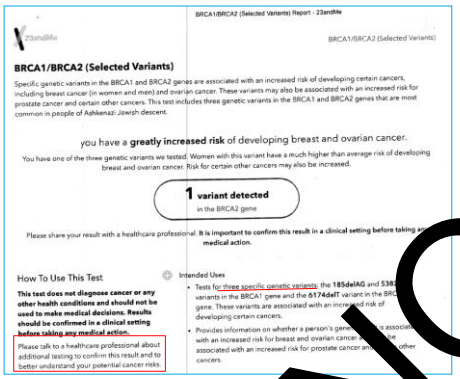
- Li-Fraumeni syndrome ($1000-$2000)
- PALB2 gene ($1000-$2000)
- CHEK2 gene ($1000-

Hereditary Cancer Test: $249 self-pay or insurance accepted

Color's Provider Platform makes ordering testing easy and fast. Save time and place your order online or request your patient to purchase while at home. Alternatively, collect the patient's sample in the office using a Color kit. You can choose if results are released at the same to your patient, or after a delay. Your patient will provide their personal and family history on our HIPAA-compliant website.

23andMe … Did You Know?

- BRCA1/BRCA2 (Selected Variants)
  - BRCA1 185delAG and 5382insC variants
  - BRCA2 6174delT variant
  - Ashkenazi Jewish Founder Mutations



Demystifying the Genetics Reports: Core Elements

What should I focus on?

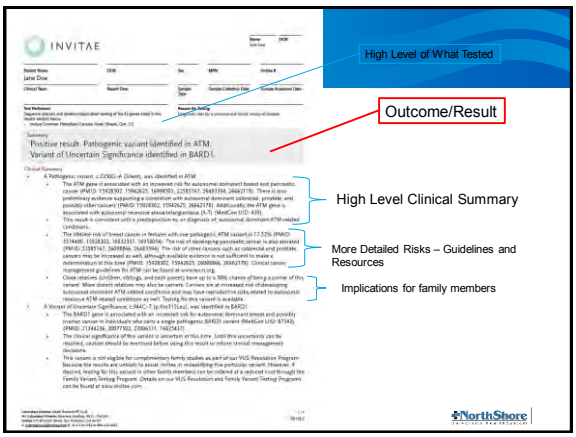
1. Outcome - Result
2. Interpretation
   - Clinical
     - Patient and Family
   - Scientific

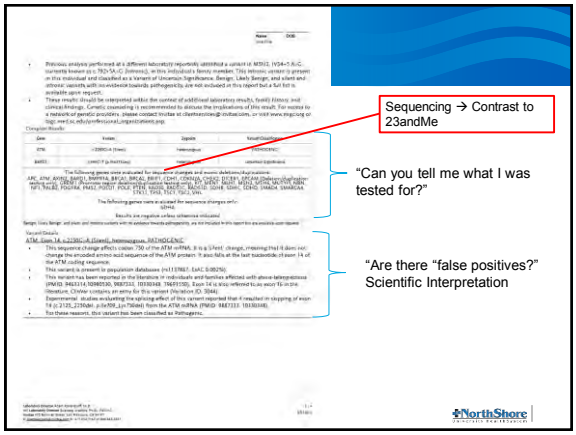
There's an over abundance of information!

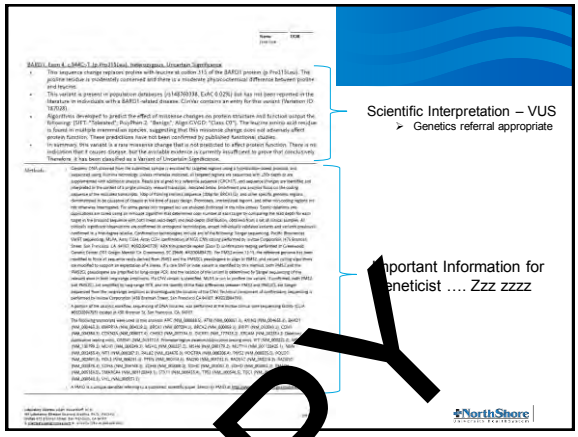
Demystifying the Genetics Reports

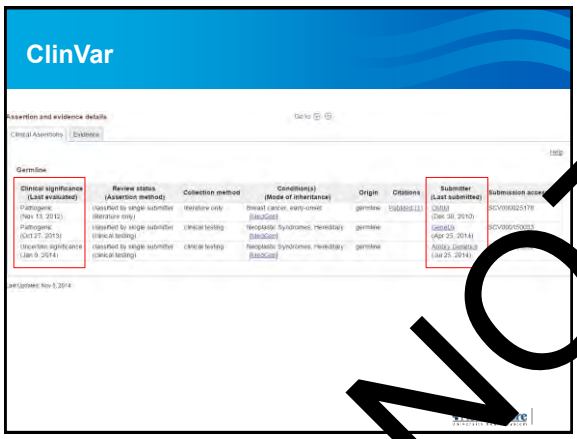
Outcome - Result of genetic testing

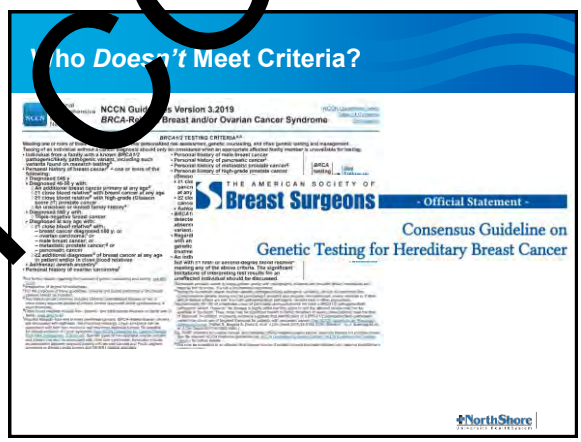
- Pathogenic / Likely Pathogenic variant (mutation) → "Positive"
- Benign or Likely Benign variant → "Negative"
  - Many labs do not report out LB/B variants
  - Family history may still be significant
- Variant of Uncertain Significance
  - "Don't Panic" → Majority end up being reclassified as benign
  - Center for Medical Genetics available
- Get the correct mindset for the information …

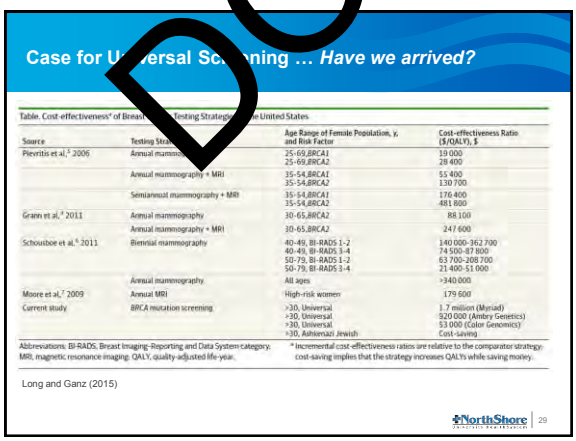


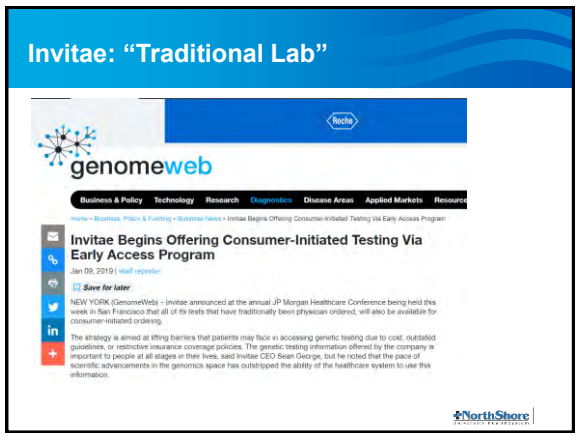




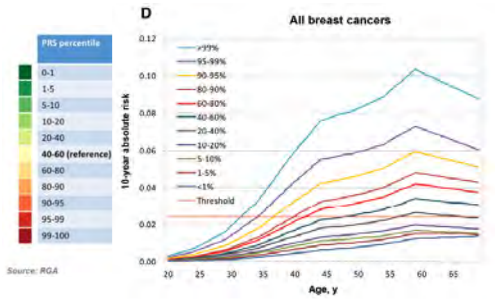








Polygenic Risk Scores … *What's Next?*



JNCI J Natl Cancer Inst (2015) 107(5)

Family History Remains Important

Table 1. Various risk assessment models and the factors considered in assessing the risk of breast cancer.

Gail model	Claus model	BRCAPRO model	Tyrer–Cuzick model	BOADICEA model
• Age of the person • Age at menarche • Age at first live birth • Breast biopsies (AH) • Family history – First-degree relatives	• Age of the person • Age at menarche • Age at first live birth • Family history – First-degree relatives – Second-degree relatives	• Age of the person • Family history – First-degree relatives – Second-degree relatives – Third-degree relatives – Age at onset of breast cancer – Bilateral breast cancer – Ovarian cancer – Male breast cancer	• Age of the person • Body mass index • Age at menarche • Age at first live birth • Age at menopause • Hormone replacement therapy use • Breast biopsies (ADH, LCIS) • Family history – First-degree relatives – Second-degree relatives – Age at onset of breast cancer – Bilateral breast cancer – Ovarian cancer – Male breast cancer	• Age of the person • Family history – First-degree relatives – Second-degree relatives – Third-degree relatives – Age at onset of breast cancer – Bilateral breast cancer – Ovarian cancer – Male breast cancer

AH, atypical hyperplasia; LCIS, lobular carcinoma in [illegible]; BRCA, breast and ovarian [illegible] of disease incidence and carrier estimation algorithm.

DOI: 10.3332/ecancer.2013.363

Take home points

- Cost of testing continues to decrease
- Criteria for genetic testing continues to expand
- Emergence of polygenetic risk scores potential to change landscape of risk assessment
- Family history remains important tool

Thank yo…

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