Barriers to Cascade Testing: Impact of a no-additional cost family genetic testing program on uptake of hereditary cancer risk assessment

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Disclosure statement

- I am an employee and stockholder of Invitae
Background

- Precision primary disease prevention - Cascade family variant testing (FVT)

- Cascade testing - designated by the Centers for Disease Control and Prevention as Tier 1 genomic application for HBOC and Lynch syndrome and is clinically indicated per multiple professional guidelines for family members of probands with a known variant (NCCN, JACC)

- Uptake of cascade FVT - varies between 10-30% (reference)

- Missed opportunity for preventive clinical screening and intervention
Background

- Proposed barriers to cascade FVT
  - Cost
  - Logistics
  - Awareness and understanding of hereditary disease
  - Shortage of genetics professionals
  - Long wait lists for appointments
  - Geography
  - Variable insurance coverage for GC
  - PCPs unfamiliar with ordering/acting on cascade FVT results
  - Family dynamics and communication barriers
  - Limit options for patients to initiate the cascade FVT process with their clinicians
Methods

- Policy – no-additional cost cascade FVT testing
  - Proband positive for family variant
  - All first degree blood relatives (c/w current guidelines)
  - Targeted FVT
  - Post-test genetic counseling available (no-additional charge)
  - 90 day limitation (motivator, good to identify earlier than later for prevention, need a better answer...)

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Methods

- Policy implemented July 2017
- Retrospectively analyzed de-identified cascade FVT case data for 6 months pre-policy and 12 months post policy
Results

- Overall change in cascade FVT uptake post-policy vs pre-policy
Probands with at least one relative being tested

All

Hereditary Cancer
Proband with multiple relatives tested

Hereditary Cancer

# of family members in FVT families

- >1 year
- <1 year
- <6 month
- <90 days

All

# of family members in FVT families

- >1 year
- <1 year
- <6 month
- <90 days

2017 Jan
2017 July
2017 July
2018 May

>1 year
<1 year
<6 month
<90 days

2017 Jan
2017 July
2017 July
2018 May

>1 year
<1 year
<6 month
<90 days
Cascade FVT uptake by cancer gene
## Clinical impact of cascade FVT

### Management guidelines for cascade FVT genes

<table>
<thead>
<tr>
<th>Gene</th>
<th>Cancer risk</th>
<th>Management recommendations¹,²,³,⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATM</td>
<td>Breast cancer</td>
<td>Annual mammogram and consider breast MRI starting at 40 years</td>
</tr>
<tr>
<td>BRCA2</td>
<td>Breast, ovarian and prostate cancer</td>
<td>Breast screening, RRM, RRSO</td>
</tr>
<tr>
<td>CHEK2</td>
<td>Breast and colon cancer</td>
<td>Annual mammogram and consider breast MRI starting at 40 years old</td>
</tr>
<tr>
<td>FH</td>
<td>Renal cell cancer</td>
<td>Annual abdominal MRI</td>
</tr>
<tr>
<td>MITF</td>
<td>Melanoma, Renal cell cancer</td>
<td>Monthly skin exams, renal ultrasound</td>
</tr>
<tr>
<td>MUTYH (het)</td>
<td>Colon cancer (moderate at most)</td>
<td>Colonoscopy at 40 years old for unaffected proband with colon cancer in 1st degree relative</td>
</tr>
<tr>
<td>NBN</td>
<td>Breast cancer</td>
<td>Annual mammogram and consider breast MRI starting at 40 years old</td>
</tr>
<tr>
<td>PALB2</td>
<td>Breast cancer</td>
<td>Annual mammogram and consider breast MRI starting at 30 years old</td>
</tr>
<tr>
<td>PMS2</td>
<td>Colon and ovarian cancer</td>
<td>Colonoscopy every 1-2 years starting at 20-25 years of age</td>
</tr>
</tbody>
</table>

RRM – risk reducing mastectomy; RRSO – risk reducing salpingo-oophorectomy; het – heterozygote.

¹Daly et al. Genetic/Familial High-Risk Assessment: Breast and Ovarian, 1.2018, nccn.org
²Provenzale et al. Genetic/Familial High-Risk Assessment: Colorectal, 3.2017, nccn.org
Future directions

- Barriers to cascade FVT
  - Cost
  - Logistics
  - Awareness and understanding of hereditary disease
  - Shortage of genetics professionals
  - Long wait lists for appointments
  - Variable insurance coverage for GC
  - PCPs unfamiliar with ordering/acting on cascade FVT results
  - Family dynamics and communication barriers
  - Limit options for patients to initiate the cascade FVT process with their clinicians

- Which is the next biggest barrier? How do we address it?
Conclusions

- Uptake of cascade FVT testing is significantly increased when the barrier of cost is removed
  - Breadth of families receiving cascade FVT
  - Depth of cascade FVT within individual families
- Genes for which cascade FVT are ordered have established management guidelines and implications for disease prevention in tested family members
- Substantial progress remains to be made in reaching all family members who are eligible for cascade FVT
- Additional research is needed to identify solutions for the remaining barriers to full implementation of FVT and its commensurate potential for precision preventive medicine
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