Familial, Hereditary, and Early Age Onset Colorectal Cancer: A Module Designed to Assist Primary Care Clinician’s in the Identification of Individuals at Increased Risk and Facilitate Earliest Possible Stage Diagnosis.

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CRC Under Age 50

- While CRC rates are falling steadily in those over age 50, diagnosis before age 50 is increasing
- Risk of CRC decreased sequentially for birth cohorts from 1890 to 1950, but has increased for every generation born since 1950
- In addition to those under age 50, risk is also rising in the 50-54 year old cohort
CRC Under Age 50

Siegel et al, CA 2017
CRC Trends Under Age 50

- Age-specific risk of colon cancer for someone born in 1990 is double that of someone born in 1950.
- For rectal cancer, the risk has quadrupled.

Siegel et al, JNCI 2017
CRC Under Age 50

Cause(s) of this trend not known. Potential contributors –

- Rising rates of:
  - Obesity
  - Sedentary lifestyle
  - Type II diabetes
  - Antibiotic use (humans and livestock)
  - Hormone use in livestock

- Decreased use of aspirin in the young (Reye’s)

- Unidentified environmental risk factors (pesticides, …)
Although rates are rising, the under 50 population still represents an overall small proportion (11%) of all CRC cases.

Rising rate in those age 50-54 reinforces the need to start screening promptly at age 50 (this group has much lower screening rates than older age groups).

Imperative to recognize those needing screening before age 50 due to family history or other risk factors.
CRC Under Age 50

Need increased awareness among clinicians and young adults of symptoms and the need to take action to facilitate earlier detection

- Rectal bleeding
- Abdominal pain
- Change in bowel habits
- Weight loss

*Remember: Guidelines are for screening only! Not relevant for symptomatic patients – regardless of age*
Who is at high risk for cancer?

Family History is the key…
Family History

An important **first step** in risk assessment for genetic diseases and other hereditary health conditions

Americans know that family history is important to health. A recent survey found that 96 percent of Americans believe that knowing their family history is important. Yet, the same survey found that only one-third of Americans have ever tried to gather and write down their family's health history.
Most cancers are **not** inherited

- **10-15% familial**
- **5-10% hereditary**
- **75-85% sporadic**
1st-, 2nd-, and 3rd-Degree Relatives

- Paternal grandfather
- Paternal grandmother
- Aunt
- Father
- Mother
- Sister
- Child
- Brother
- Maternal grandfather
- Maternal grandmother
- Uncle
- First cousin
High Risk Families

- Strong family history of cancer
- Need referral for genetic counseling & consideration of genetic testing
- Need intensive cancer surveillance
  - Depends on the syndrome but often includes colonoscopy every 1-2 years starting in the teens-20s
- The first degree relatives of a person with a hereditary cancer predisposition syndrome have a 50% chance that they have inherited it
- Cancer risks vary but range from 20-100%
High Risk Clues:
- Cancer in 2 or more close relatives (on same side of family)
- Multiple generations affected
- Early age at diagnosis
- Rare cancers (sebaceous skin cancer)
- Multiple primary tumors (colon and uterus; more than one colon cancer)
- Multiple colon polyps (>10)
- Patients with certain pathology findings
  - Abnormal IHC or MSI+ testing
Lynch syndrome family
Moderate Risk Families

- 1-2 cases of a cancer in the family
- Do not need referral for genetic counseling
- Do need increased cancer surveillance
- Generally the first degree relatives of a person with a cancer are about twice as likely to develop that same cancer than someone without that family history (10% lifetime risk)
Familial Colorectal Cancer Risks

**Table 1.** Selected Familial Relative Risk (FRR) Estimates for Proband Considering Only First-Degree Relative (FDR) Family History

<table>
<thead>
<tr>
<th>No. of affected FDRs</th>
<th>No. of probands</th>
<th>FRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2,232,396</td>
<td>0.89 (0.87-0.91)</td>
</tr>
<tr>
<td>1</td>
<td>87,089</td>
<td>1.91 (1.82-2.00)</td>
</tr>
<tr>
<td>≥1</td>
<td>94,931</td>
<td>2.05 (1.96-2.14)</td>
</tr>
<tr>
<td>2</td>
<td>6966</td>
<td>3.01 (2.66-3.38)</td>
</tr>
<tr>
<td>3</td>
<td>762</td>
<td>4.43 (3.24-5.90)</td>
</tr>
<tr>
<td>4</td>
<td>92</td>
<td>7.74 (3.71-14.24)</td>
</tr>
<tr>
<td>≥5</td>
<td>22</td>
<td>19.86 (7.29-43.24)</td>
</tr>
</tbody>
</table>

**Table 2.** Familial Relative Risk (FRR) Estimates for Proband With 0 or 1 Affected First-Degree Relatives (FDRs) and Increasing Numbers of Affected Second-Degree Relatives (SDRs)

<table>
<thead>
<tr>
<th>No. of affected FDRs</th>
<th>No. of affected SDRs</th>
<th>No. of probands</th>
<th>FRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>1,965,853</td>
<td>0.86 (0.84-0.88)</td>
</tr>
<tr>
<td>0</td>
<td>1</td>
<td>224,609</td>
<td>1.05 (0.99-1.11)</td>
</tr>
<tr>
<td>0</td>
<td>2</td>
<td>33,407</td>
<td>1.20 (1.05-1.38)</td>
</tr>
<tr>
<td>0</td>
<td>≥3</td>
<td>8527</td>
<td>1.48 (1.11-1.93)</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>65,192</td>
<td>1.82 (1.72-1.93)</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>16,760</td>
<td>2.12 (1.90-2.35)</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>3776</td>
<td>2.31 (1.80-2.93)</td>
</tr>
<tr>
<td>≥3</td>
<td></td>
<td>1361</td>
<td>3.37 (2.20-4.93)</td>
</tr>
</tbody>
</table>

**Table 4.** Selected Familial Relative Risks (FRRs) for Proband With Affected First-Degree Relatives (FDRs) or Second-Degree Relatives (SDRs) Diagnosed at Certain Ages

<table>
<thead>
<tr>
<th>Proband</th>
<th>No. of probands</th>
<th>FRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 affected FDR diagnosed &lt;50 y of age</td>
<td>6291</td>
<td>3.31 (2.79-3.89)</td>
</tr>
<tr>
<td>≥1 affected FDR diagnosed between 50 and 59 y of age</td>
<td>12,094</td>
<td>2.53 (2.24-2.85)</td>
</tr>
<tr>
<td>≥1 affected FDR diagnosed ≥50 y of age</td>
<td>89,340</td>
<td>2.02 (1.93-2.11)</td>
</tr>
<tr>
<td>≥1 affected FDR diagnosed between 60 and 69 y of age</td>
<td>25,084</td>
<td>2.22 (2.04-2.40)</td>
</tr>
<tr>
<td>≥1 affected FDR diagnosed ≥60 y of age</td>
<td>78,629</td>
<td>1.99 (1.90-2.09)</td>
</tr>
<tr>
<td>≥1 affected FDR diagnosed between 70 and 79 y of age</td>
<td>32,445</td>
<td>1.97 (1.83-2.12)</td>
</tr>
<tr>
<td>≥1 affected FDR diagnosed ≥70 y of age</td>
<td>56,065</td>
<td>1.97 (1.86-2.08)</td>
</tr>
<tr>
<td>≥1 affected SDR diagnosed &lt;50 y of age</td>
<td>19,616</td>
<td>1.84 (1.61-2.09)</td>
</tr>
</tbody>
</table>

Familial Colorectal Cancer Screening Recommendations

- ≥1 FDR dx at any age
  - Colonoscopy every 5-10 years beginning at age 40 (or 10 years before earliest dx of CRC)
- ≥1 SDR diagnosed <50
  - Colonoscopy every 5-10 years beginning at age 50
- FDR with advanced adenoma(s)
  - Colonoscopy every 5-10 years beginning at age 40 or age of onset of adenoma in relative
- Otherwise follow Average Risk recommendations
  - Colonoscopy every 10 years beginning at age 50
NCCRT Family History & Early-onset CRC Module

- Call for proposals in Spring of 2017 to develop a module for primary care physicians on best practices in colorectal cancer risk assessment, screening and early detection for early-onset, familial, and hereditary cancers
- Awarded to The Jackson Laboratory
- Emily Edelman and Therese Ingram will be updating us on their progress on The Family History & Early-Onset Colorectal Cancer Toolkit