Trends in Colorectal Cancer Incidence Among Younger Adults-Disparities by Subsite, Age, Sex, Race, Ethnicity, and Stage

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Millennials (ages 18-35) are now the largest living generation in the US\textsuperscript{1}, making it important to understand and characterize the rising trend of colorectal cancer (CRC) incidence in this population, as well as other younger generations of Americans.
What do you know about the health and lifestyle habits of those under 50?

• We know they drink more,\textsuperscript{21-23} and they engage in riskier sexual behaviors\textsuperscript{24,25} than earlier generations

• HPV is associated with cancers in other organs,\textsuperscript{26} and we know that alcohol has a greater impact on the rectal subsite\textsuperscript{27}

• Recent birth cohorts in the US show that younger generations are reaching a higher prevalence of obesity earlier in life, resulting in a greater duration and degree of obesity in their lifetime\textsuperscript{28}
Recent studies indicate CRC has been rising in younger adults who are under the recommended screening age of 50.\(^2-8\)

The American Cancer Society (ACS) made new recommendations that adults aged 45 years and older with an average risk of CRC should undergo regular screening.

In New Jersey (NJ), an average of 435 younger adults (approximately 10% of all CRC cases) are diagnosed each year.\(^9\)
• Right and left sided colon cancers have markedly different underlying biological characteristics, and are distinct from rectal cancers.

• This has important implications for disease severity, choice of therapies and prognosis, which makes it very important to understand who is most at risk for CRC in younger adulthood in today’s population.
We set out to characterize the at risk population of younger adults for CRC in NJ and compared NJ to the US to better inform cancer control and prevention efforts in a population that would not otherwise be considered for interventions.
Methods

CRC sites were based on primary site and histology coded to the International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3)\textsuperscript{13}

CRC sites included C18.0, 18.2-20.9, and C26.0; diagnosis of appendix (C18.1) was excluded. ICD-O-3 Histological types 9590-9989, 9050-9055 and 9140 were also excluded

Cases with unknown age or county of residence were excluded, as were cases reported only through autopsy reports or death certificates
Methods

We explored 2 times frames: 1979-2014 and 1992-2014

- SEER 13 registries reported on expanded race/ethnicity starting in 1992, which allowed us to include Hispanic and Asian or Pacific Islanders (APIs) in our race/ethnicity subanalyses which compared NJ to the US

- We kept the longer time trends to offer the full picture over a longer time span for greater power, and to demonstrate where it is most likely the changes occurred
CRC subsites were defined as:

- **proximal** includes the cecum, ascending colon, hepatic flexure, and transverse colon (C18.0, C18.2-18.4)

- **distal** includes the splenic flexure, descending and sigmoid colon (C18.5-C18.7)

- **rectal** which includes the rectosigmoid junction and rectum (C19.9, C20.9)

Large intestine, NOS (C18.8-18.9, 26.0) were excluded from the subsite specific analyses. Appendix excluded.
1979-2014

- A total of 181,909 invasive CRC cases in NJ ages 20 and older were included in the analyses, after excluding 5,364 (2.9%) cases ascertained only from death certificate and autopsy reports
  - 12,080 (6.6%) were 20-49 and 169,829 (93.4%) were 50 and older

- Compared to SEER 9 population-based cancer registries (Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle-Puget Sound, San Francisco- Oakland, Utah)\(^\text{14}\) by age group (20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80+) and sex (male, female)

- Younger adults were further examined by subsite (proximal, distal, rectal), age group (20-39, 20-49, 40-49), sex and race (black, white)
1992-2014

• 113,501 invasive CRC cases were included in the analyses
  o **8,588 (7.6%)** were 20-49 and **104,913 (92.4%)** were 50 and older

• Compared to SEER 13 (SEER 9 plus San Jose-Monterey, Los Angeles, Alaska Native Registry, rural Georgia)\textsuperscript{15} by **sex, race** (black, white, Asian or Pacific Islander [API], **ethnicity** (Hispanic, Not Hispanic)

• Younger NJ adults (20-49) were compared to older NJ adults (50+) by **sex, race, ethnicity, cancer subsite** (colon, proximal, distal, rectal), and **stage** (in situ/local [early], regional/distant [late])

- The stage analyses included 123,420 cases (both in situ and invasive CRC)
  - 9,217 (7.5%) were 20-49, and 114,203 (92.5%) were 50 and older
• Rates were age-adjusted to the 2000 US population standard
• 95% Confidence Intervals (CIs)
• Annual Percent Changes (APCs)
• Pearson’s chi-square
• Statistical significance for all analyses was set at p<0.05
• SEER*Stat software (version 8.3.4, NCI)\textsuperscript{16}
• JoinPoint Regression Program (version 4.4.0.0, NCI)\textsuperscript{17,18}
• SAS version 9.4\textsuperscript{19}
Results
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Age Group, Years</th>
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<th>p-value</th>
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<tbody>
<tr>
<td></td>
<td>Ages 20-49</td>
<td>Ages ≥50</td>
<td></td>
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<tr>
<td>Sex</td>
<td>N=8,588 (100%)</td>
<td>N=104,913 (100%)</td>
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<tr>
<td></td>
<td>Female</td>
<td>4,010 (46.7%)</td>
<td>52,721 (50.3%)</td>
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<tr>
<td></td>
<td>Male</td>
<td>4,578 (53.3%)</td>
<td>52,192 (49.7%)</td>
<td>p&lt;.0001</td>
</tr>
<tr>
<td>Race</td>
<td></td>
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<tr>
<td>White</td>
<td>6,542 (76.2%)</td>
<td>91,251 (87.0%)</td>
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<tr>
<td>Black</td>
<td>1,444 (16.8%)</td>
<td>10,912 (10.4%)</td>
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<tr>
<td>API</td>
<td>477 (5.6%)</td>
<td>2,263 (2.2%)</td>
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<tr>
<td>Other</td>
<td>125 (1.5%)</td>
<td>487 (0.5%)</td>
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<tr>
<td>Ethnicity</td>
<td></td>
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<tr>
<td>Hispanic (of any race)</td>
<td>1,125 (13.1%)</td>
<td>6,279 (6.0%)</td>
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<td>p&lt;.0001</td>
</tr>
<tr>
<td>Not Hispanic (of any race)</td>
<td>7,463 (86.9%)</td>
<td>98,634 (94.0%)</td>
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<tr>
<td>Cancer Subsite</td>
<td></td>
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<tr>
<td>Colon</td>
<td>5,192 (60.5%)</td>
<td>75,882 (72.3%)</td>
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<tr>
<td>Proximal</td>
<td>2,286 (44.0%)</td>
<td>41,606 (54.8%)</td>
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<tr>
<td>Distal</td>
<td>2,499 (48.1%)</td>
<td>28,161 (37.1%)</td>
<td></td>
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</tr>
<tr>
<td>Other</td>
<td>407 (7.8%)</td>
<td>6,115 (8.1%)</td>
<td></td>
<td>p&lt;.0001</td>
</tr>
<tr>
<td>Rectal</td>
<td>3,396 (39.5%)</td>
<td>29,031 (27.7%)</td>
<td></td>
<td>p&lt;.0001</td>
</tr>
<tr>
<td>Stage*</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1992-2014</td>
<td>n=9,217</td>
<td>n=114,203</td>
<td></td>
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</tr>
<tr>
<td>Early</td>
<td>3,278 (35.6%)</td>
<td>46,639 (40.8%)</td>
<td></td>
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<tr>
<td>Late</td>
<td>5,320 (57.7%)</td>
<td>57,905 (50.7%)</td>
<td></td>
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</tr>
<tr>
<td>Unstaged</td>
<td>619 (6.7%)</td>
<td>9,659 (8.5%)</td>
<td></td>
<td>p&lt;.0001</td>
</tr>
</tbody>
</table>

*Includes in situ. **Early stage is defined as in situ and local stages.***Late stage includes regional and distant stages.

Note: Percentages do not always add up to 100% due to rounding.
Figure 1: Annual Percent Change (APC) in Younger Adult (20-49 years) Colorectal Cancer Incidence Rates by Race/Ethnicity and Year, 1992-2014. (a) NJ Males (b) NJ Females (c) US Males (d) US Females.

Abbreviations: API, Asian or Pacific Islander. Persons of Hispanic ethnicity may be of any race or combination of races. The categories of race and ethnicity are not mutually exclusive. Rates are per 100,000 and age-adjusted to the 2000 US Standard Population (19 age groups - Census P25-1130). An asterisk denotes that the APC is statistically significant (p < 0.05).
Figure 2: Annual Percent Change (APC) in Younger Adult (20-49 Years) Invasive Colorectal Cancer Incidence Rates by Subsite, Age Group, Sex, Race and Year in NJ, 1979-2014. The scale of the y-axis varies to depict the trends.

(a) Proximal by Age Group
(b) Distal by Age Group
(c) Rectal by Age Group
(d) Proximal by Sex
(e) Distal by Sex
(f) Rectal by Sex
(g) Proximal by Race
(h) Distal by Race
(i) Rectal by Race

Rates are age-adjusted to the 2000 US Standard Population (10 age groups - Census P2S-1130). An asterisk denotes that the APC is statistically significant (p < 0.05).
<table>
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</thead>
<tbody>
<tr>
<td>All Histologies (8000-9992)</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Adenocarcinoma (8050, 8140-8147, 8160-8162, 8180-8221, 8250-8507, 8520-8551, 8560, 8570-8574, 8576, 8940-8941)</td>
<td>90.4%</td>
<td>91.5%</td>
<td>89.5%</td>
<td>88.6%</td>
<td>89.8%</td>
</tr>
<tr>
<td>Adenocarcinoma, NOS (8140)</td>
<td>66.7%</td>
<td>70.4%</td>
<td>66.4%</td>
<td>62.0%</td>
<td>61.9%</td>
</tr>
<tr>
<td>Adenocarcinoma in adenomatous polyp (8210)</td>
<td>2.7%</td>
<td>2.5%</td>
<td>3.7%</td>
<td>5.8%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Adenocarcinoma in villous adenoma (8261)</td>
<td>3.4%</td>
<td>2.0%</td>
<td>1.8%</td>
<td>1.6%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Mucinous adenocarcinoma (8470-8473, 8480, 8482)</td>
<td>4.9%</td>
<td>6.1%</td>
<td>7.2%</td>
<td>6.9%</td>
<td>6.0%</td>
</tr>
<tr>
<td>Mucin-producing adenocarcinoma (8481)</td>
<td>5.5%</td>
<td>4.4%</td>
<td>3.3%</td>
<td>2.3%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Signet ring adenocarcinoma (8490)</td>
<td>2.4%</td>
<td>1.9%</td>
<td>1.6%</td>
<td>1.8%</td>
<td>1.8%</td>
</tr>
<tr>
<td>Other adenocarcinomas (8050, 8141-8147, 8160-8162, 8180-8204, 8211-8221, 8250-8260, 8262-8264, 8270-8463, 8500-8507, 8514, 8520-8551, 8560, 8570-8574, 8576, 8940-8941)</td>
<td>4.8%</td>
<td>4.1%</td>
<td>5.6%</td>
<td>8.2%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Other specific carcinomas (8012-8015, 8030-8046, 8150-8155, 8170-8175, 8230-8249, 8508, 8510-8513, 8561-8562, 8575, 8580-8671)</td>
<td>2.8%</td>
<td>3.1%</td>
<td>7.3%</td>
<td>8.4%</td>
<td>8.5%</td>
</tr>
<tr>
<td>Neuroendocrine carcinoid (8240-8245)</td>
<td>2.7%</td>
<td>2.8%</td>
<td>6.5%</td>
<td>7.0%</td>
<td>7.1%</td>
</tr>
</tbody>
</table>
### What do we know about NJ’s population?

#### Mean age and percent of the population by Race/Ethnicity in NJ and the US, 2015

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>NJ</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Percent</td>
<td>Mean Age</td>
</tr>
<tr>
<td>White</td>
<td>68.3%</td>
<td>42.7</td>
</tr>
<tr>
<td>Black</td>
<td>13.5%</td>
<td>35.3</td>
</tr>
<tr>
<td>Asian</td>
<td>9.0%</td>
<td>36.2</td>
</tr>
<tr>
<td>Hispanic (of any race)</td>
<td>19.0%</td>
<td>31.4</td>
</tr>
</tbody>
</table>
• **Foreign born:** NJ 22% vs. US 13%

• **NJ Asians:** 41% self-identify as Asian Indian vs. US 20%

• **NJ Hispanics:** Puerto Rican 28% vs. US 9%
  South American 21% vs. US 6%
  Dominican 13% vs. US 3%

• **Few NJ Hispanics identify as Mexican,** 14.0% vs. US 63.0%
**Strengths and Limitations:**

- High rates of microscopic confirmation of cases
- Population-based cancer registry, thus eliminating sampling biases
- High quality data

- One study limitation, common to time trend analyses using cancer registry data, is that the most recent few years of data may be incomplete due to reporting delays. This may result in underestimates of incidence rates and underestimates of APCs, which appear to level off from 2012 to 2014

- We may have lacked the power to detect significant changes in rates over time in some of our subgroup analyses due to small numbers

- There is potential for anal cancers to be misclassified as rectal SSC. However, rectal SSC comprises less than 0.5% of the NJ CRC data in younger adults, making the effects of any misclassification minimal
Conclusions

- Rising trends in CRC incidence among NJ men and women less than 50 years old
  - Rising trends most notable for rectal cancers
  - Among men
  - Ages 20-39
  - Whites
Next Steps

• Large, case-level, studies are needed to understand the role of genetics, human papillomavirus (HPV), and cultural and behavioral factors in the rise of CRC among younger adults

• Careful studies of the risks and benefits of lowering the current screening age, perhaps specifically for low-cost, low-risk methods such as fecal immunochemical test kits or fecal DNA tests, should also be considered

• Surveillance among survivors will then be key to understanding prevention and/or early detection of subsequent primaries

• Public and clinician awareness could promote early stage diagnoses in symptomatic younger adults
Average Annual Age-Adjusted Incidence Rate of Invasive Colorectal Cancer (CRC) in New Jersey (NJ) Residents Ages 20-49 By County, 1992-2014
Thank you!

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