

Colorectal Cancer Disparity

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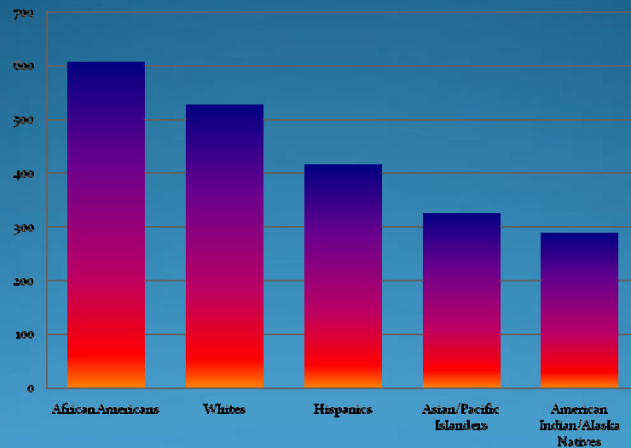


- “Despite notable progress in the overall health of the Nation.....
 - there are continuing disparities in the burden of illness and death experienced by
 - African Americans, Hispanics or Latinos, American Indians and Alaska Natives, and Native Hawaiian and Other Pacific Islanders, compared to the U.S. population as a whole.”
 - “The demographic changes anticipated over the next decade magnify the importance of addressing disparities in health status.”

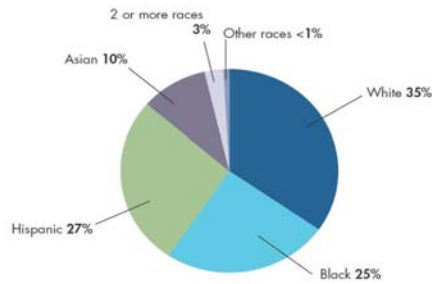
Objectives

1. Review US epidemiologic information on ethnic disparities in cancer, especially colorectal cancer (CRC)
2. NYC & South Bronx health status related to CRC
3. The Lincoln Hospital experience
4. Carcinogenesis and tumor host interactions

Cancer Incidence per 100,000 population



New York City is racially and ethnically diverse



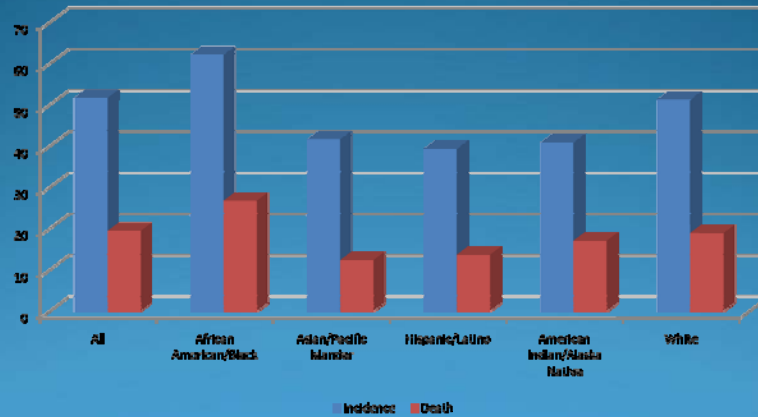
Source: U.S. Census 2000 / NYC Department of City Planning



Cancer among Minority

- African Americans have the **highest death rate and shortest survival of any racial and ethnic group** in the US for most cancers.
- Death rate for all cancers combined continued to be 33% higher in African American men and 16% higher in African American women than in white men and women, respectively
- Cancer survival rates are **generally similar** or lower among Hispanics compared to non-Hispanic whites.
- For all cancers combined, and for the most common cancer (prostate, breast, colorectal, and lung), incidence and death rates are lower among Hispanics than among non-Hispanic whites.

Colorectal Cancer (CRC) Disparity

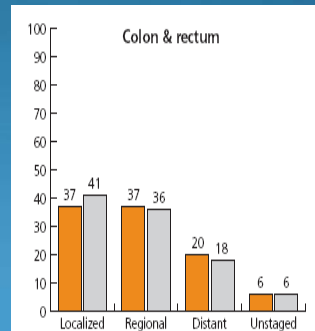
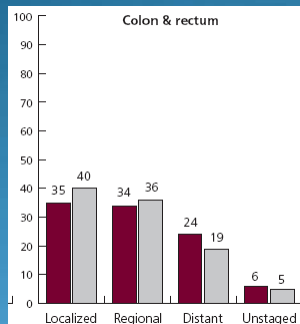


Statistics are for 2000-2004, age-adjusted to the 2000 U.S. standard million population, and represent the number of new cases of invasive cancer and deaths per year per 100,000 men and women

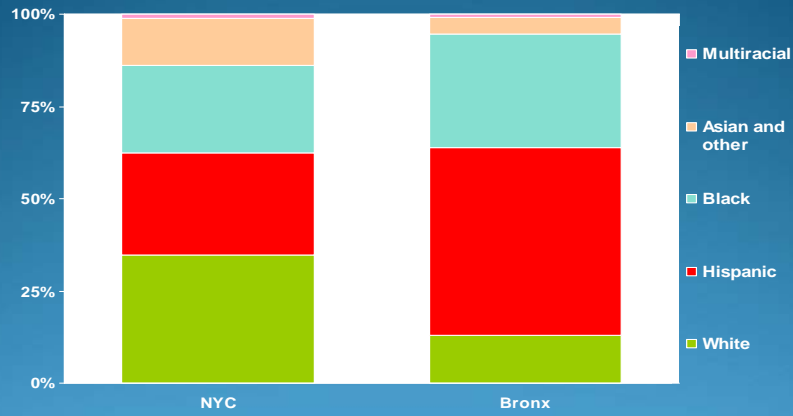
CRC Stage of distribution

African Americans vs. Whites

Hispanics vs. Whites

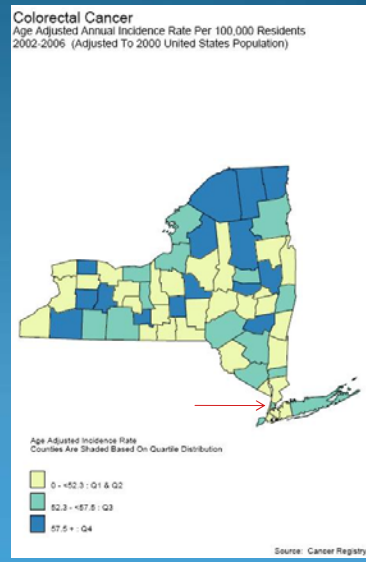
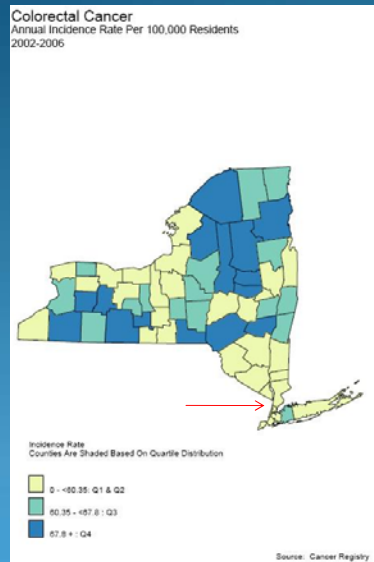


Population by Race New York City and Bronx, 2006



Source: NYC Dept. of City Planning

Incidence of CRC in the Bronx





Patient navigator Program

Screening for CRC has increased by 300%*

> 2000 colonoscopies per year

Program

- Patient navigation

- Direct endoscopic referral system (DERS)

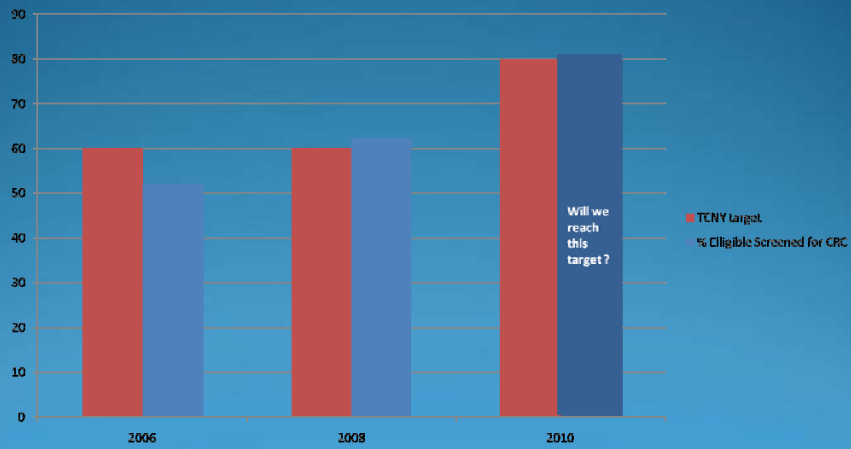
- GI suite modifications

Improved screening by Colonoscopy from 5 to 15 % in the service area*

*Nash D, Azeez S, Vlahov D, et al. Evaluation of an intervention to increase screening colonoscopy in an urban public hospital setting. J Urban Health 2006 Mar; 83(2):231-43



CRC screening in Hunts point & Mott Haven



Study of Colorectal tumors among minority New Yorkers

4,043 consecutive colonoscopies

2-year period

Age and gender distribution of colorectal tumor type, location,
and stage of colorectal tumors among urban minorities

99% were Hispanic or African American

two-thirds were women

Colorectal tumors study

- 960 (23.7%), had adenomas, and 82 (2.0%) had colorectal cancer
- Gender related findings
 - Women had higher visit volume adjusted odds to undergo colonoscopy (OR 1.35; CI 1.26-1.44, $P < .001$)
 - Men had higher odds for both adenomas and cancers (OR 2.38, CI 2.0-2.82, $P < .001$).
- Age related findings
 - The odds of colorectal cancers were higher at age greater than 70 years (OR 1.91; CI 1.09-3.27, $P < .05$), specifically among men (OR 2.27, 95% CI 1.07-4.65, $P < .05$)
 - However, 38% of cancers were noted among the 50- to 59-year-old subjects.
- Ethnicity related findings
 - Significantly higher adjusted odds of Hispanic Americans undergoing colonoscopy compared to African Americans in our sample.
- Proximal location
 - 51% of all abnormalities and 35.4% of cancers were found proximal to splenic flexure

Ethnic disparity in mortality after diagnosis of colorectal cancer among inner city New Yorkers

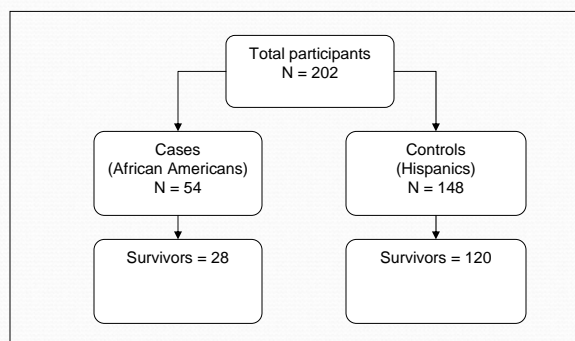
- 5-year data on demographics and clinical features of CRC patients at LMMHC
- African Americans (AAs) and Hispanics
- Adjusted cancer-related deaths and early deaths (within 6 months of diagnosis) were compared

CRC Ethnic disparity study

- 202 CRC subjects
- Hispanics, 148 (73%); AAs, 54 (27%)
- Women, 107 (53%)
- Mean age, 64.5 years
- CRC was diagnosed by colonoscopy in 157 (78%) and by surgery in 45 (22%) cases
- One hundred twenty-two (60%) had stage 0-2 CRC
- 69 (34%) had proximal colonic lesions.

CRC Ethnic disparity study

- Fifty-four of 202 (20%) patients died
- 24 (11.9%) were early deaths (within 6 months of follow-up)
- Study period (median, 27 months)



CRC Ethnic disparity study

There were no differences in

- demographic,
- clinical features,
- or treatment

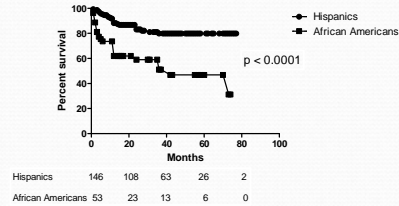
between Hispanics and AAs

($p = NS$)

Clinical feature	Cases (African Americans N=54)	Controls (Hispanics N=148)	OR (95% CI)	P value
Age (median, IQR) years	64 (56-73)	65 (57-72.5)	0.97 (0.97-1.02)	0.790
Women n (%)	28 (51.8)	67 (45.3)	1.3 (0.69- 2.43)	0.407
Insured n (%)	41 (76)	113 (76.3)	0.98 (0.47-2.03)	0.950
Active smokers n (%)	19 (35.2)	37 (25)	1.63 (0.83-3.19)	0.154
Family h/o cancer n (%)	3 (5.6)	2 (1.4)	4.29 (0.69-26.43)	0.116
Screening colonoscopy n (%)	9 (16.7)	35 (23.7)	0.65 (0.29-1.45)	0.290
Diagnosis by colonoscopy n (%)	42 (77.8)	115 (77.7)	1.00 (0.47-2.12)	0.991
Lesions proximal to hepatic flexure n(%)	22 (40.7)	47 (31.8)	1.48 (0.78-2.81)	0.235
Adenocarcinoma-in-situ n (%)	12 (22.2)	31 (21)	1.08 (0.51- 2.29)	0.845
AJCC stage < 2 n (%)	35 (64.8)	87 (58.8)	1.29 (0.67- 2.47)	0.439
Metastatic disease n (%)	20 (37)	47 (31.8)	1.26 (0.66- 2.43)	0.481
> 12 lymph nodes resected during surgery n (%)	15 (27.8)	37 (25)	1.15 (0.57- 2.33)	0.690
Appropriate Rx n (%)	49 (90.7)	128 (86.5)	1.53 (0.54- 4.31)	0.419
Chemotherapy n (%)	14 (25.9)	44 (29.7)	0.83 (0.41- 1.67)	0.597
Treatment complete n (%)	51 (94.4)	135 (91.2)	1.64 (0.45- 5.93)	0.456
*Deaths n (%)	26 (48.2)	28 (18.9)	3.98 (2.03- 7.81)	0.000
**Deaths in 6 months n (%)	15 (27.8)	9 (6.1)	5.94 (2.42- 14.6)	0.000
***Deaths in 1 year n (%)	21 (38.9)	19 (12.8)	4.32 (2.08 8.96)	0.000
****Deaths in 3 years n (%)	24 (44.4)	28 (18.9)	3.43 (1.74- 6.74)	0.000

CRC Ethnic disparity study

- Significantly higher odds of death (OR, 3.98; 95% CI, 2.03-7.81)
- Especially early death (OR, 5.94; 95% CI, 2.42-14.6) was observed among AAs



CRC Study Highlights

- First to compare inner city minority subjects with CRC
- Increased odds of death in AAs, despite similar clinical features and living environment
- Tumor behavior or host response among AAs could explain this difference



Carcinogenesis and Genetic markers

Colonic adenomas progress to adenocarcinomas (Morson 1974)

- Adenoma–carcinoma sequence has become established as a stepwise pattern of mutational activation of oncogenes and inactivation of tumour suppressor genes that result in cancer (Vogelstein *et al.* 1988)

The transition from normal epithelium to adenoma to carcinoma is associated with acquired molecular events



Molecular Events Associated With Colon Carcinogenesis

At least five to seven major deleterious molecular alterations may occur

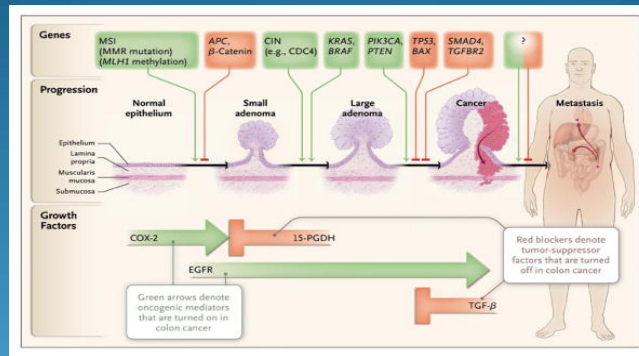
- when a normal epithelial cell progresses in a clonal fashion to carcinoma.

Two major pathways by which these molecular events can lead to colorectal cancer.

- 85% of colorectal cancers are due to chromosomal instability (CIN)
- 15% are due to events that result in microsatellite instability (MSI or MIN, also known as replication error [RER])

Molecular Basis of Colorectal Cancer

Markowitz, S & Bertagnolli, M - NEJM 2010



Micro satellite Instability (MSI)

- The key characteristics of MSI cancers are
 - a largely intact chromosome complement
 - defects in the DNA mismatch repair system
- Mitotic instability of microsatellites is the hallmark of MSI cancers.



MSI

- The rate of adenoma-to-carcinoma progression appears to be faster in microsatellite-unstable tumors compared with microsatellite-stable tumors.
- Characteristic histologic changes such as increased mucin production can be seen in tumors that demonstrate MSI, suggesting that at least some molecular events contribute to the histologic features of the tumors.



MSI – does not explain everything

CRCs with MSI have a significantly **better prognosis** compared to those with intact mismatch repair.

Carolien M Kets. Et al. Unfavorable pathological characteristics in familial colorectal cancer with low-level microsatellite instability. *Modern Pathology* (2006) 19, 1624-1630

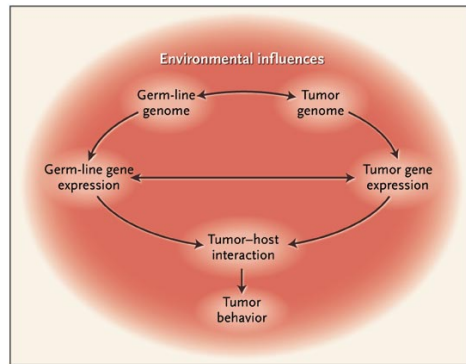
Familial CRC can be divided into two groups: Tumors with high-level MSI and tumors with low-level or no MSI. However, tumors with low-level MSI show unfavorable pathological characteristics compared to tumors with no and tumors with high-level MSI. These differences suggest a distinct underlying biology of CRC with low-level MSI.

Popat, S., Hubner, R., Houlston, R.S. **Systematic Review of Microsatellite Instability and Colorectal Cancer Prognosis**. *J Clin Oncol* 2005 23: 609-618

Incidence of MSI-H tumors was 3-fold higher in this study group of AA patients
Hassan Ashktorab, et al. High Incidence of Microsatellite Instability in Colorectal Cancer from African Americans . *Clin Cancer Res* March 2003 9:112-117

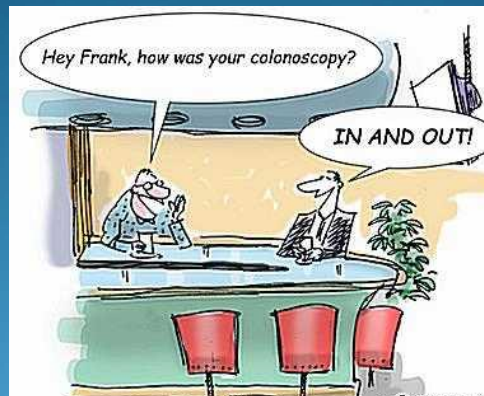


Multifactorial Colorectal Carcinogenesis
Markowitz, S & Bertagnolli, M, NEJM 2010



•The molecular events that drive the initiation, promotion, and progression of colorectal cancer occur on many interrelated levels.

•This dynamic process involves interactions among environmental influences, germ-line factors dictating individual cancer susceptibility, and accumulated somatic changes in the colorectal epithelium.



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