Genetics and Outcomes in Colorectal Cancer Disparities

Florida Society of Clinical Oncology

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MICHIGAN MEDICINE
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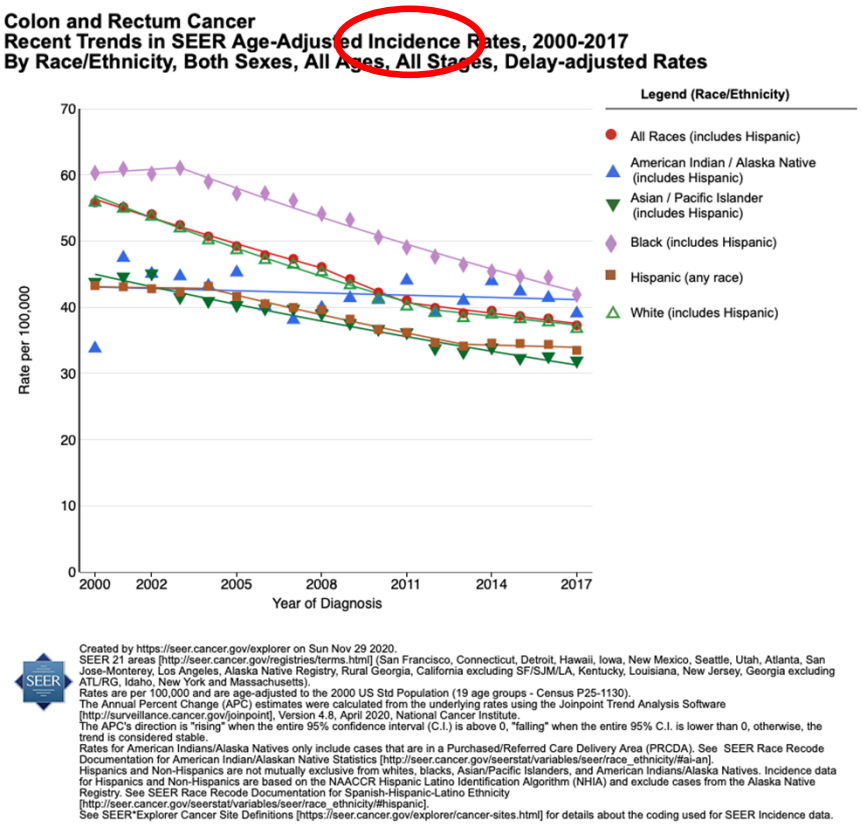
Epidemiology of CRC Disparities

Trends in SEER Age-adjusted CRC Incidence and Mortality

A



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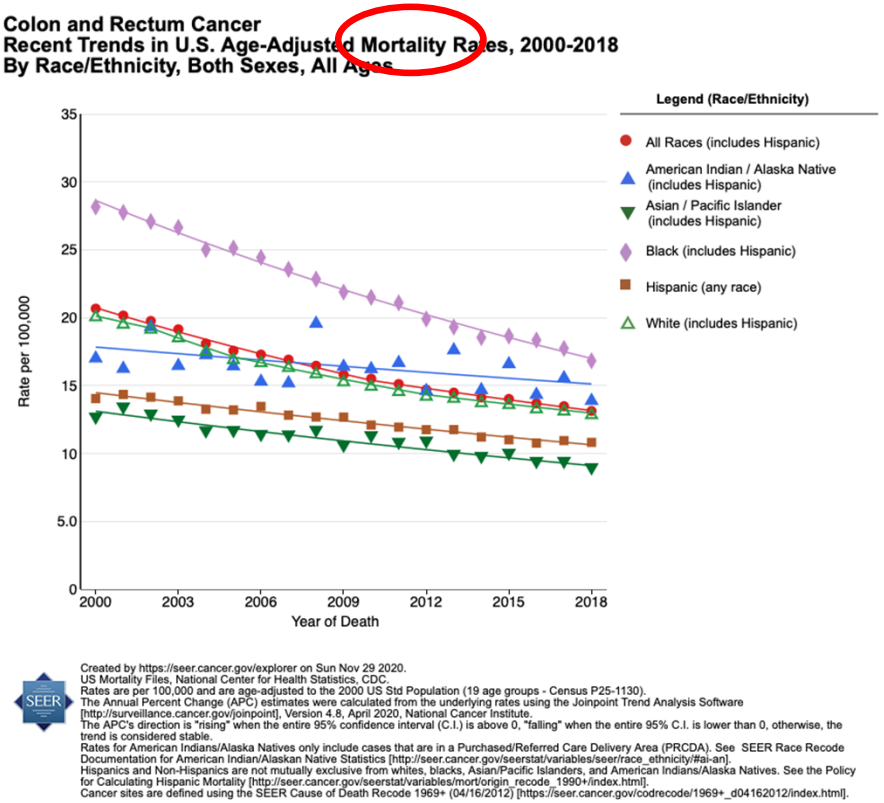


Carethers JM. *Adv Cancer Res* 2021;**151**:197-229.

Global Cancer 5-Year Survival Rates

Table 5. Five-year Net Survival Rates* (%) among Adults 15 Years of Age and Older in Select Countries by Cancer Site, 2010-2014

	Esophagus	Stomach	Colon	Rectum	Liver	Lung	Female Breast	Cervix	Prostate
Asia									
Chinese registries	30	36	58	57	14	20	83	68	69
Indian registries	4	9	39	30	6†	4	66	59	44
Israel	26	32	72	68	19†	27	88	67	96
Kuwait	25†	22	59	58	19	13	75	57	84
Malaysia (Penang)	14†	30	56	58	10†	10	65†	57†	88
South Korea	31	69	72	71	27	25	87	77	90
Thai registries	7	13	47	44	7	9	69†	54†	68
Turkish registries	19	25	55	53	16	15	82	61	84
Northern America									
Canada	16	30	67	67	19	21	88	67	94
US registries	20	33	65	64	17	21	90	63	97
Central and Southern America									
Brazilian registries	10†	21†	48†	42†	11†	9	75†	60	92
Chilean registries	9	17	44†	33†	4†	5†	76†	57†	82†
Colombian registries	11†	17†	35†	38†	5†	9†	72†	49†	80†
Costa Rica	21†	41	60	54	24†	20†	87	78†	93
Europe									
Austria	19	35	64	64	15†	20	85	64	90
Belgium	24	38	68	67	21	18	86	65	94
Czech Republic	10	21	56	52	7	11	81	61	85
Denmark	14	20	62	65	8	17	86	70	86
Estonia	5	29	58	55	4	17	77	67	86
German registries	21	34	65	62	13	18	86	65	92
Italian registries	14	31	64	61	20	16	86	67	90
Polish registries	9	21	53	48	11	14	77	55	78
Slovenia	9	29	62	60	7	15	84	66	85
Spanish registries	13	28	63	60	17	14	85	65	90
UK registries	16	21	60	63	13	13	86	64	89
Oceania									
Australian registries	24	32	71	71	19	19	90	66	95
New Zealand	15	26	64	66	19	15	88	67	90

*Survival rates are age-standardized. †Data are subject to limitations. Please see source.

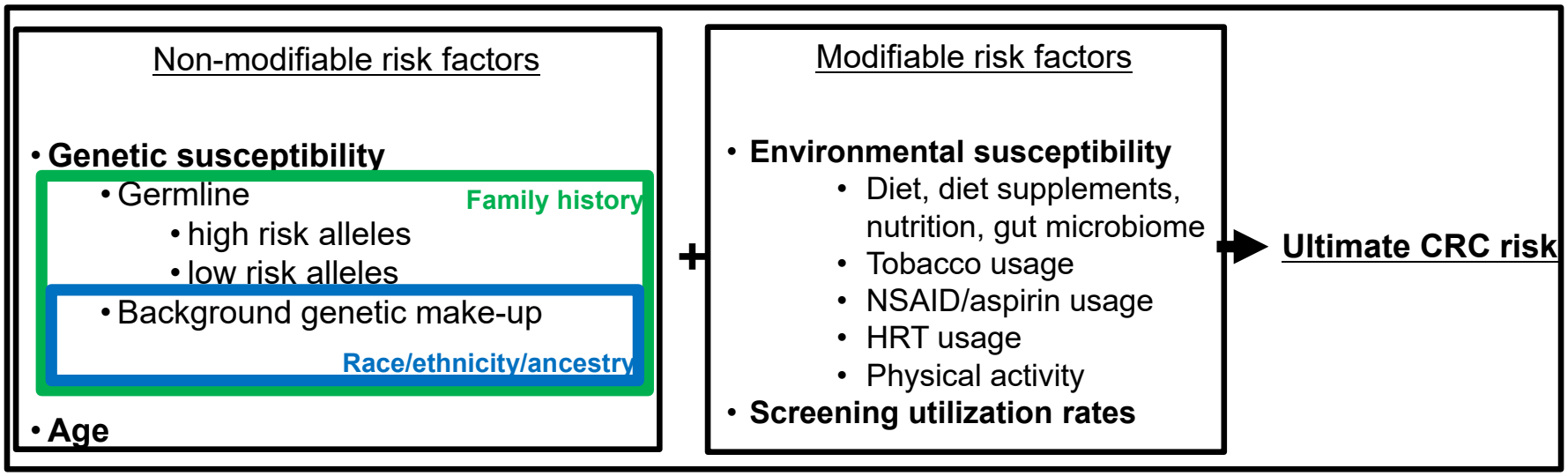
Source: Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet*. Jan 30 2018. doi: 10.1016/S0140-6736(17)33326-3.

- CRC survival (all stages) ranges from 30% (India) to 71% (South Korea, Australia), depending on country
- No real data from African countries in report

American Cancer Society. *Global Cancer Facts & Figures 4th Edition*. Atlanta: American Cancer Society; 2018.

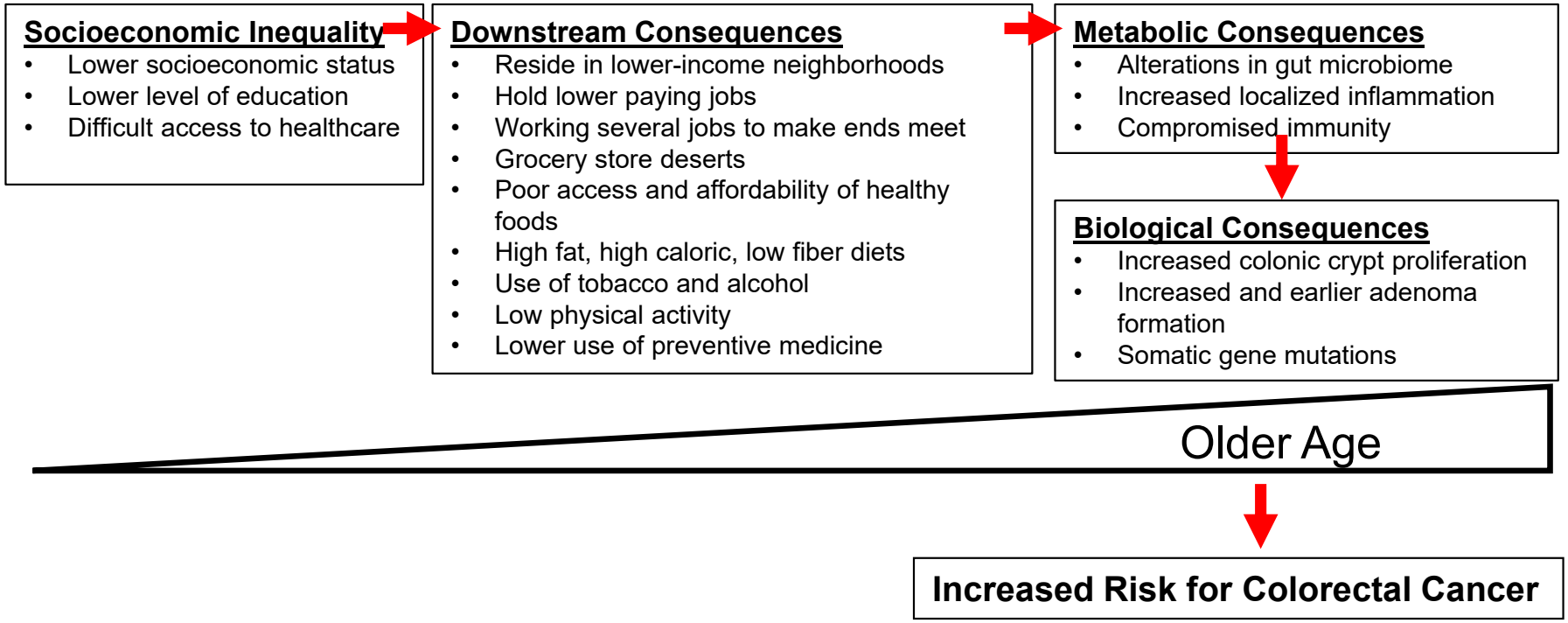
Root Causes of CRC Disparities

Risk Factors for Colorectal Cancer



Carethers JM. *Adv Cancer Res* 2021;**151**:197-229.

Connections and Consequences Initiated by Socioeconomic Disparities for CRC Risk



Carethers JM. *Adv Cancer Res* 2021;**151**:197-229.

Unique Biological, Genetic, Immunologic and Screening Changes for CRC Disparities

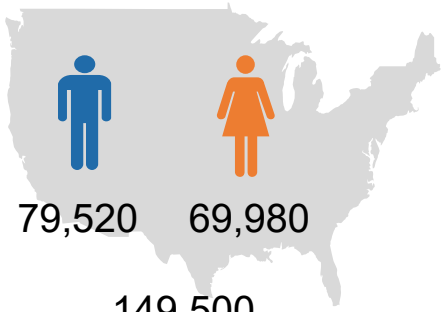
Summary of Differences in Black CRCs and Patients

Biological differences for Black American CRC risk as compared to White CRC risk
Increased number of adenomas >9mm
Increased proximal number of adenomas >9mm
Earlier onset of sporadic CRC
Increased proximal CRCs
Increase sulfidogenic bacteria in colon
Increased pro-inflammatory *Fusobacterium* and *Enterobacter* species in colon
Genetic differences for Black American CRC risk
Decreased frequency of MSI-H CRCs
Increased frequency of inflammation-associated microsatellite alterations/EMAST
Unique somatic *FLCN*, *EPHA6*, and *HTR1F* mutation
Increased frequency of KRAS mutation
Immunologic differences for Black American CRC risk
Decreased high numbers of $CD8^+$ T lymphocytes within CRC
Decreased numbers of granzyme B^+ T lymphocytes withing CRC
Screening and surveillance differences for Black American CRC risk
Lower frequency of population CRC screening uptake
Lower frequency of colonoscopy screening uptake
Lower frequency of follow-up after positive non-invasive CRC screening test

Carethers JM. *Adv Cancer Res* 2021;**151**:197-229.

Screening Utilization Contributions to CRC Disparities and Mitigation Strategies

General Guidelines for Screening and Surveillance for Colorectal Cancer



Men and Women → Symptomatic → Diagnostic Work-up

Asymptomatic

NEW: Moving to age 45 years (ACS, USPSTF)

No consideration of race until July 2017

Age < 50 years

Age ≥ 50 years

Negative Family History → No Screening

Positive Family History

Negative Family History → Av. Risk Screening**

Tier 1 Tests Preferred
- FIT
- Colonoscopy

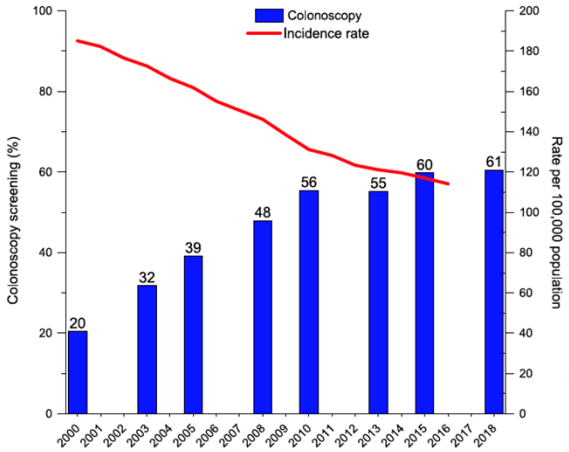
HNPCC* or FAP → Genetic Counselling & Special Screening

2 or more first-degree relatives affected* or 1 first-degree relative affected at age < 60 years → Colonoscopy Beginning age 40 years, or 10 years earlier than the youngest diagnosis* in the family, whichever comes first

1 first-degree relative affected at age ≥ 60 years → Average-risk screening, but beginning at age 40 years

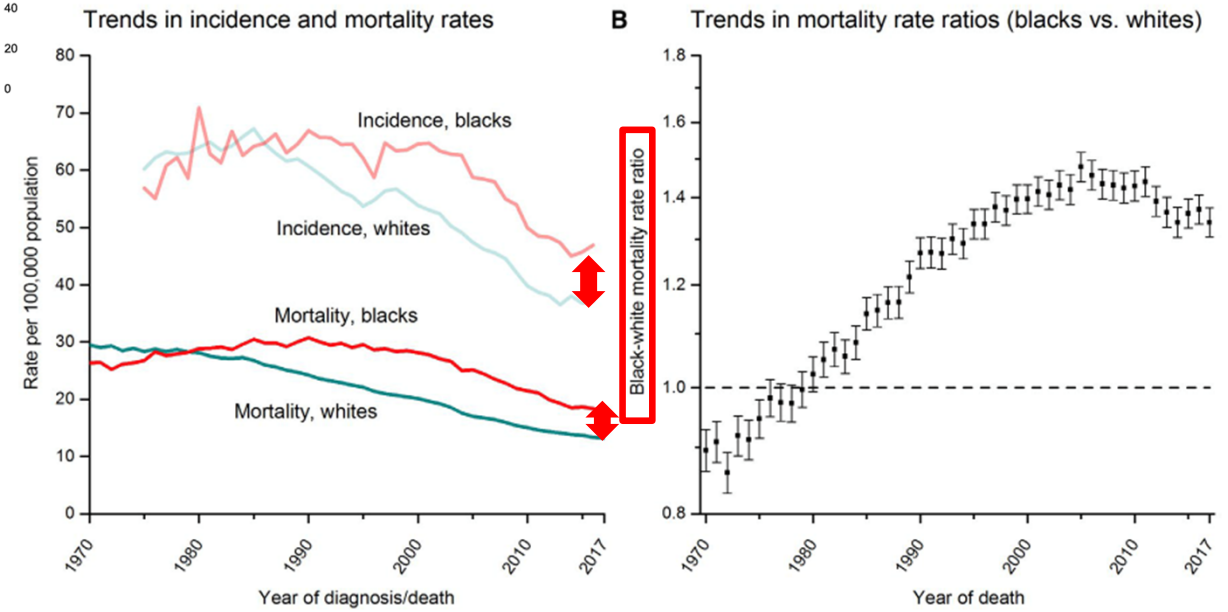
Colonoscopy

CRC Screening and CRC Incidence Trends



CRC Screening Rates in 2020

- 65% Whites
- 62% Blacks



Siegel RL et al. *CA Cancer J Clin* 2020;**70**:1-20
Siegel R *et al*. *CA Cancer J Clin* 2021;**71**:7-33

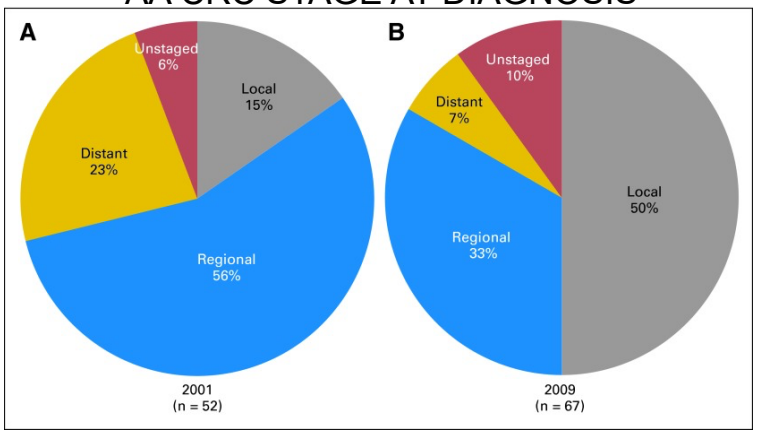
Strategies to Reduce Disparity of CRC in African Americans

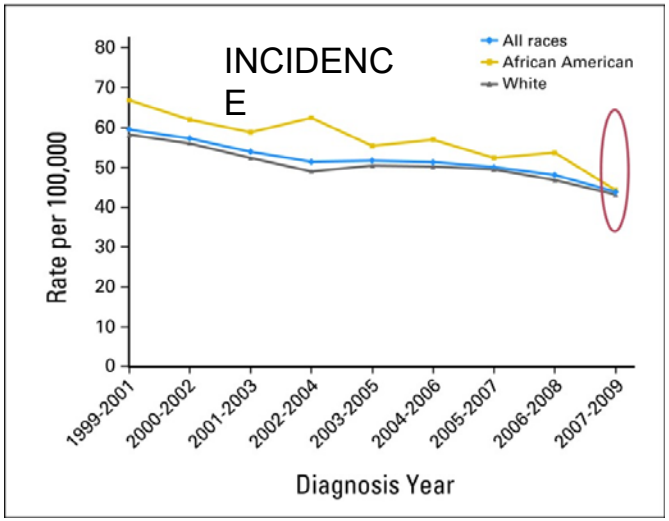
Strategy	Advantages	Disadvantages
Patient education	• Direct to consumer • Addresses patient-level barriers (e.g., fear, mistrust, etc)	• Cost • Ability to effectively reach certain target populations (i.e. those with low health literacy)
Physician education	• AAs report lower rates of physician recommendation for screening	• No data on effectiveness • Cost • Broad target population (e.g., gastroenterologists, primary care, etc)
Patient navigation	• Evidence for benefit in increasing colonoscopy screening for AAs • Cost effective	• Cost and insurance coverage • Training • Implementation
Increased screening by any method at age 50	• Low screening rates among AAs • Most CRCs develop after age 50 • AAs might prefer non-colonoscopy screening	• Confusion about preferred modality • AAs have increased risk of right-sided neoplasia
Modify age for screening	• Reduces burden of early-onset disease • Raises awareness of increased risk • Life years gained by earlier screening	• Increased confusion in guidelines • No prospective study of effectiveness • Most CRCs develop after age 50

Kupfer SS, Carr RM, Carethers JM. *Gastroenterology* 2015;**149**:1302-1304.

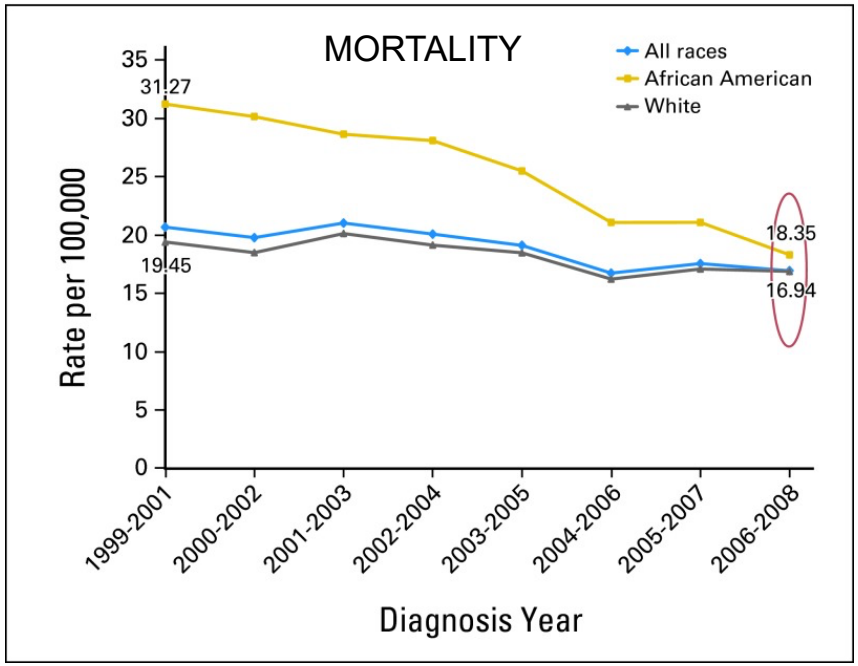
Delaware Cancer Consortium

AA CRC STAGE AT DIAGNOSIS





- Funded through state
- Colonoscopy preferred
- 10,000 Navigations
- AA: 47.8% in 2001 to 73.5% in 2009
- White: 58.0% in 2001 to 74.7% in 2009



Grubbs SS *at al*. *J Clin Oncol* 2013;**31**:1928-1930

Similarities Between Cancer Disparities and COVID-19

CANCER

- Series of genetic diseases
  - Germline predisposition
  - Somatic DNA mutations
- Local environmental influences
  - Inflammation
  - Microbiome
- Onset over months to years
- Asymptomatic screening is part of routine health care

common to both

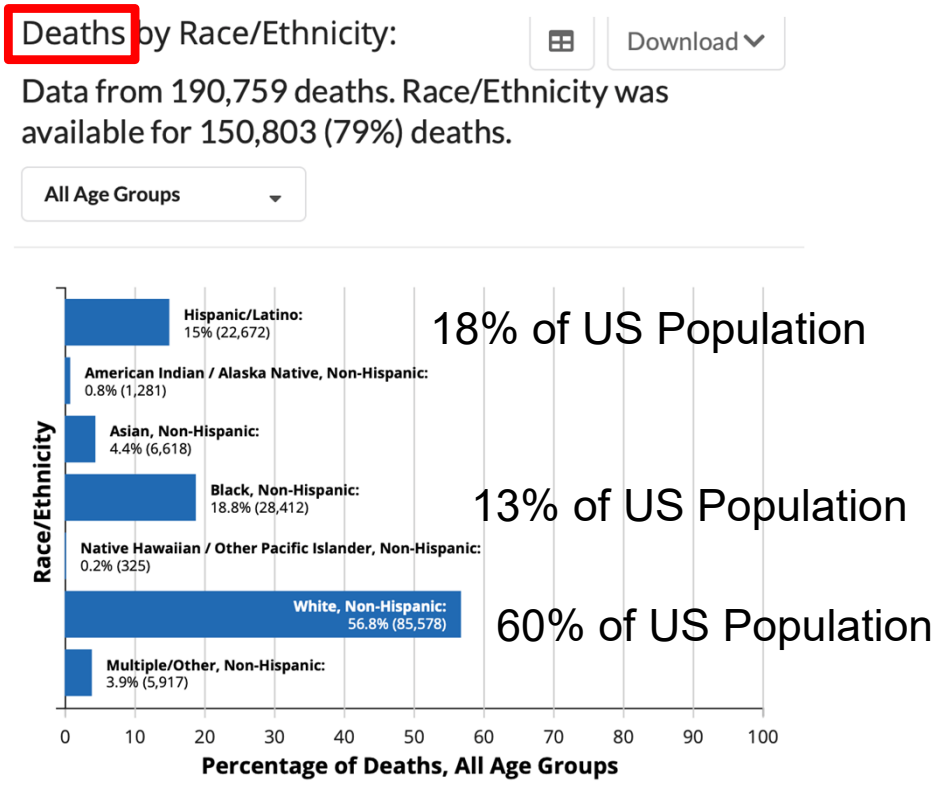
- Socioeconomic disparity
  - Level of Income and employment
  - Housing and location
  - Level of medical insurance
- Level of education
- Lifestyle factors and co-morbidities
  - Tobacco
  - Alcohol
  - Diet and obesity
- Reduced access to medical care
  - Delayed prevention or care
- Fear of clinical trial participation
- Higher risk of acquiring disease
- Higher risk of death from disease
- Survivorship medical and socioeconomic issues

COVID-19

- Single infectious disease
- Local environmental influences
  - ACE2 receptor
- Onset over hours to days
- Symptomatic screening
  - With widespread testing, can move to asymptomatic screening

Newman LA, Winn RA, Carethers JM. *Clin Cancer Res* 2021;**27**:24-27.

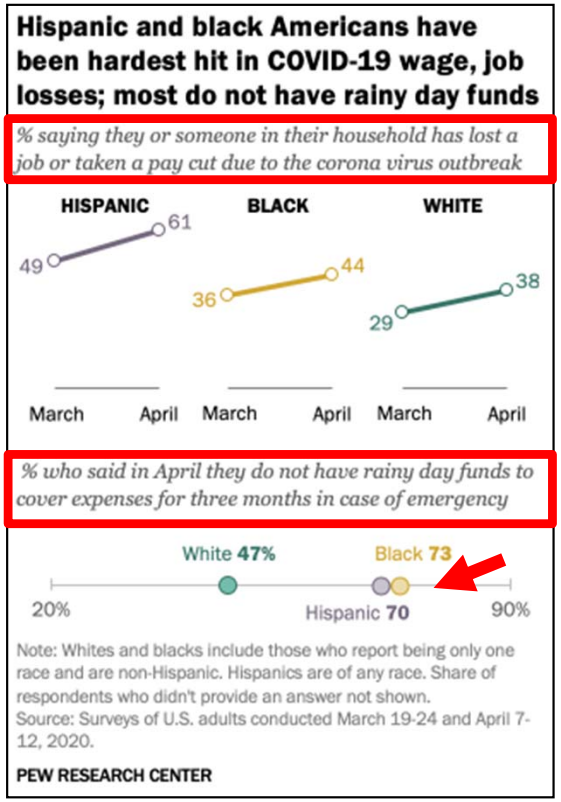
COVID-19 Effects on Race/Ethnicity



18% of US Population

13% of US Population

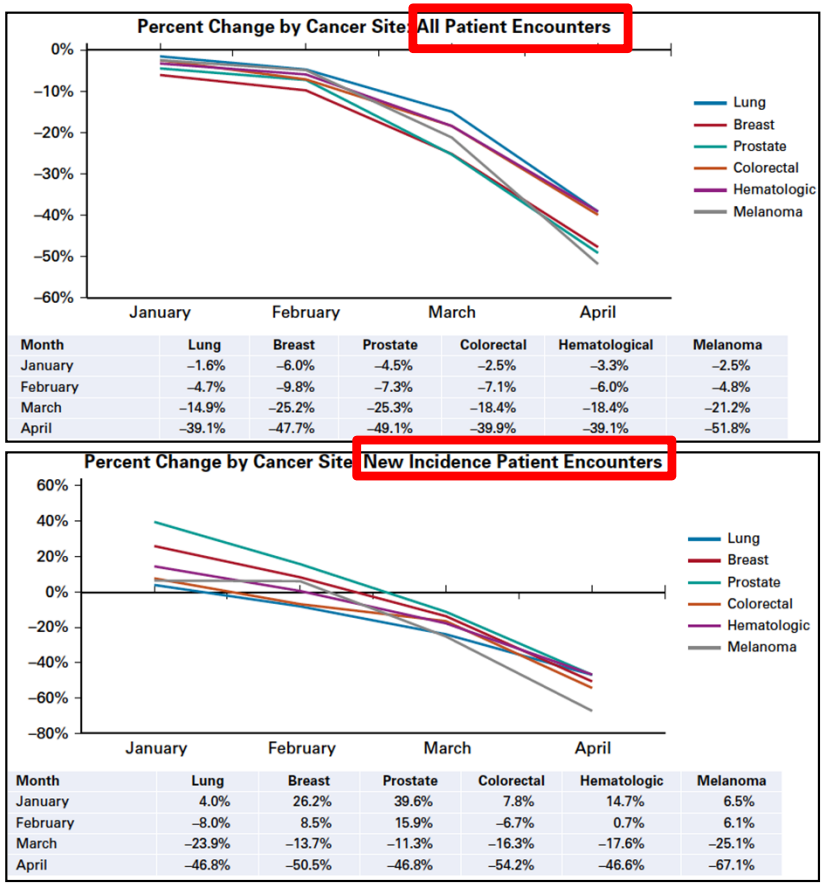
60% of US Population



https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html

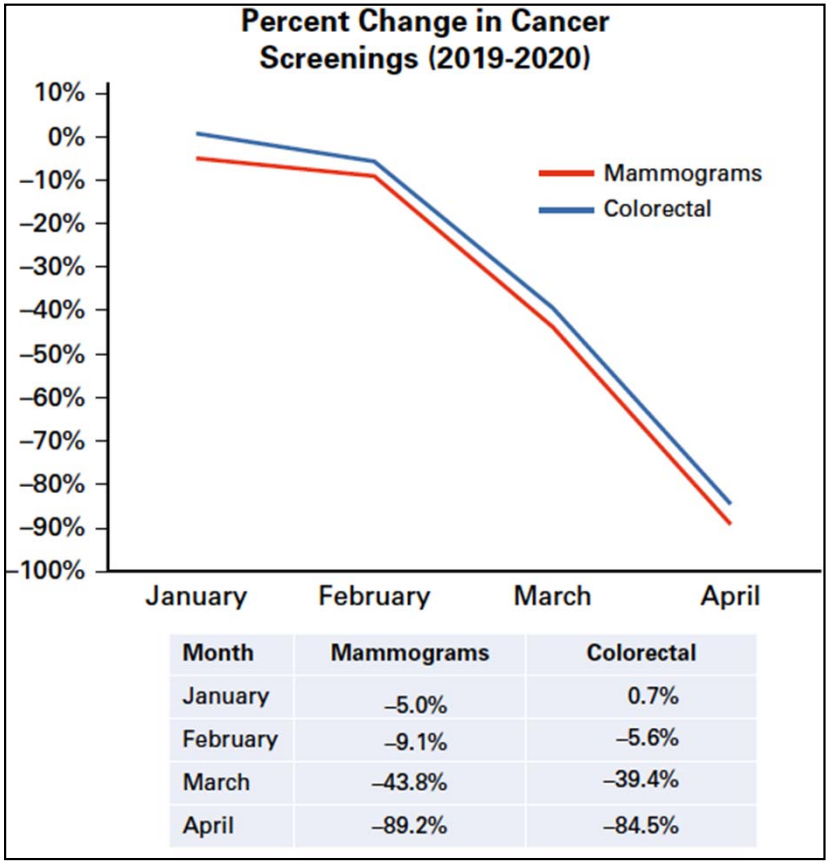
https://www.pewresearch.org/fact-tank/2020/05/05/financial-and-health-impacts-of-covid-19-vary-widely-by-race-and-ethnicity

COVID-19 Effect of Cancer Care



Month	Lung	Breast	Prostate	Colorectal	Hematological	Melanoma
January	–1.6%	–6.0%	–4.5%	–2.5%	–3.3%	–2.5%
February	–4.7%	–9.8%	–7.3%	–7.1%	–6.0%	–4.8%
March	–14.9%	–25.2%	–25.3%	–18.4%	–18.4%	–21.2%
April	–39.1%	–47.7%	–49.1%	–39.9%	–39.1%	–51.8%

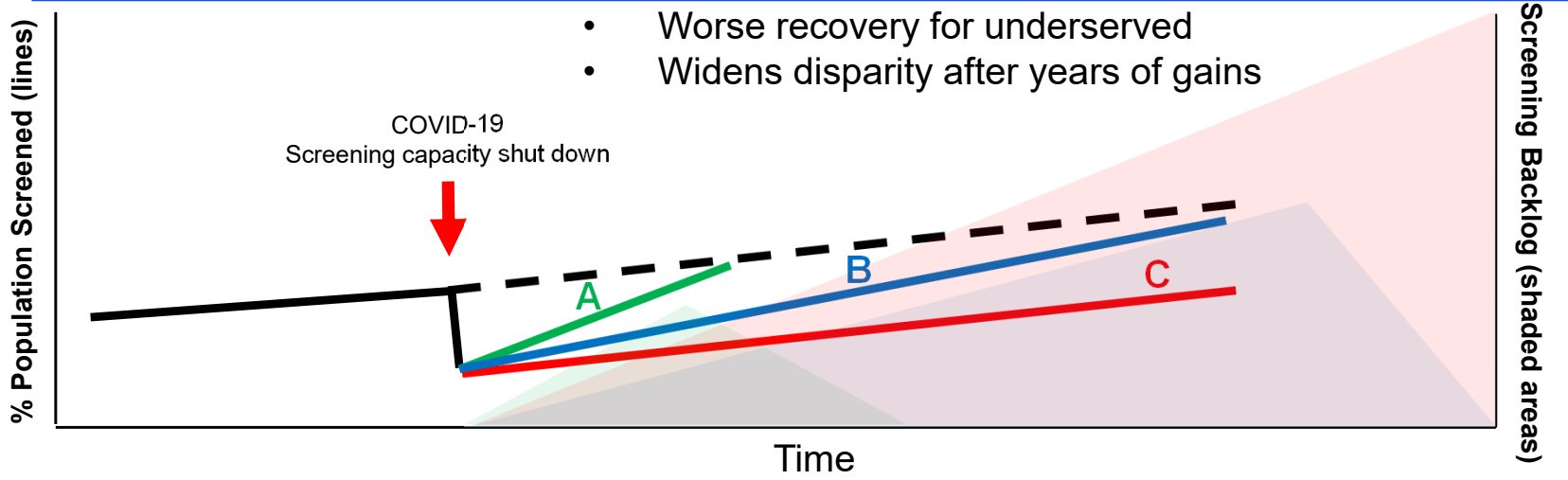
Month	Lung	Breast	Prostate	Colorectal	Hematologic	Melanoma
January	4.0%	26.2%	39.6%	7.8%	14.7%	6.5%
February	–8.0%	8.5%	15.9%	–6.7%	0.7%	6.1%
March	–23.9%	–13.7%	–11.3%	–16.3%	–17.6%	–25.1%
April	–46.8%	–50.5%	–46.8%	–54.2%	–46.6%	–67.1%



Month	Mammograms	Colorectal
January	–5.0%	0.7%
February	–9.1%	–5.6%
March	–43.8%	–39.4%
April	–89.2%	–84.5%

London JW *et al. JCO Clin Cancer Inform* 2020;**4**:657-665.

Cancer Screening in the COVID-19 Era



	Scenario	Factors affecting scenario	Relative # cancer deaths from baseline trajectory
A	**rapid return to screening trajectory within 6-12 months**	• **no further COVID-19 shutdowns of clinical capacity** • **unrestricted screening capacity**	**~1000 annually**
B	**delayed return to trajectory over 1-3 years**	• **restricted/delayed screening capacity due to COVID-19 testing (preventing some screening services) and social distancing**	**1000-5000 annually**
C	**prolonged return to trajectory over several years**	• **prolonged screening capacity restraints due to large backlogs of delayed screening** • **potential public and individual awareness for screening wanes** • **exacerbation of fears for clinic settings due to ongoing pandemic**	**≥5000-10,000 annually**

Carethers JM, *et al. Cancer Prev Res* 2020;**13**:893-896.
Sharpless NE. *Science* 2020;**368**:1290.

COVID-19 and Disparities

- Potential exacerbation of disparities with:
  - Disruption and access for acute medical care
  - Long term consequences with disruption of preventive care
  - Food insecurity
- Additional issues
  - Use of video vs phone for telehealth in COVID-19 / post-COVID-19 era
  - Worsening enrollment and outreach for underrepresented minorities to participate in clinical trials

Issues and Messaging

- Don’t delay preventive healthcare just because of COVID-19
  - Exceptions are if you are positive, and it is not an emergency
  - With excessive delay, will cost some lives
- At-Home CRC screening
  - Lesser in cost
  - Need to mail to home
    - Some still have difficulty in completing test correctly
    - May require navigation
  - Provider / Health System must follow up on negative and positive tests
    - Positive tests need colonoscopy (may require additional navigation)
    - Some patients may still be hesitant due to COVID-19
  - Loopholes for screening vs diagnostic colonoscopy and out-of-pocket costs

Colon Cancer is Preventable – Let's Get Screened!

Chadwick Boseman (2016)

Ruth Bader Ginsburg (1999)

Sharon Osbourne (2003)

Elizabeth Montgomery (1995)

Audrey Hepburn (1993)
Ronald Reagan (1985)

Eartha Kitt (2008)

Vince Lombardi (1970)

Clarence Williams III (2021)

Thank You!