Screening for Colon Cancer in South Africa

22nd Annual Controversies and Problems in Surgery Symposium 2018

Reidwaan Ally

University of Witswatersrand

WHO principles of early detection

Condition

- The condition should be an important health problem.
- There should be a recognisable latent or early stage.
- The natural history of the condition, including development from latent to declared disease should be adequately understood.

Test

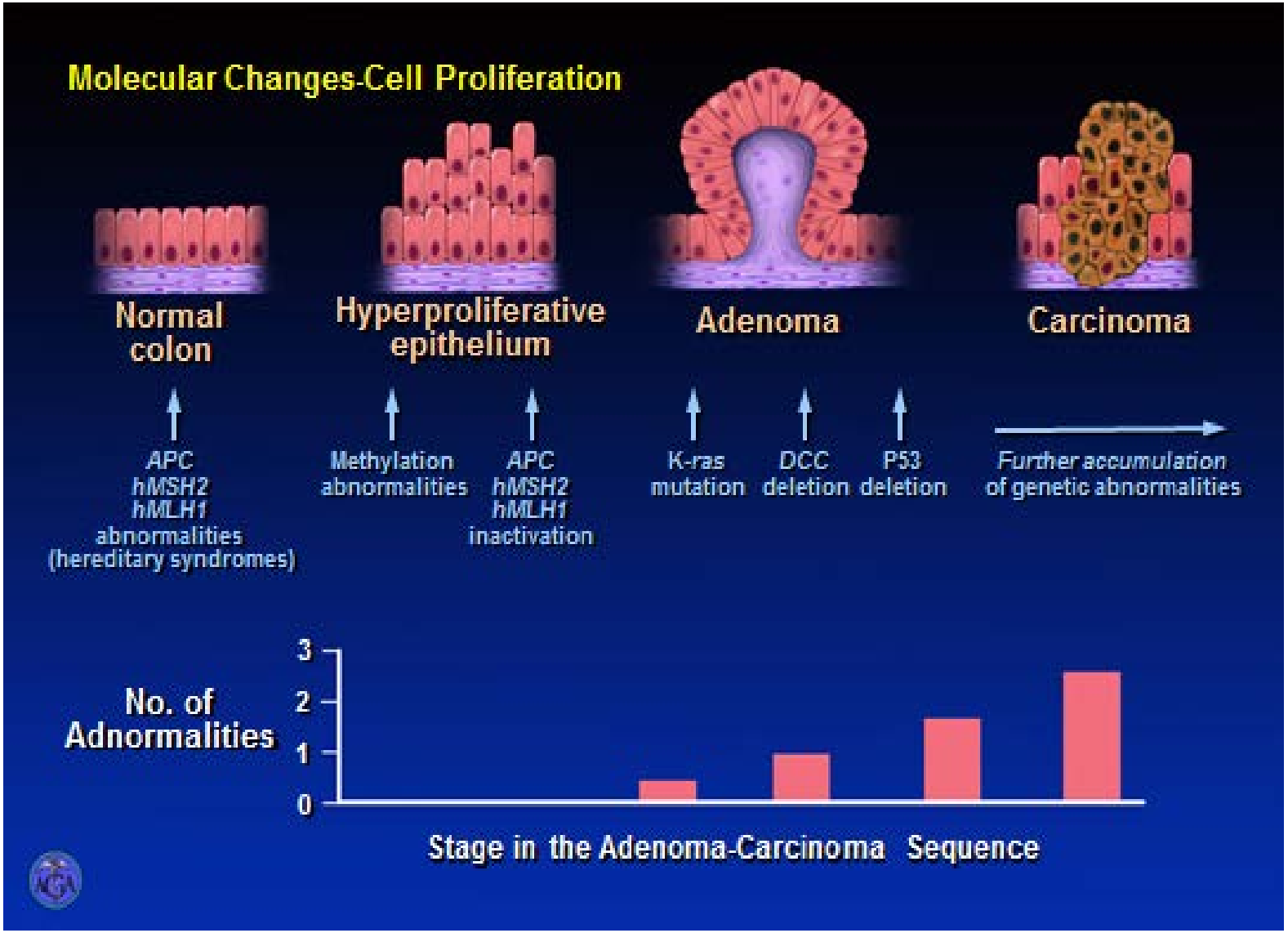
- There should be a suitable test or examination.
- The test should be acceptable to the population.

Treatment

- There should be an accepted treatment for patients with recognised disease.

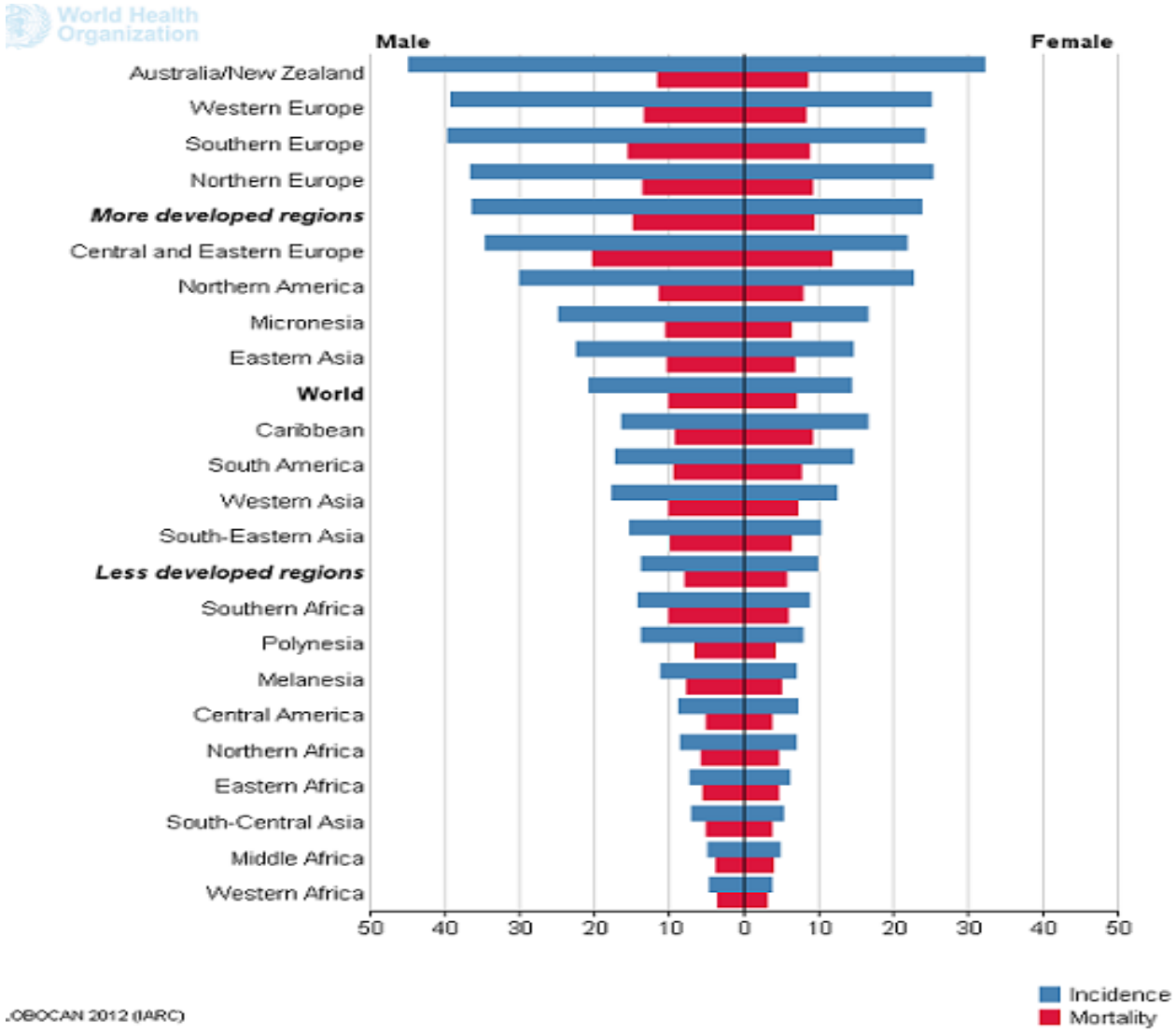
Screening Program

- There should be an agreed policy on whom to treat as patients.
- Facilities for diagnosis and treatment should be available.
- The cost of case-findings (including diagnosos and treatment of patients diagosed) should be economically balanced in relation to possible expenditiure on medical care as a whole.
- Case-finding should be a continuing process and not 'once and for all' project.


Molecular Changes-Cell Proliferation
Normal colon
Hyperproliferative epithelium
Adenoma
Carcinoma
APC
hMSH2
hMLH1
abnormalities
(hereditary syndromes)
Methylation abnormalities
APC
hMSH2
hMLH1
inactivation
K-ras mutation
DCC deletion
P53 deletion
Further accumulation of genetic abnormalities
No. of Adnormalities
3
2
1
0
Stage in the Adenoma-Carcinoma Sequence

Globocan 2012

per 100,1000	ETHIOPIA	SOUTH AFRICA	HIGHEST
Oesophageal	7,1 - 11,2	> 12,9	>12,9
Stomach	2,4 - 5,2	7,2 - 12,7	>23,8
Colorectal	2,6 - 7,1	13,0 - 20,5	>31
Liver	4,5 – 8,5	4,2 - 8,5	>25,9


World Health Organization
Male
Female
Australia/New Zealand
Western Europe
Southern Europe
Northern Europe
More developed regions
Central and Eastern Europe
Northern America
Micronesia
Eastern Asia
World
Caribbean
South America
Western Asia
South-Eastern Asia
Less developed regions
Southern Africa
Polynesia
Melanesia
Central America
Northern Africa
Eastern Africa
South-Central Asia
Middle Africa
Western Africa
50 40 30 20 10 0 10 20 30 40 50
Incidence
Mortality
GLOBOCAN 2012 (IARC)

Statistics at a Glance —

At a Glance

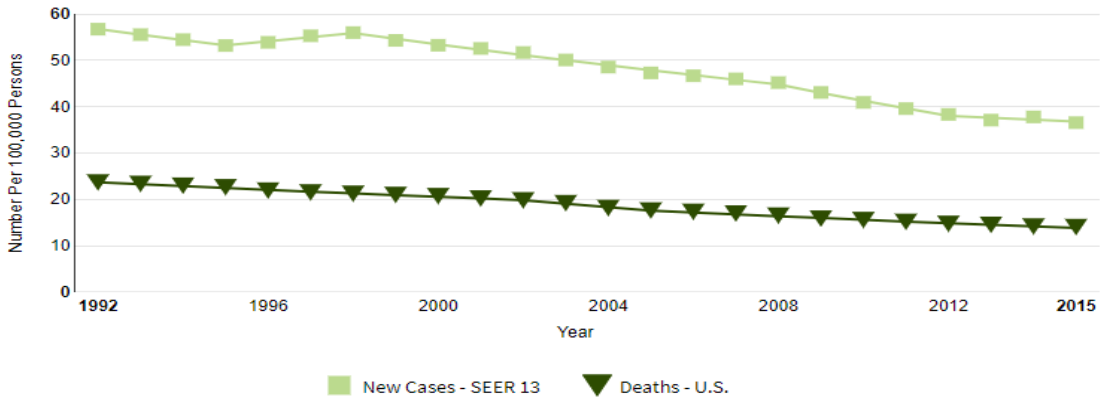
Estimated New Cases in 2018	140,250
% of All New Cancer Cases	8.1%

Estimated Deaths in 2018	50,630
% of All Cancer Deaths	8.3%

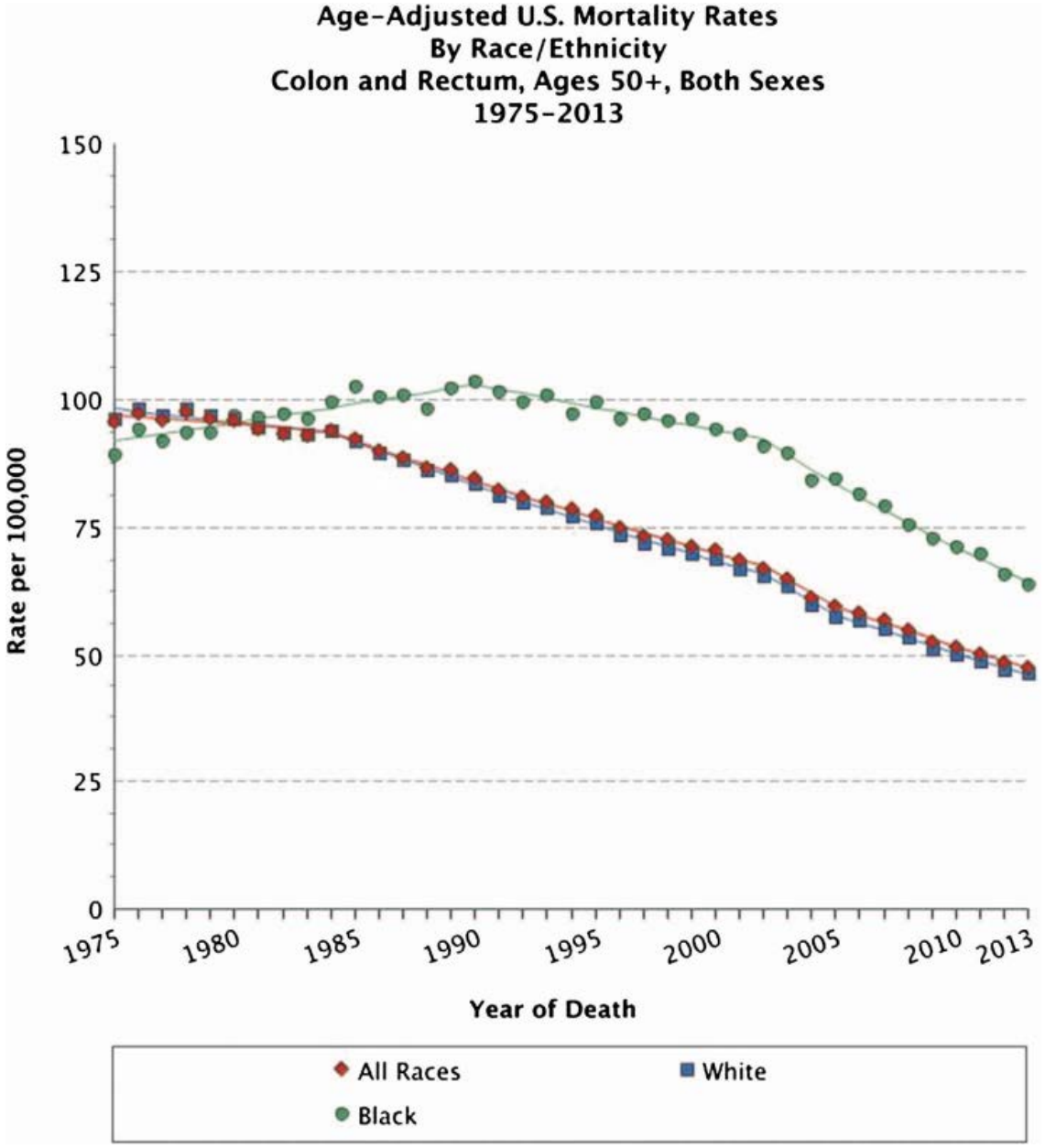
Percent Surviving 5 Years

64.5%

2008-2014



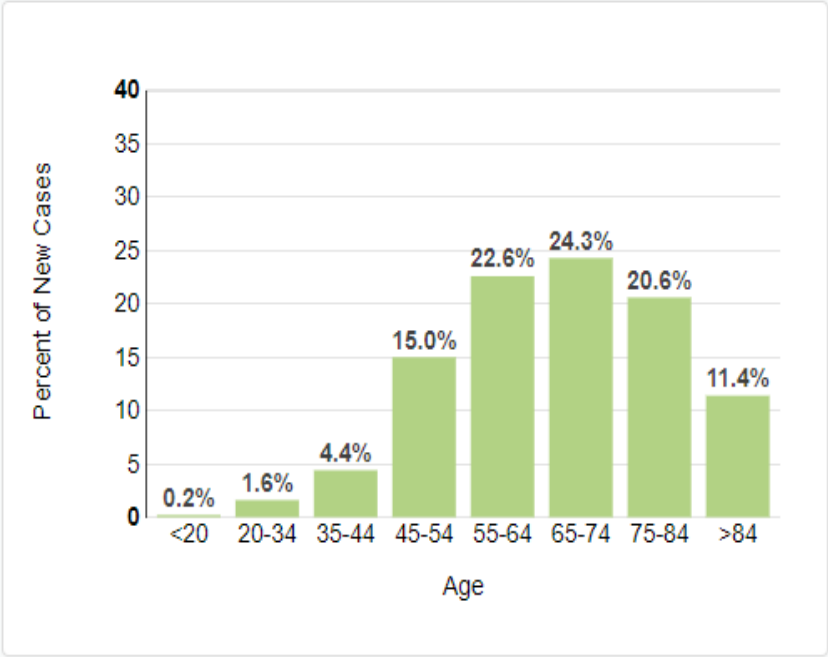
Modeled trend lines were calculated from the underlying rates using the Joinpoint Trend Analysis Software.


Age-Adjusted U.S. Mortality Rates
By Race/Ethnicity
Colon and Rectum, Ages 50+, Both Sexes
1975-2013
Rate per 100,000
150
125
100
75
50
25
0
1975
1980
1985
1990
1995
2000
2005
2010
2013
Year of Death
All Races
White
Black

Number of New Cases per 100,000 Persons by Race/Ethnicity & Sex: Colorectal Cancer

SEER 18 2011-2015, Age-Adjusted

Percent of New Cases by Age Group: Colorectal Cancer

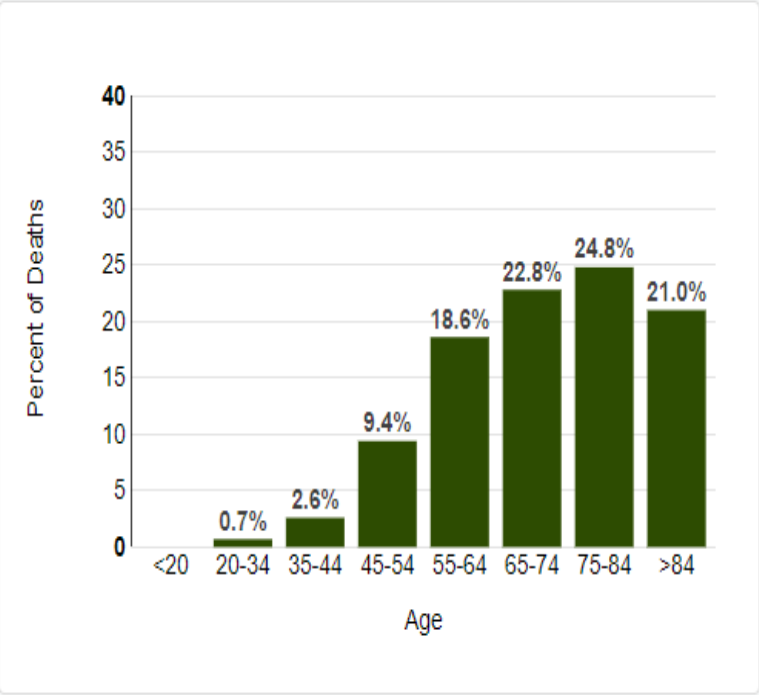


Colorectal cancer is most frequently diagnosed among people aged 65-74.

Median Age At Diagnosis
67

SEER 18 2011-2015, All Races, Both Sexes

Percent of Deaths by Age Group: Colorectal Cancer



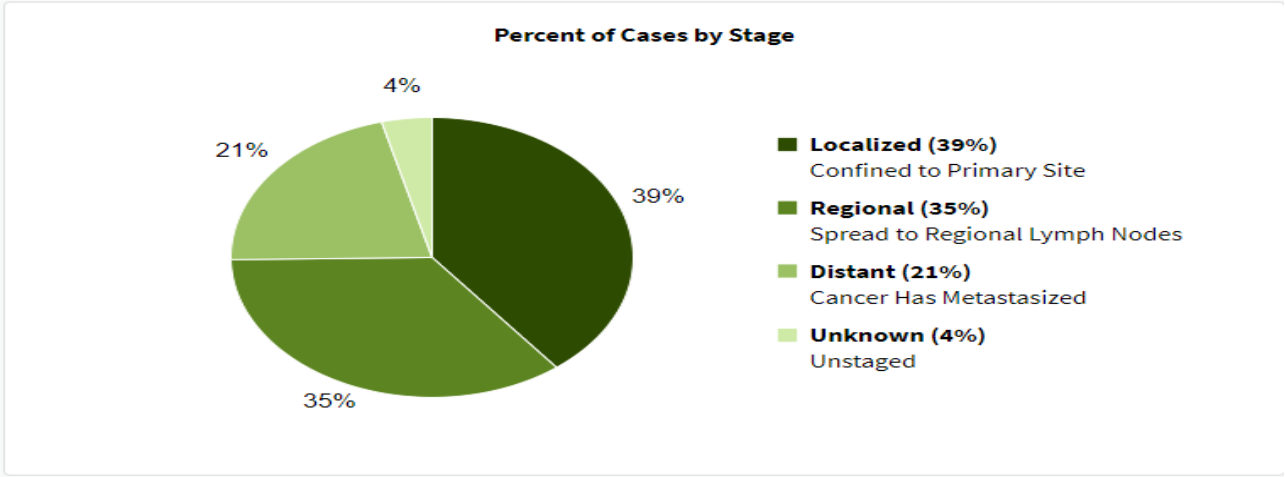
The percent of colorectal cancer deaths is highest among people aged 75-84.

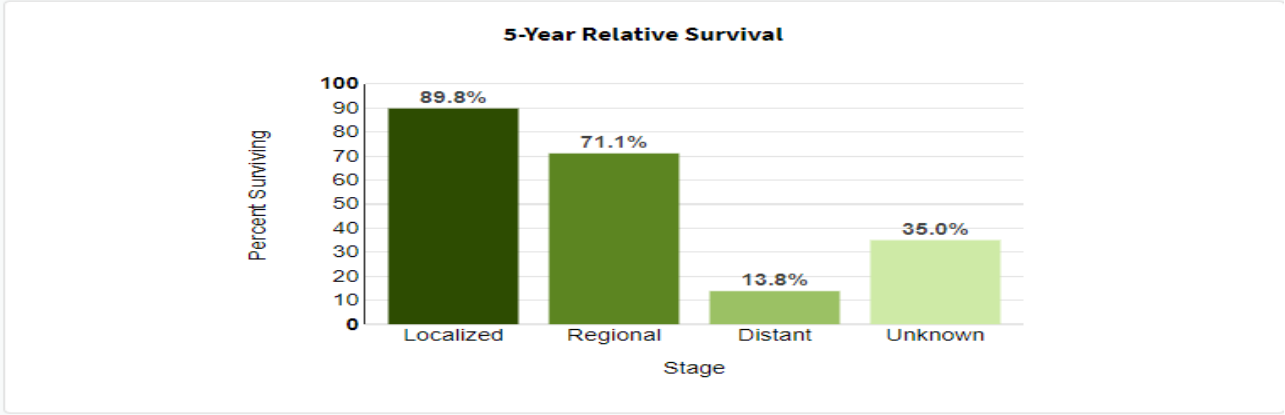
Median Age At Death

73

U.S. 2011-2015, All Races, Both Sexes

Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Colorectal Cancer





SEER 18 2008-2014, All Races, Both Sexes by SEER Summary Stage 2000

GETTING SCREENED CAN MAKE ALL THE DIFFERENCE

If found early, colon cancer is highly treatable[1]:

Stage I = 94%* survival rate

Stage II = 82%* survival rate

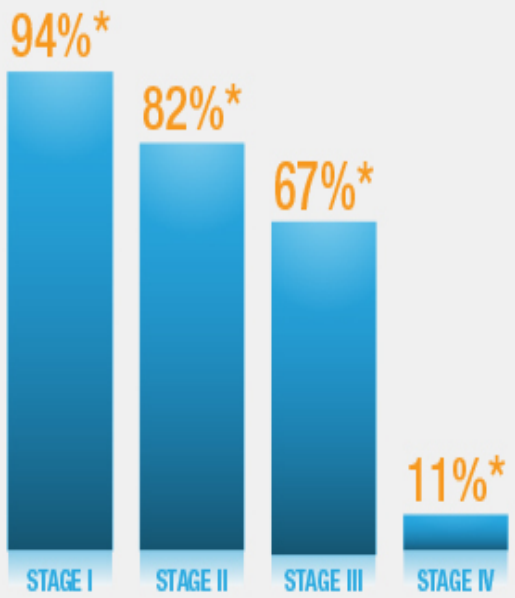
Stage III = 67%* survival rate

Stage IV = 11%* survival rate

*Based on 5-year survival rate.

1. Lansdorp-Vogelaar I, van Ballegooijen M, Zauber A, Habbema J, Kulpers E. Effect of rising chemotherapy costs on the cost savings of colorectal cancer screening. *J Natl Cancer Inst.* 2009;101:1412-1422.

BeSeenGetScreened.com



Increasing Rates of Young Rectal Cancer

- Colorectal cancer rates have declined overall in the past few decades, 30% of cases are now diagnosed in people younger than 55 years, according to 2017 data from the American Cancer Society
- Updated its guidelines and now recommends that colorectal cancer screening begin at age 45, rather than age 50

DDW
Digestive Disease Week®

Increasing Rates of Young Rectal Cancer

- Rates of rectal cancer are increasing in young people, and those affected are overwhelmingly female and white
- The work shows an annual increase in rates of the malignancy in people younger than 50 years of about 3%.

DDW
Digestive Disease Week®

Increasing Rates of Young Rectal Cancer

- Analyzed data on 68,699 patients with rectal cancer from the 2010 to 2012 National Inpatient Sample database.
- During that 3-year period, 2748 (4%) of the cases diagnosed were in people younger than 50 years.
- But in that younger age group, the incidence rose over each of the 3 years, by 2.8%, 3.0%, and 3.4%.
- Notably, the younger people diagnosed with rectal cancer were more likely to be women than men (62% vs 39%).
- More research is needed to discern the reason for this, authors pointed out.

DDW
Digestive Disease Week®

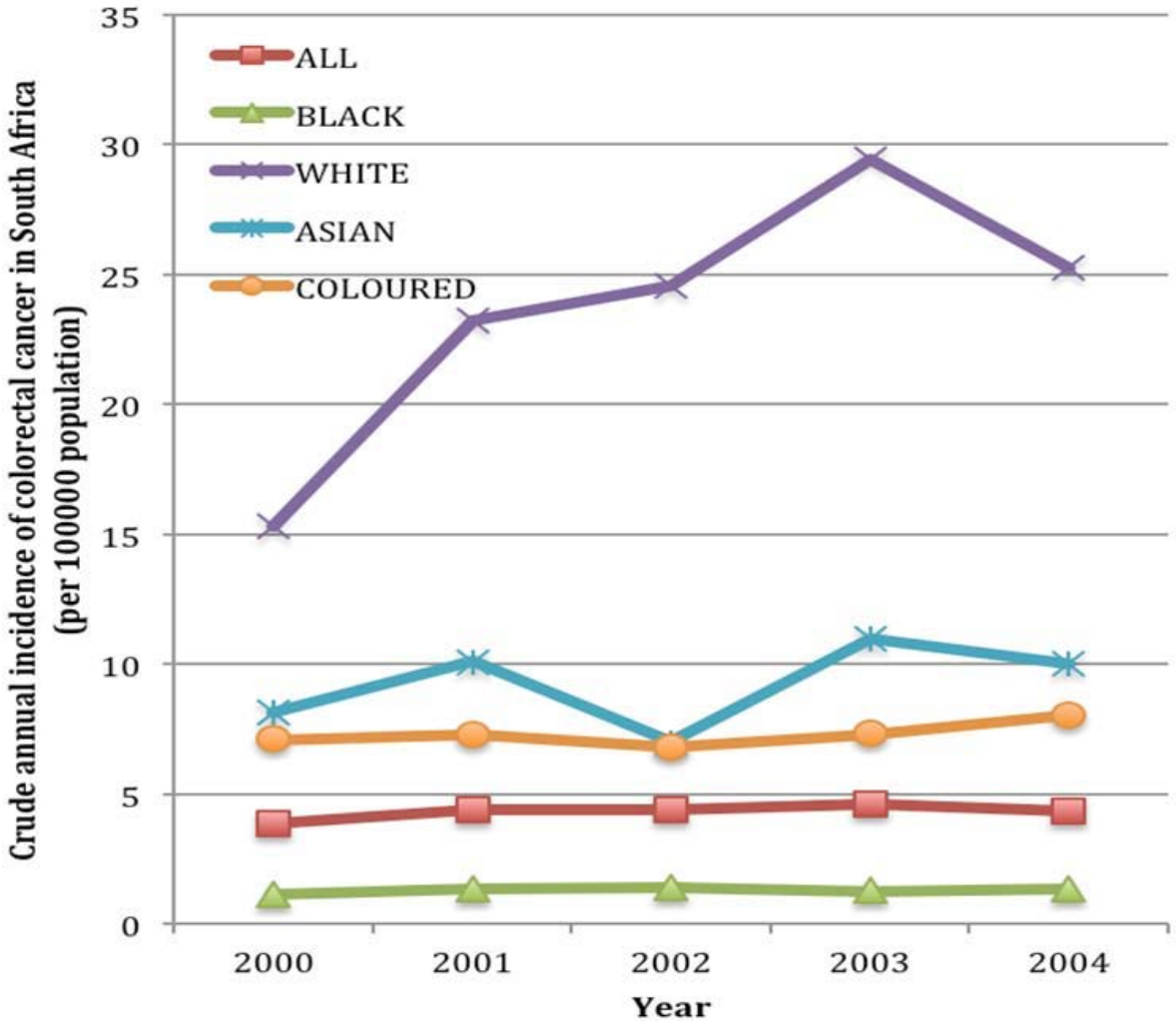
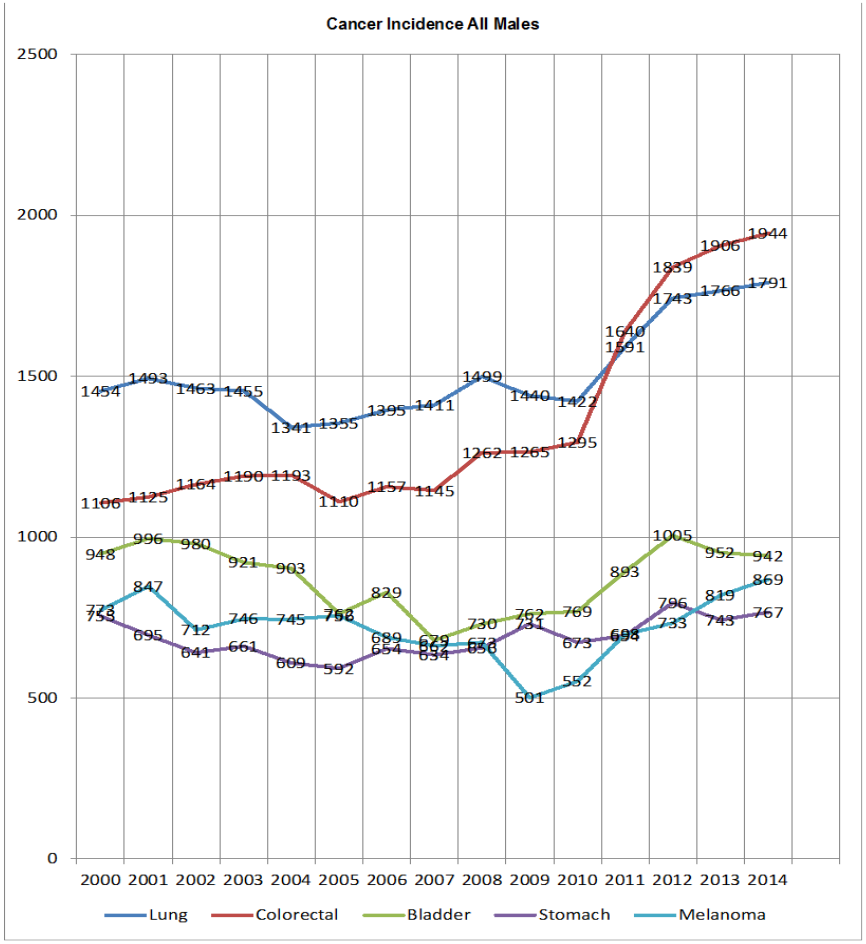
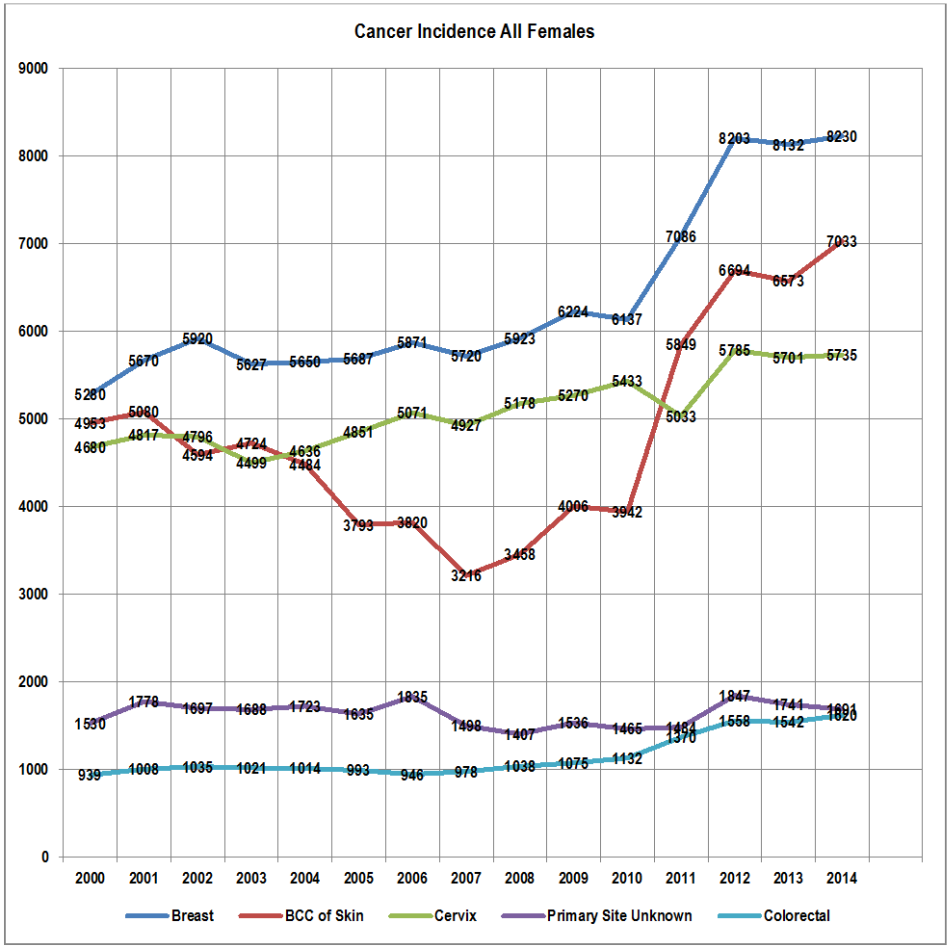


Figure 9 Crude incidence of colorectal cancer in South Africa (per 100 000 population) by ethnicity for 2000–2004.

2014 Cancer Registry





Herbst et al CANSA fact sheet

Cancer Epidemiology 44 (2016) 96–100

Contents lists available at ScienceDirect

Cancer Epidemiology

The International Journal of Cancer Epidemiology, Detection, and Prevention

journal homepage: www.cancerepidemiology.net

Short communication

The incidence and histo-pathological characteristics of colorectal cancer in a population based cancer registry in Zimbabwe

Leolin Katsidzira[a,b,*], Eric Chokunonga[c], Innocent T. Gangaidzo[a], Simbarashe Rusakaniko[d], Margaret Borok[a,c], Zvifadzo Matsena-Zingoni[e], Sandie Thomson[b], Raj Ramesar[f], Jonathan A. Matenga[a]

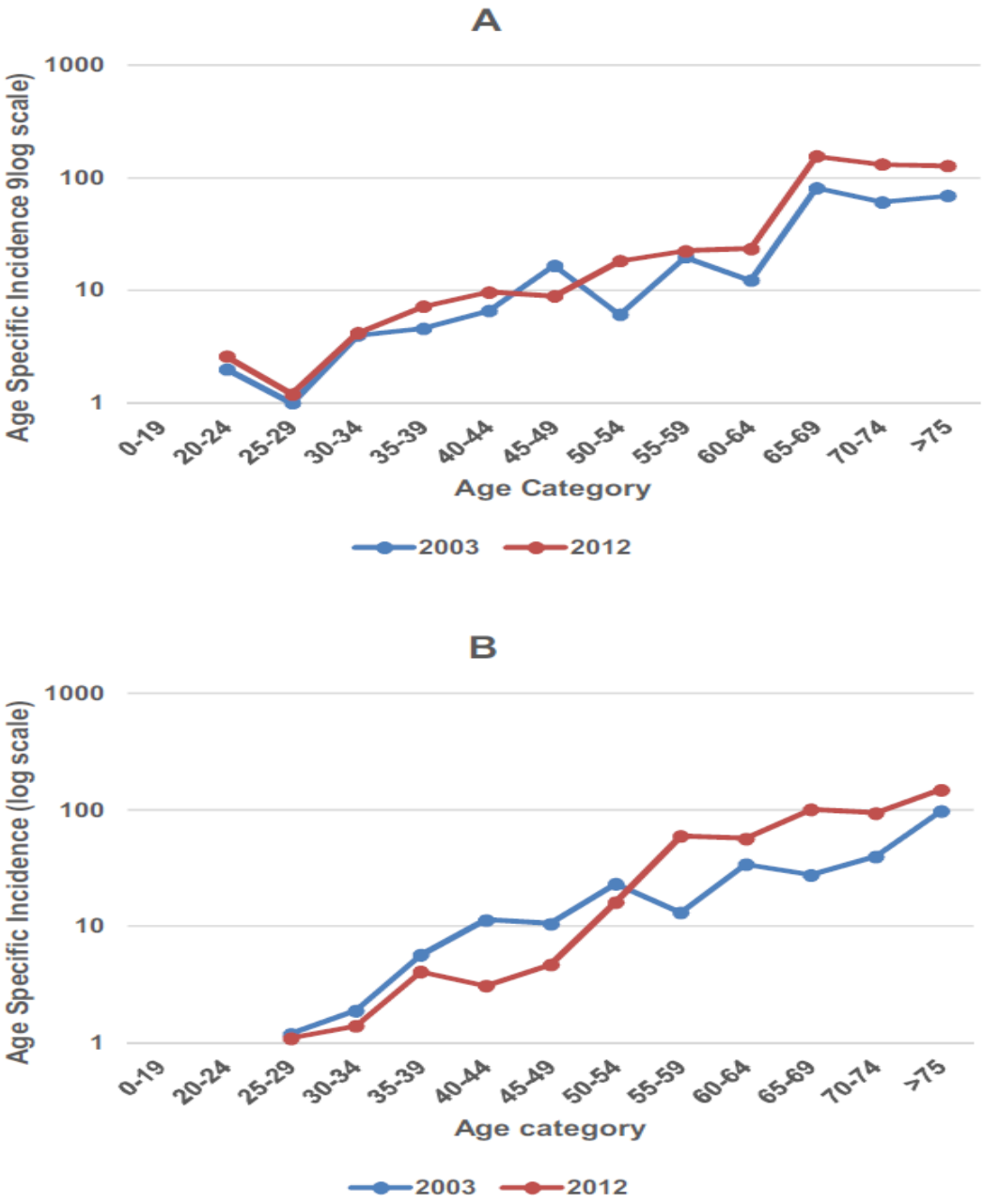

A
1000
100
10
1
Age Specific Incidence 9log scale)
0-19
20-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
65-69
70-74
>75
Age Category
2003
2012
B
1000
100
10
1
Age Specific Incidence (log scale)
0-19
20-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
65-69
70-74
>75
Age category
2003
2012

Table 1
Comparison of demographic and pathological characteristics between different population groups.

Variable	Black Africans n = 886	Caucasians n = 216	P value
Gender			
Males	471 (53%)	136 (63%)	0.009
Mean age (SD)[a]	52.9 (16.6)	69.5 (10.8)	<0.001
Site			
Colon	487 (55%)	135 (62%)	
Rectum	399 (45%)	81 (38%)	0.133
Histology[b]			
Adenocarcinoma	768 (87%)	202(94%)	
Mucinous adenocarcinoma	59 (7%)	10(4%)	
Signet ring cell carcinoma	37 (4%)	3(1%)	
Other	22 (2%)	1(1%)	0.024

[a] 39 black Africans and 4 Caucasians had missing ages.
[b] Fisher's exact test.

Table 2
Differences in demographic and pathologic characteristics between young adults and older individuals among black Africans with colorectal cancer.

Variable	Age < 40 n = 223	Age > 40 n = 624	P value
Sex			
Male	119 (53%)	332 (53%)	
Female	104 (47%)	292 (47%)	0.970
Site			
Colon	111 (50%)	347 (55%)	
Rectum	112 (50%)	277 (45%)	0.305
Histology			
Adenocarcinoma	172 (77%)	565 (90%)	
Mucinous adenocarcinoma	20 (9%)	36 (6%)	
Signet ring cell carcinoma	22 (10%)	12 (2%)	
Others	9 (4%)	11 (2%)	<0.001

NB: Age was unavailable in 39 cases and they are not included in this table.

unusually high frequency of colorectal cancer among young black adults. Mucinous and signet ring cell carcinomas are more common among black Africans, and this is particularly striking in young patients. These features contribute to the poor survival of colorectal cancer in this population. The higher incidence of colorectal cancer in later years may represent improved detection of the condition rather than a true increase in the population.

Int. J. Cancer: **112,** 860–864 (2004)

Publication of the International Union Against Cancer

CANCER SURVIVAL IN A SOUTHERN AFRICAN URBAN POPULATION

Adam GONDOS[1]*, Eric CHOKUNONGA[2], Hermann BRENNER[1], Donald Maxwell PARKIN[3], Risto SANKILA[4], Margaret Z. BOROK[2], Z. Michael CHIRENJE[5], Anna M. NYAKABAU[6] and Mary Travis BASSETT[2]

TABLE II – COMPARISON OF PATIENTS' MEDIAN AGE AT DIAGNOSIS, ZIMBABWEAN CANCER PATIENT POPULATIONS AND SEER CANCER PATIENT POPULATIONS, 1993–1997

Cancer site	Zimbabwe (Harare)		USA (SEER)	
	Black patients	White patients	Black Americans	White Americans
Oesophagus	58	—	63	69
Stomach	62	—	68	72
Colorectal	54	67.5	68	72
Liver	56	—	62	69
Larynx	59	71	62	66
Lung	59	67.5	65	70
Skin melanoma	56	50	64	57
Breast	46	63	57	64
Cervix	46.5	—	50	47
Ovary	45	—	62	64
Prostate	68	70	68	70
Bladder	58	73	71	71
Eye	30	—	3.5	63
Lymphomas	36	—	47	64
Kaposi sarcoma	26	—	37	39

Viewpoint

The shifting epidemiology of colorectal cancer in sub-Saharan Africa

Leolin Katsidzira, Innocent Gangaidzo, Sandie Thomson, Simbarashe Rusakaniko, Jonathan Matenga, Raj Ramesar

Lancet Gastroenterol Hepatol 2017; 2: 377–83

The perception that colorectal cancer is rare in sub-Saharan Africa is widely held; however, it is unclear whether this is due to poor epidemiological data or to lower disease rates. The quality of epidemiological data has somewhat

DGC-Data

SA-MRC / CERC grant

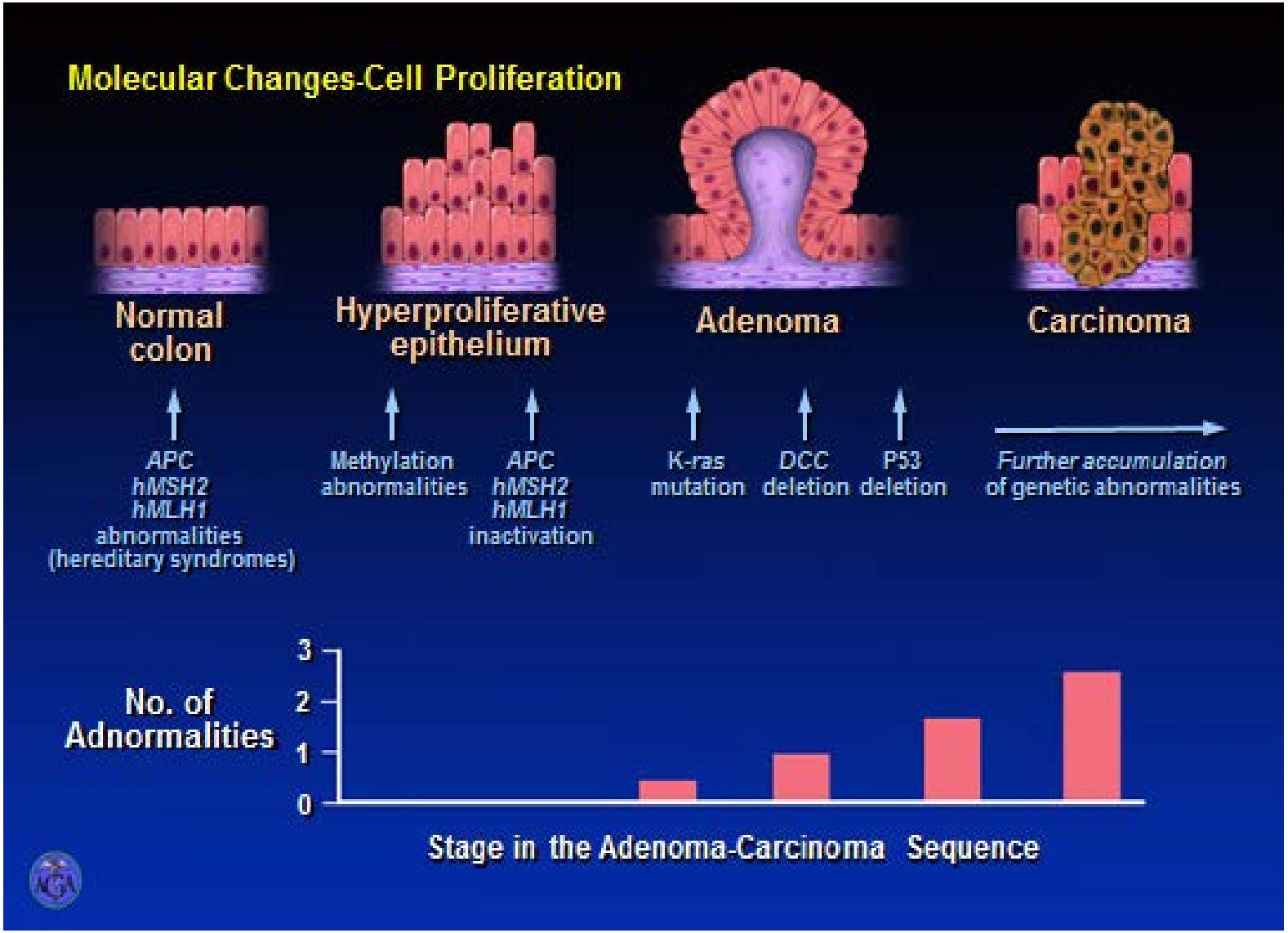
Table 1: Characteristics of colorectal cancer patients

Patient Characteristics		N	%
Demographic characteristics			
Age			
Overall age (median & IQR)	59 (49 - 67)		
Age group			
<=50 years		104	28.97
Over 50		255	71.03
Self-reported race			
Black		189	52.65
White		119	33.15
Indian/Asian		27	7.52
Coloured/ mixed race		24	6.69
Gender			
Male		182	50.7
Female		177	49.3

Clinical features			
Family History of CRC			
Yes		15	4.18
No		344	95.82
Site of malignancy			
Right		64	17.83
Left		100	27.86
Rectal		187	52.09
Missing		8	2.23
AJCC Stage			
Stage 1/2		73	20.33
Stage 3/4		193	54.32
Not staged		91	25.35
Elective vs Emergency			
Elective		162	45.4
Urgent/Emergency		36	10.03
Missing		160	44.57

Risk factors for mortality among colorectal cancer patients

	Univariate Models		Multivariate Model	
Age group		P value		P value
Over 50	Reference			
<=50	1.18 (0.71 - 1.94)	0.525	1.25 (0.67 - 2.31)	0.475
Self-reported race (Black vs other)				
Other	Reference		Reference	
Black	2.19 (1.30 - 3.68)**	0.003	1.59 (0.83 - 3.05)	0.161
AJCC Stage				
Stage 1/2	Reference			
Stage 3/4	4.33 (1.72 - 10.86)**	0.002	3.32 (1.31 - 8.41)**	0.012
Education				
Less than matric	Reference		Reference	
Matric or better	0.32 (0.18 - 0.55)**	<0.001	0.31 (0.16 - 0.59)**	<0.001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DCC deletion
P53 deletion
Further accumulation of genetic abnormalities
No. of Adnormalities
3
2
1
0
Stage in the Adenoma-Carcinoma Sequence

COLON CANCER SCREENING METHODS*

BESEEN GETSCREENED

	FIT	FOBT	CT COLONOGRAPHY (Virtual Colonoscopy)	FLEXIBLE SIGMOIDOSCOPY	COLONOSCOPY
DESCRIPTION	Designed to detect occult blood (blood not seen with the naked eye) in the stool, which may indicate colon cancer.	Designed to detect occult blood (blood not seen with the naked eye) in the stool, which may indicate colon cancer.	Uses computed tomography to create both two-dimensional and three-dimensional views of the inside of the colon and rectum to detect precancerous growths (polyps).	A test where the lower part of the colon and rectum are viewed by the doctor with a sigmoidoscope—a flexible, lighted tube about the thickness of a finger with a small video camera on the end.	A procedure that allows your doctor to look inside the rectum and the entire colon to check for cancer or precancerous growths (polyps) with a thin, flexible tube with a camera attached to it.
HOW IT WORKS	You collect a sample of your bowel movement at home and return the test kit to your doctor or a lab.	You collect a sample of your bowel movement at home and return the test kit to your doctor or a lab.	Your doctor will administer the test in the office, which takes only a few minutes in the scanner, with downtime before and after.	Your doctor will administer the test in the office, which takes approximately 20 minutes.	Your doctor will administer the test in the operating room.
FREQUENCY	EVERY YEAR	EVERY YEAR	EVERY 5 YEARS	EVERY 3-5 YEARS	EVERY 10 YEARS
PREPARATION	• You do not need to follow any diet preparation or changes to your medications	• This test may require that you limit certain foods and medications in your diet	• This test requires fasting • Requires complete cleansing of the colon with a laxative	• This test requires fasting • Requires complete cleansing of the colon with a laxative	• This test requires fasting • Requires complete cleansing of the colon with a laxative
TYPE	NONINVASIVE	NONINVASIVE	NONINVASIVE	INVASIVE	INVASIVE
OTHER CONSIDERATIONS	• At-home stool collection • If the test result is positive, a colonoscopy is needed to find the source of the bleeding • Because there are other conditions that can cause blood in the stool, this may not be as reliable for detection of cancer	• At-home stool collection • If the test result is positive, a colonoscopy is needed to find the source of the bleeding • Because there are other conditions that can cause blood in the stool, this may not be as reliable for detection of cancer	• Useful for people who can't have or prefer not to have colonoscopies • No sedation required • Not covered by Medicare • Not recommended for high-risk patients • For diagnosis only—follow-up colonoscopy required if suspicious areas are found	• Examines the entire rectum, and half of the colon • Requires some type of sedation • Air is put into the colon • Suspicious-looking areas can be removed and biopsied during this procedure	• Examines the entire colon • Removes polyps • Patients receive sedation during the procedure • Prepping for this test requires you to use the bathroom often, stick to a clear liquid diet, and drink a special solution that helps to empty your colon

BeSeenGetScreened.com

*Data on file.

New Colorectal Cancer Screening Guidelines

Adults age 50 and older	
Tests That Detect Adenomatous Polyps and Cancer	
	Flexible sigmoidoscopy (FSIG) every 5 years, or
	Colonoscopy every 10 years, or
	Double contrast barium enema (DCBE) every 5 years, or
	CT colonography (CTC) every 5 years
Tests That Primarily Detect Cancer	
	Annual guaiac-based fecal occult blood test (gFOBT) with high test sensitivity for cancer, or
	Annual fecal immunochemical test (FIT) with high test sensitivity for cancer, or
	Stool DNA test (sDNA), with high sensitivity for cancer, interval uncertain

2011 Guidelines for Colon Cancer Screening

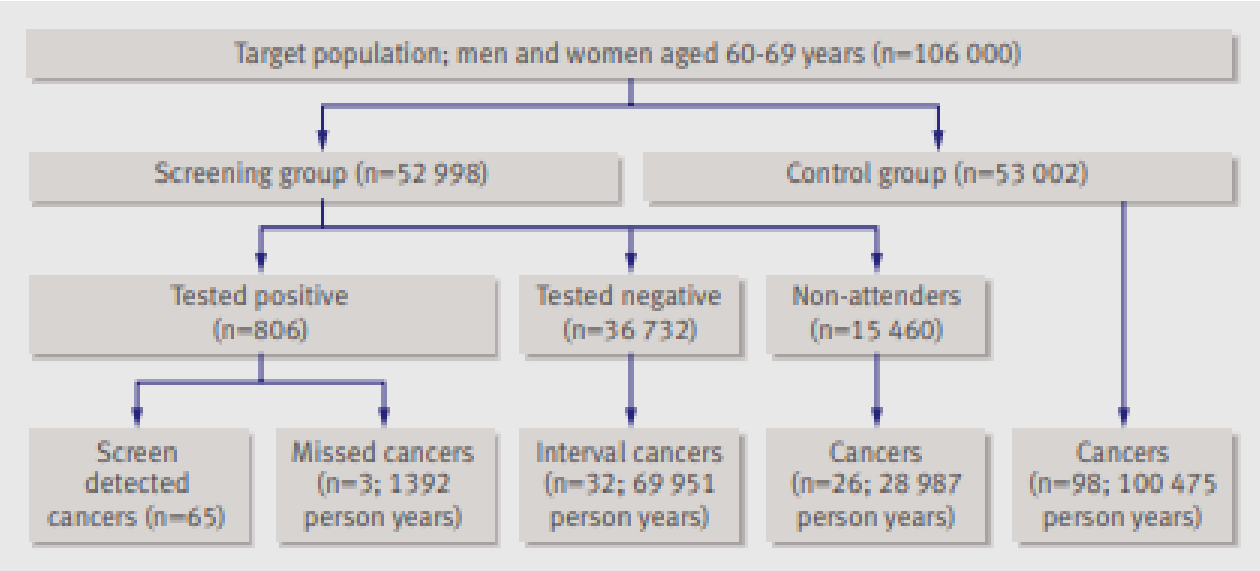
	PATIENT DESCRIPTION	EVALUATION INDICATED		
		stool hemoccult	colonoscopy	sigmoidoscopy
AVERAGE RISK	AGE 50 - No symptoms - Negative family hx (Age 45 for African-Americans)	Annually after colonoscopy	Colonoscopy now, then every 10 years if negative	If colonoscopy is not available, sigmoidoscopy plus air contrast Barium Enema would be an alternative choice
HIGH RISK	ANY AGE ADULT with personal history of colon polyps or cancer 1st degree relative with colon cancer or colon polyps before age 60	Annually after colonoscopy	Colonoscopy every 3-5 years Colonoscopy 10 years earlier than when 1st degree relative was diagnosed	
	Unexplained blood in stool or iron deficiency anemia	————	Colonoscopy now	————
	Ulcerative colitis or Crohn's disease	————	Yearly with biopsies after 7 years of disease	————
OTHER	Other GI symptoms, abdominal pain, narrow stools, constipation or diarrhea, "gas" or distension may indicate the need for a colonoscopy. These are guidelines only. The need for a colonoscopy is based on the patient's individual medical history.			

BMJ

RESEARCH

Test, episode, and programme sensitivities of screening for colorectal cancer as a public health policy in Finland: experimental design

Nea Malila, director of Mass Screening Registry,[1] Tiina Oivanen, chief medical officer,[2] Outi Malminiemi, hospital chemist,[3] Matti Hakama, professor[1,4]



Flow chart of Finnish colorectal cancer screening programme. Screen detected cancers provide no follow-up time in current analysis

DISCUSSION

We found high attendance in the screening programme for colorectal cancer that was run as a public health policy in Finland. The faecal occult blood test was able to detect a major proportion (55%) of cancers in the detectable preclinical phase and more than one third (38%) in the total target population.

Only the faecal occult blood test has been evaluated for effect on mortality when screening for colorectal cancer.[8 9] With screening every two years the reduction in mortality from colorectal cancer varies between 25% at 18 years of follow-up[10] and 12% at eight years of follow-up.[4] In one trial with a follow-up of 18 years, a 20% reduction in incidence of colorectal cancer was also seen.[11] In light of these results several organisa-

Our Reality

- We have a young population
- At the moment we have less colorectal cancer than Europe
- We probably have significant differences of colorectal cancer in different groups of patients
- We can probably expect a significant increase in colorectal cancer (aging population & urbanization)

The Private Sector

- Currently serves about 15% of the population
- Likely that the incidence of CRC is higher in this group
- Resource rich

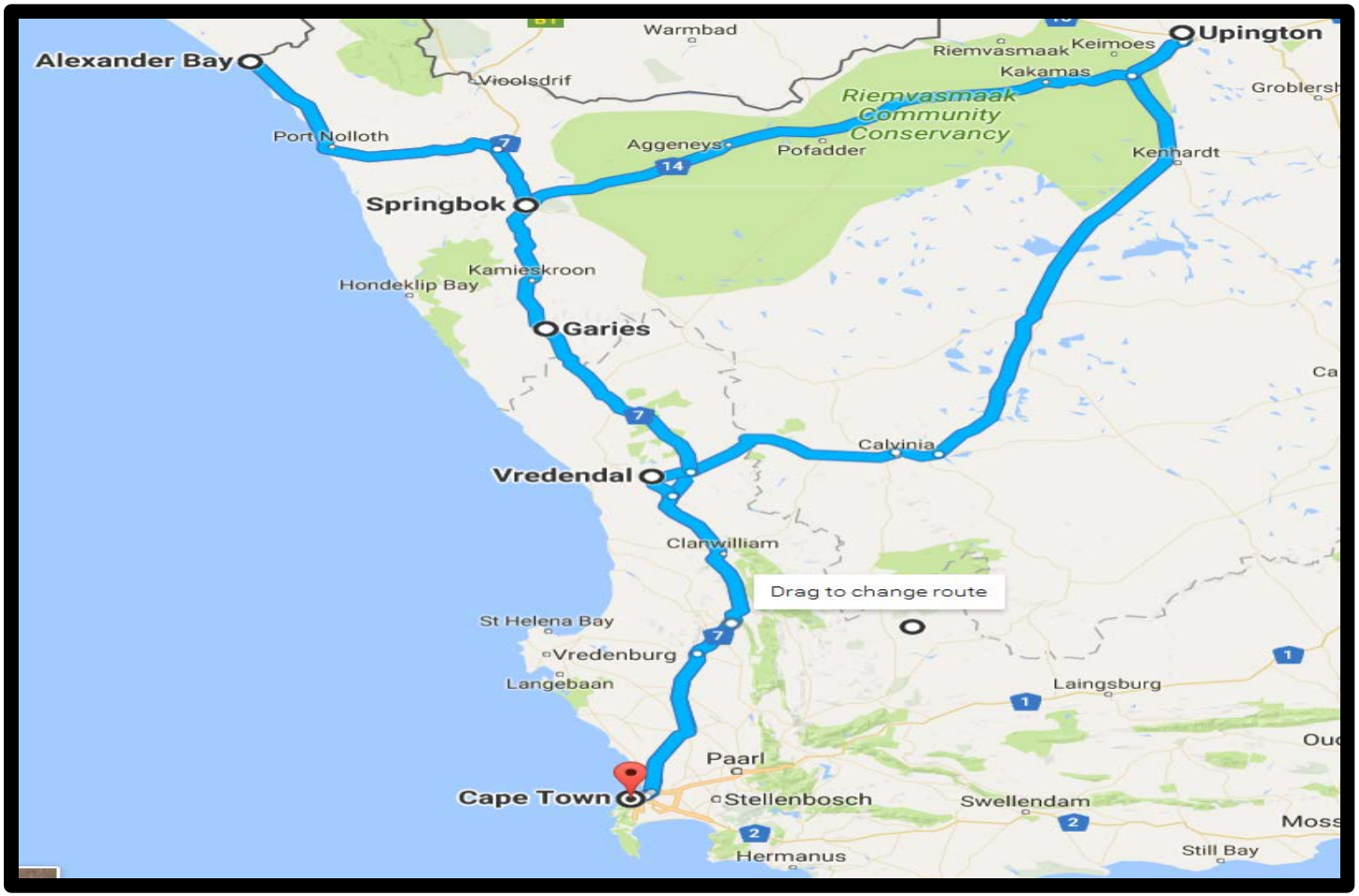
The State Sector

- Can we afford a population based bowel cancer screening program (FOB)
- With the current prevalence of colorectal cancer do we need a bowel cancer screening program . HOWEVER , because of the aggressive nature and early onset ????
- We definitely need more research to evaluate emerging trends – small population based studies (100,000 – Finland)

But

- In a low incidence area do inherited cancer syndromes play a proportionally larger role
- What about targeted surveillance for high risk groups.

HNPCC and the Northern Cape



- 1985 HNPCC diagnosed in a Northern Cape Community
- 1996 R Ramasar identified the first mutation

What is the incidence of CRC in the Northern Cape?

SAJS

General Surgery

Incidence and histological features of colorectal cancer in the Northern Cape province, South Africa

M. Q. WENTINK
M. RÄKERS

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Colorectal Surgery Unit, Department of Surgery, University of Cape Town and Groote Schuur Hospital

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P. A. GOLDBERG, M.MED.

Colorectal Surgery Unit, Department of Surgery, University of Cape Town and Groote Schuur Hospital

3.7/100 000 and histological features suggestive of increased HNPCC

In a low incidence areas does HNPCC play a bigger role?

SAJS

General Surgery

Mismatch repair deficiency in colorectal cancer patients in a low-incidence area

F Vergouwe, A Boutall, D Stupart, U Algar, D Govender, G D van der Linde, A Mall, R Ramesar, P A Goldberg

- 21.8% of cases deficient for hMLH1 or hMSH2
- It would appear that more cancers follow a MMR gene pathway but we have yet to demonstrate that this is due to HNPCC

How do we survey this group?

Original article doi:10.1111/j.1463-1318.2006.01172.x

Mobile colonoscopic surveillance provides quality care for hereditary nonpolyposis colorectal carcinoma families in South Africa

D. W. Anderson*, P. A. Goldberg*, U. Algar*, R. Felix† and R. S. Ramesar†

*Colorectal Unit, Department of Surgery and †MRC/UCT Human Genetics Research Unit, Division of Human Genetics, Institute for Infectious Diseases and Molecular Medicine, University of Cape Town and Groote Schuur Hospital, Cape Town, South Africa

Received 17 November 2005; accepted 28 July 2006

Does targeted surveillance work?

Original article

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Surveillance colonoscopy improves survival in a cohort of subjects with a single mismatch repair gene mutation

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- 129 patients colonoscopic surveillance 49 refused
- Cancers diagnosed 14/129 and 13/49
- Death from colorectal cancer 3/129 (2%) and 6/49 (12%) (P=0.021)

Northern Cape Lynch Syndrome Surveillance trip

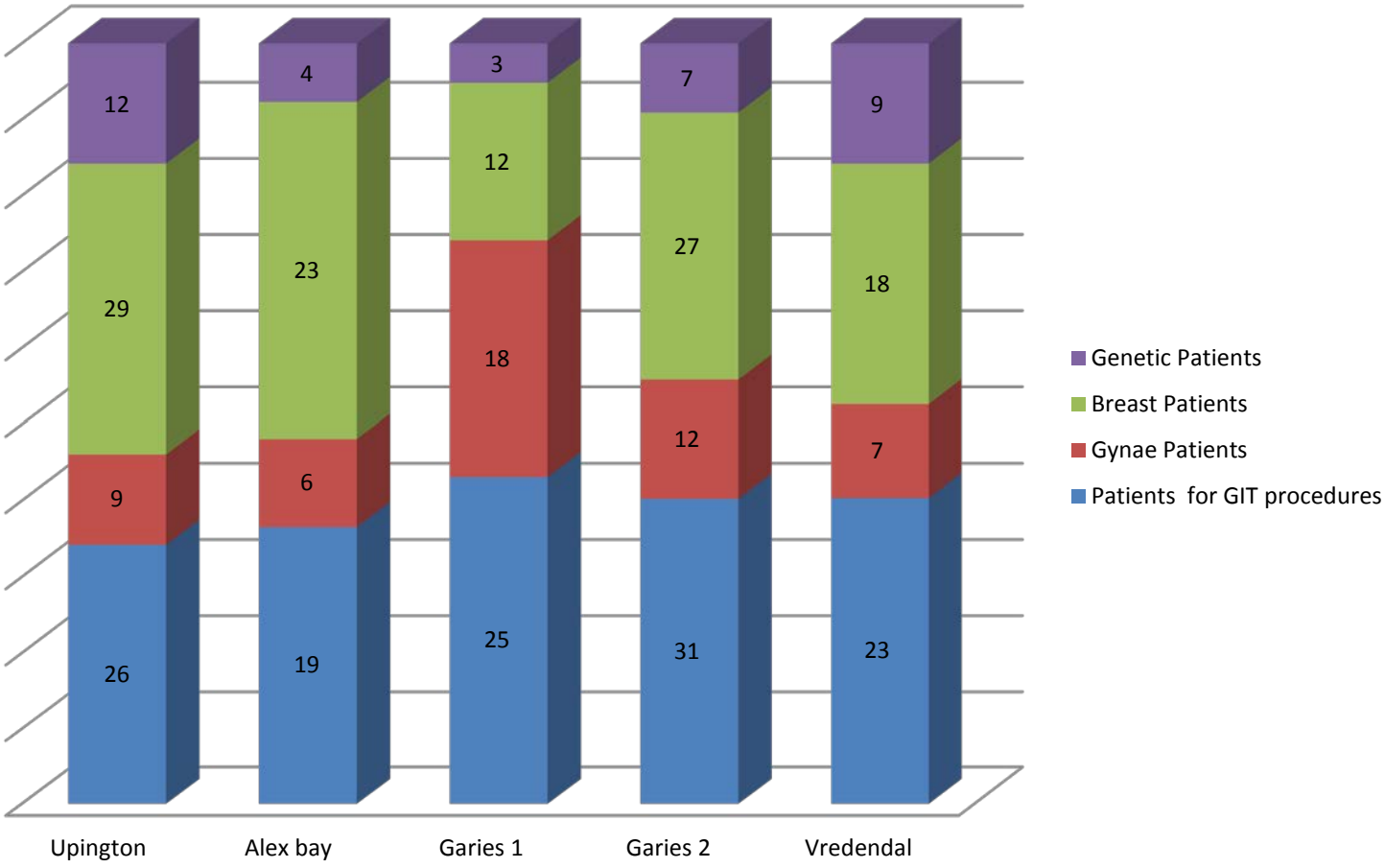
2016 Report

'Splash of Red'

Sunday 27th August - Friday 2nd September

1	Paul Goldberg	GSH Colorectal Surgery	Endoscopist
2	Adam Boutall	GSH Colorectal Surgery	Endoscopist
3	Reid Ally	Baragwanath Hosp. GIT	Endoscopist
4	Faizel Kimmie	KHC Surgery	Endoscopist
5	Klaus Matzel	Coloproctology, University Erlangen, Germany	Endoscopist

Numbers of patients seen per speciality and town



Surveilance/Screening

- Managed to serve a remote high risk community in a low incidence area by
  - Performing targeted outreach colonoscopy
  - With a confirmed survival benefit
  - By offering sub-total colectomy we simplified surveillance and reduced metachronous cancers

Personal History: Surveillance after Initial Colonoscopy

Colonoscopy Findings:	Recommended Interval:
Colon cancer	1 year after cancer resection
No polyp	10 years
Hyperplastic , left- sided	10 years
1-2 Tubular Adenomas < 1 cm	5 – 10 years
Adenoma with low grade dysplasia	5 – 10 years
3-10 Tubular adenomas > 1 cm	3 years
Villous adenoma > 25% villous	3 years
Adenoma with high grade dysplasia	3 years
> 10 adenomas	3 years (genetic testing should be considered- FAP/HNPCC)
Sessile adenomas with piecemeal resection	2-6 months after resection

Conclusion

- Research into colorectal cancer : incidence/pathobiology is desperately needed.
- Cost effectiveness of screening - FOB
- Targeted screening in low incidence, higher risk areas (Young people with aggressive cancer)
- Train : safe and effective colonoscopy