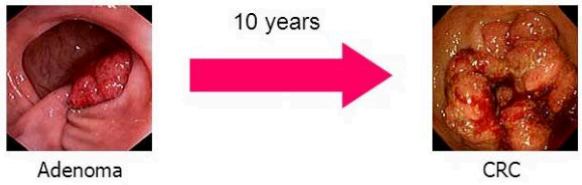
Debate: General surveillance/screening for colon cancer in a resource constrained environment is imperative

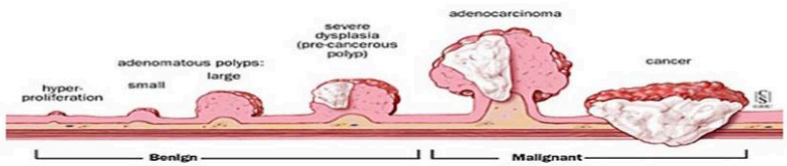
UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Dr. Meryl Oyomno
Department of surgery, University of Pretoria

INTRODUCTION



Screening is the systematic application of a test to identify individuals at sufficient risk of a specific disorder (e.g. colorectal cancer CRC) to warrant further investigation or direct preventive action, amongst asymptomatic persons



- associated with cure and improved survival

CRC screening tests

Average risk individual

- Fecal occult blood test FOBT (1yr)
- Fecal immunochemical test FIT (1yr)
- Multi-targeted stool DNA test (MT-sDNA) (3yr)
- Flexible sigmoidoscopy FS (5yr)
- Colonoscopy (10yr)
- CT colonography (5yr)
- Capsule colonoscopy
- Septin 9 assay.

Table 2. **Screening Tests for Colorectal Cancer**

Screening Test	Sensitivity	Specificity	Cost	Interval	Patient Information
gFOBT	Variable	Variable	Low	Annual	Two samples from 3 consecutive stools at home Low risk Positive result requires follow-up colonoscopy
iFOBT	Variable	Variable	Medium	Annual	Stool sample Low risk Positive result requires follow-up colonoscopy
sDNA	Variable	High	High	Uncertain	Adequate stool sample (30-g minimum) Low risk Positive result requires follow-up colonoscopy
DCBE	Low	Low	Low	5 y	Complete bowel preparation Risks include perforation and bleeding Positive result requires follow-up colonoscopy
Flexible sigmoidoscopy	Medium	Medium	High	5 y	Complete bowel preparation Low risk Positive result requires follow-up colonoscopy
Colonoscopy	High	High	High	10 y	Complete bowel preparation Risks include perforation and bleeding
CTC	Medium	Medium	High	5 y	Complete bowel preparation Low risk Polyps require follow-up colonoscopy

CTC = computed tomography colonography; DCBE = double-contrast barium enema; gFOBT = guaiac-based fecal occult blood test; iFOBT = immunochemical-based fecal occult blood test; sDNA = stool DNA panel.

CRC Surveillance

Table 4 Colorectal Cancer Post-Treatment Surveillance: Common Practices, Data, and Author Recommendations

	Studies For or Against Use	Author Recommendations
Colonoscopy	**FOR:** Frazier et al—high sensitivity and specificity for identifying high-risk polyps or tumors[34] Rex et al and Green et al—CRC patients at high risk for developing second primary, particularly within 2 yrs[35,36]	Recommended at year 1 and, if normal, at 5-yr intervals thereafter; shorter interval (3-yr) recommended if high-risk polyps found at year 1
CT (chest/abdomen)	**FOR:** Pfister et al—can identify liver/lung lesions amenable to curative resection when asymptomatic[37] Tsikiris et al—CT detected asymptomatic recurrence, particularly in second year [39] **AGAINST:** Grossmann et al—routine anatomic imaging did not improve survival at interim analysis[49] Primrose et al—annual CT in addition to CEA did not improve survival (when compared against CEA with CT scan at 12–18 mos) at interim analysis[50]	Recommended annually for 3 yrs for those with stage II or stage III disease deemed at high risk for recurrence
CEA	**FOR:** Tjandra et al—associated with higher probability of detection of recurrence when asymptomatic[40] Makela et al—CEA elevation most common indicator of disease recurrence[47] Tsikiris et al—CEA detected most recurrences, particularly in second year[39]	Recommended every 3 mos for first 3 yrs then every 6 mos for 2 yrs, given that highest rate of recurrence is within 3 yrs and 95% of recurrences occur within 5 yrs

CEA = carcinoembryonic antigen; CRC = colorectal cancer.

Table 3 Published Colorectal Cancer Surveillance Guidelines

	History and Physical	CT (Chest/Abdomen/Pelvis)	CEA	Colonoscopy
ASCO (stage II/III)	Every 3–6 mos × 3 yrs; every 6 mos at years 4 and 5	Annually × 3 yrs if high risk	Every 3 mos for at least 3 yrs	At 3 yrs and then every 5 yrs thereafter
NCCN (stage I–III)	Every 3–6 mos × 2 yrs; every 6 mos in years 3–5	Annually for up to 5 yrs, especially if high risk	Every 3–6 mos × 2 yrs; every 6 mos in yrs 3–5	At years 1 and 4, then every 5 yrs
ASCRS (stage I–III)	At least every 4 mos for 2 yrs	None	At least every 4 mos for 2 yrs	Every 3 yrs
UK (stage I–III)	None	CT of abdomen and pelvis only, once within 2 yrs	None	Every 5 yrs

ASCO = American Society of Clinical Oncology; ASCRS = American Society of Colon and Rectal Cancer Surgeons; CEA = carcinoembryonic antigen; NCCN = National Comprehensive Cancer Network; UK = United Kingdom 2010 guidelines.

- **Debate:** General surveillance/screening for colon cancer in **“a resource constrained environment”** is imperative

Arguments against CRC screening

1. CRC incidence
2. Need for basic health care rather than preventative measures
3. Evidence for screening, how good is it?
4. False positives and negatives
5. Complications
6. Overall mortality
7. Means and resources
8. Poor attendance/ non-compliance
9. Personal responsibility
10. Socio-economic status SES
11. Culture

1. CRC Incidence

- Worldwide: 3rd most commonly diagnosed cancer.

- UK: ♀ 2nd most common cancer after breast Ca.

  ♂ 3rd most common cancer after prostate and lung

  >36,000 new cases diagnosed each year

- South Africa:

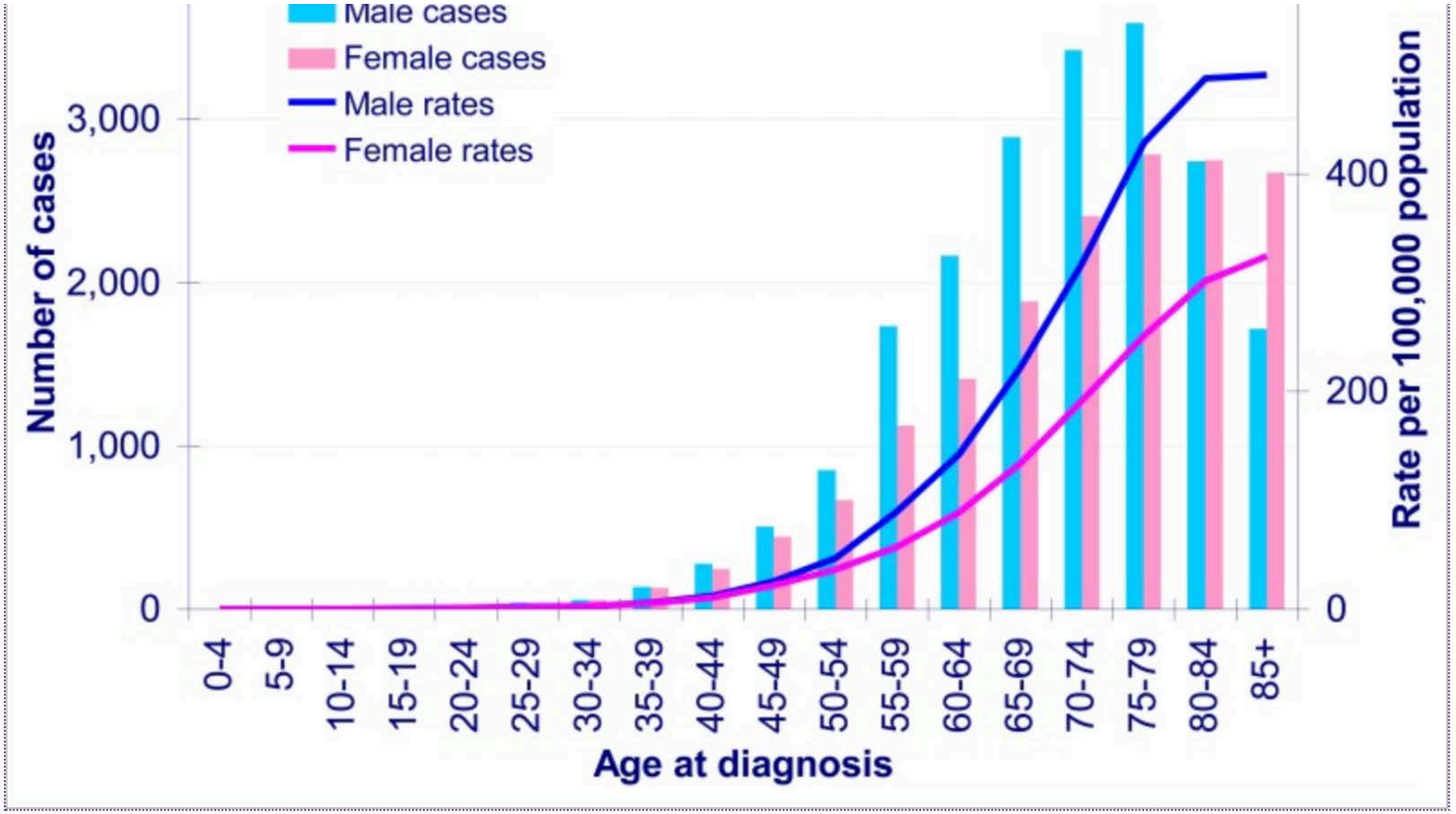


Figure 1.5 Number of new cases and age-specific incidence rates by sex, colorectal cancer, UK, 2005

From: 1 Epidemiology

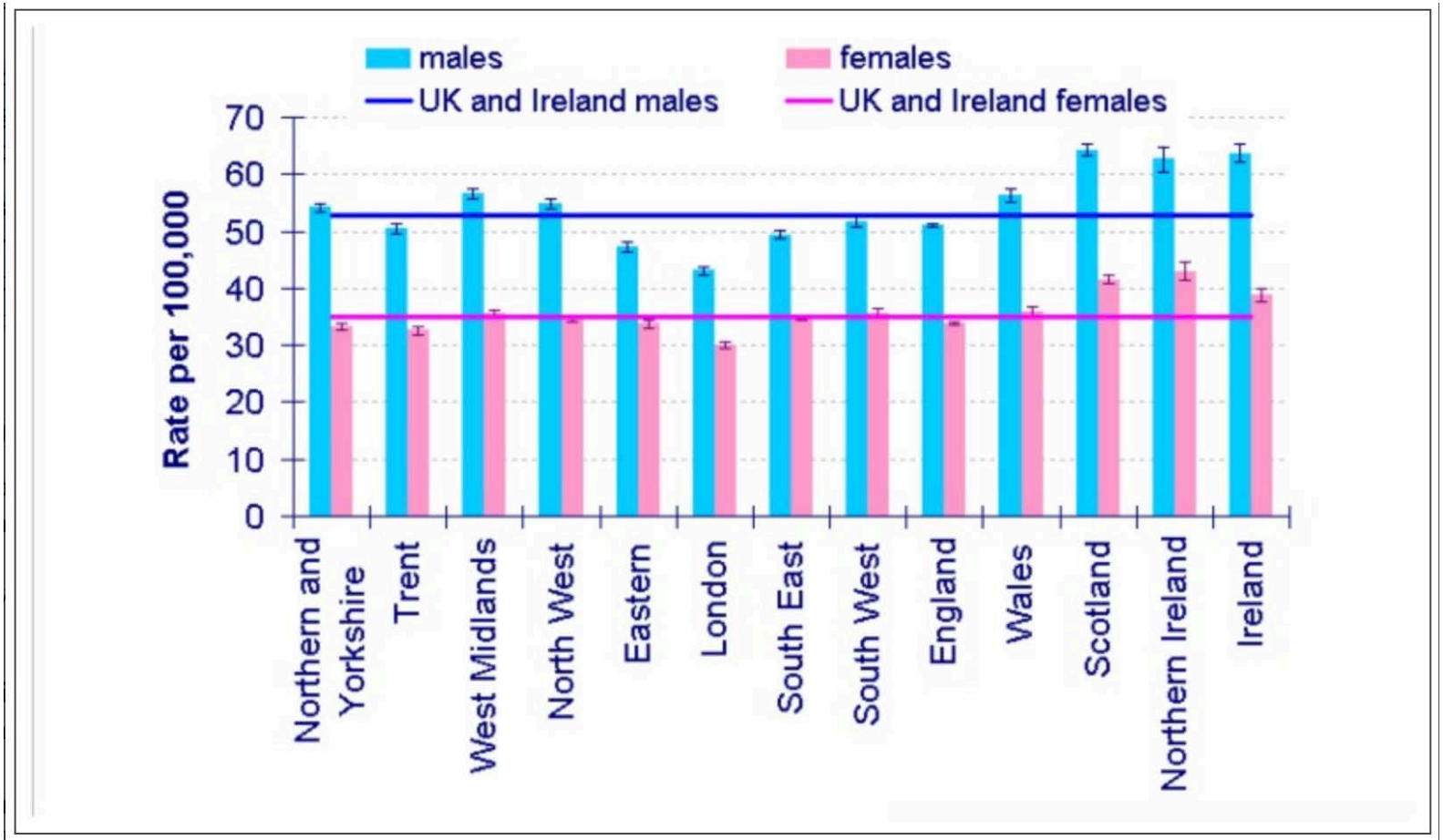


Figure 1.6

Age standardised incidence rates by sex, colorectal cancer, regions of England, Wales, Scotland, Northern Ireland and Ireland, 1991–1999.

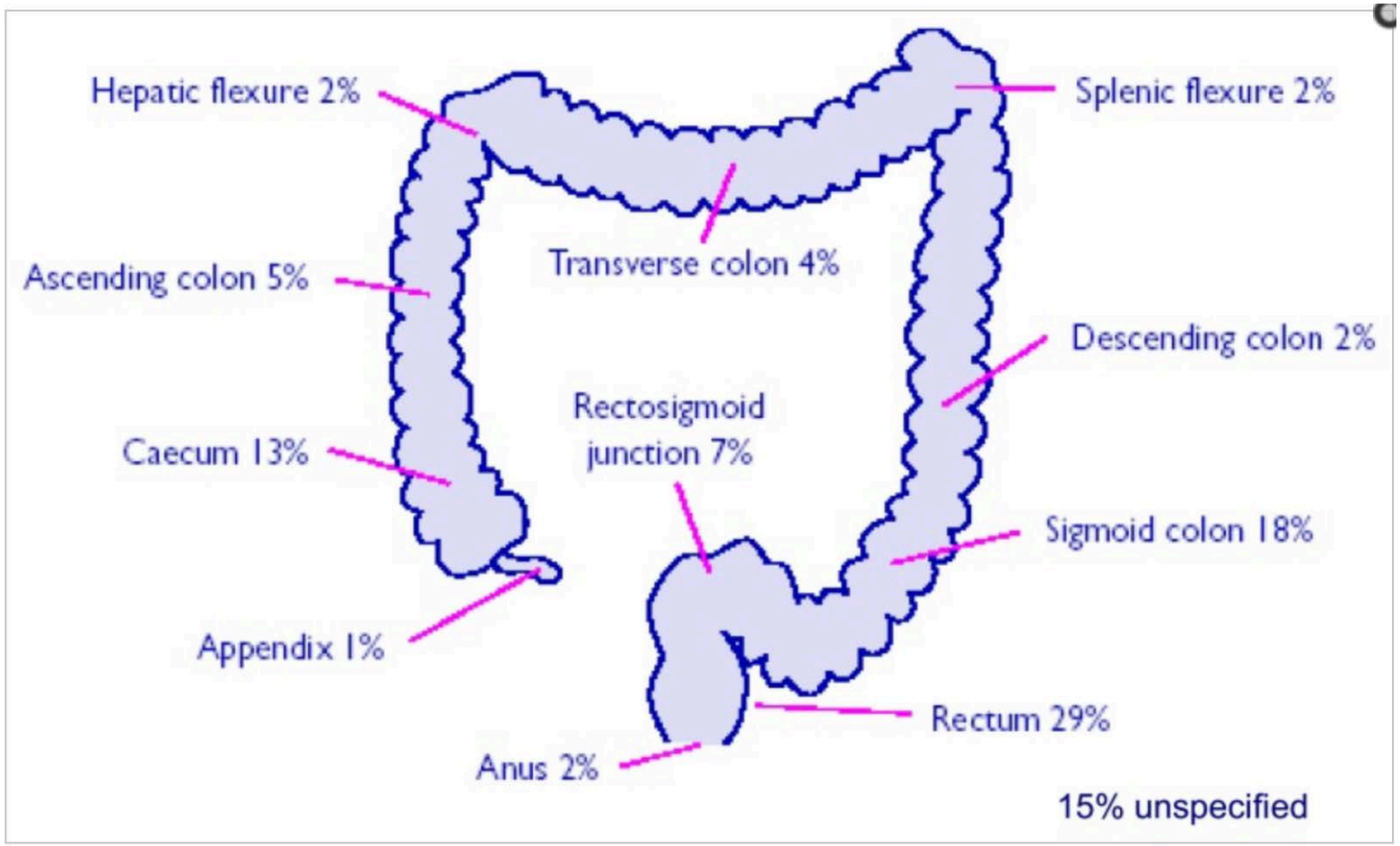


Figure 1.4 Percentage distribution of cases by site within the large bowel, England, 1997–2000

From: 1, Epidemiology

Colorectal Cancer: The Diagnosis and Management of Colorectal Cancer.
NICE Clinical Guidelines, No. 131.
National Collaborating Centre for Cancer (UK).
Cardiff: National Collaborating Centre for Cancer (UK); 2011 Nov.

2. Need for basic health care rather than preventative measures

- Developed countries have already secured certain standards of healthcare for the sick e.g. childhood vaccination, maternal health etc. and therefore screening can be next on the agenda

- Developing countries this isn't the case. There is a need to ensure equitable distribution of the little available resources.

- Focus on the basics with the little resources available e.g. childhood vaccination, decreasing maternal obstetric and neonatal mortality, so as to achieve maximal impact and good for the larger population.

3. Evidence for screening, how good is it?

Fecal occult blood test FOBT:

- RCT showed a 15 - 33% decrease in mortality from CRC after 8 - 13 yr. follow-up period
- With 5% lifetime risk of CRC and 50% mortality from the disease, the risk of dying from CRC is 2.5% without FOBT.. About 98% of us will die from something else. How do you sell these figures to doctors and the public?

Flexible sigmoidoscopy FS:

- A single FS screening between ages 55 and 64 years was associated with a substantial reduction of CRC incidence and mortality. CRC incidence was reduced by 31% (RR = 0.69; 95% CI = 0.56 to 0.86) and mortality was reduced by 38% (RR = 0.62; 95% CI = 0.40 to 0.96) compared with the control group.
- Norwegian Colorectal Cancer Prevention (NORCCAP) screening study: no difference in diagnostic yield between the FS group and the FS plus FOBT group screening with regards to detection of CRC or high-risk adenomas

Annals of Internal Medicine®

ORIGINAL RESEARCH | 5 JUNE 2018

Long-Term Effectiveness of Sigmoidoscopy Screening on Colorectal Cancer Incidence and Mortality in Women and Men: A Randomized Trial

*Øyvind Holme, MD, PhD *; Magnus Løberg, MD, PhD *; Mette Kalager, MD, PhD *; Michael Bretthauer, MD, PhD; Miguel A. Hernán, MD, DrPH; Eline Aas, PhD; Tor J. Eide, MD, PhD; Eva Skovlund, MSc, PhD; Jon Lekven, MD, PhD; Jörn Schneede, MD, PhD; Kjell Magne Tveit, MD, PhD; Morten Vatn, MD, PhD; Giske Ursin, MD, PhD; Geir Hoff, MD, PhD; for the NORCCAP Study Group† †*

Norwegian RCT (1999-2001 & 15yrs follow-up)

- Adults 54-64yrs at base line
- Screening FS vs. FS+FOBT
- Norwegian Colorectal Cancer Prevention (NORCCAP) Trial

Measurements: Age-adjusted CRC incidence and mortality stratified by sex

RESULTS:

- 98,678 persons (20,552 screened, 78,126 no screening)
- Adherence: women 64.7%, men 61.4%
- **Absolute risks for death from CRC in women: 0.60% in the screening group and 0.59% in the control group** (risk difference, 0.01 percentage point [CI, −0.16 to 0.18 percentage point]; HR, 1.01 [CI, 0.77 to 1.33]), in men were 0.49% and 0.81%, respectively (risk difference, −0.33 percentage point [CI, −0.49 to −0.16 percentage point]; HR, 0.63 [CI, 0.47 to 0.83]) (P for heterogeneity = 0.014).

CONCLUSION: Offering sigmoidoscopy screening in Norway reduced CRC incidence and mortality in men but had little or no effect in women.

4. False positives and negatives

FOBT (Haemoccult II) uses guaiac, a resin that oxidizes and changes color in the presence of hemoglobin.

Main causes of Hemoccult II inaccuracy

	False positives	False negatives
Dietary reasons	• Red meat • Horseradish • Turnips	• Vitamin C • Antioxidant
Digestive reasons	• Gingivitis • Epistaxis • Gastritis • Inflammatory disease • Diverticular disease • Anal fissures • Hemorrhoids	• Less vascularized cancers • Less voluminous cancers • Localization in the right colon or the caecum

- A poor test (30% specificity, 98% sensitivity)
- 2 – 17% positive predictive value (≈ 98% of patients with a positive FOBT, have a normal colonoscopy)

- Anxiety and psychological harm
- Wasted resources
- False sense of security
- Late diagnosis with poor outcome

5. Complications

Screening: "healthy", asymptomatic individuals

- NORCCAP Trial: 6 perforations (1:336)
- Rectal bleeding requiring admission
- Perforation rate of 1:769

Complications associated with a colonoscopy

Intestinal perforations:
Intestinal perforations occur at a rate of 1 per 2,222 colonoscopies; however, depending on the study, the rate has also been seen to vary enormously, ranging from 1 per 716 to 1 per 16,810.

Hemorrhages:
The rates for significant hemorrhages are considerable, starting with 1 in 81 in the presence of a polypctomy, to 1 in 1,352 without polypctomy.

Cardiovascular complications:
Some data report up to 20%; these are side-effects of the intestinal cleaning and the sedation.

Infections:
According to one study, 24% of endoscopes were contaminated and two cases of hepatitis C were documented in France.

Mortality:
1 in 16,745.

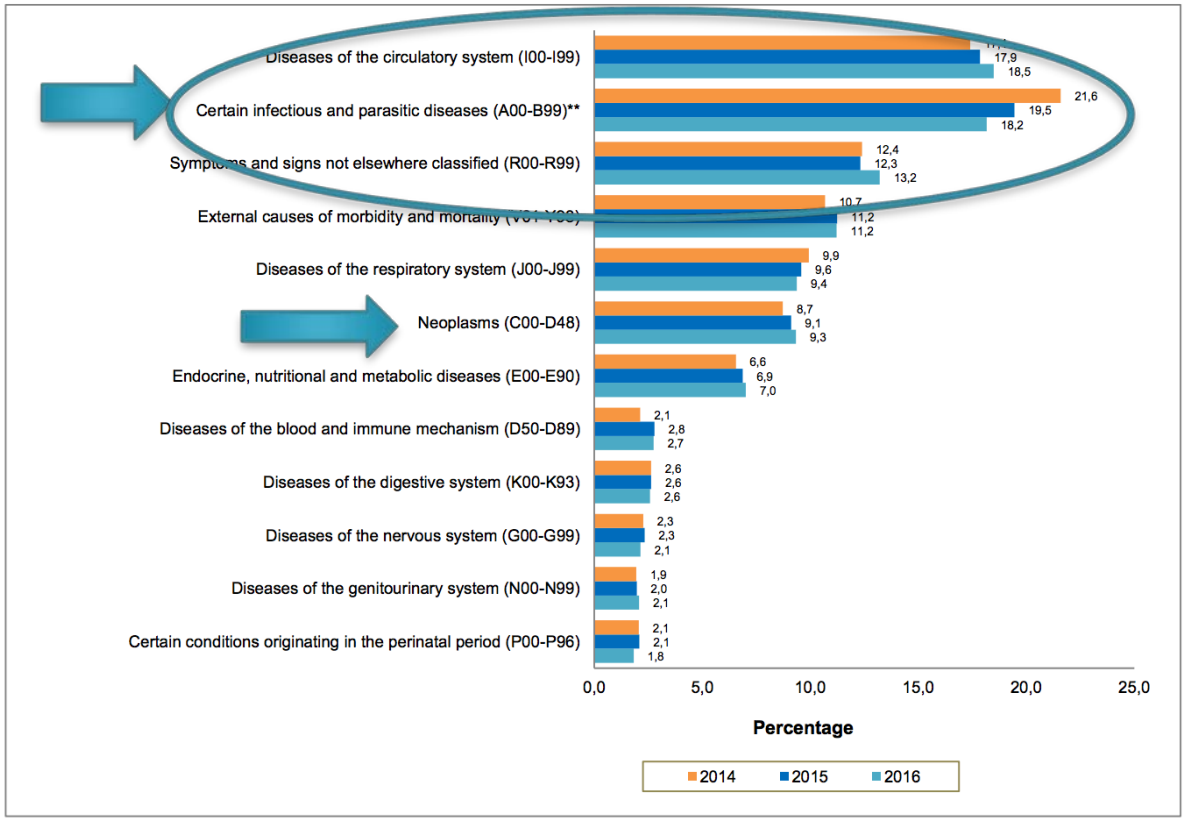
Morbidity:
The operative morbidity associated with the resection of polyps that can be resectioned per colonoscopy ranges from 1% to 7%.

- Infection secondary to contaminated scopes
- Cardiovascular complications of mechanical bowel preparation and sedation
- Mortality rate: 1 in 16,745

6. Overall mortality

STATS SA
STATISTICS SOUTH AFRICA

Figure 4.1: Percentage distribution of deaths by selected main groups of causes of death, 2014–2016



*(1) Data for 2014–2015 have been updated with late registrations/delayed death notification forms processed in 2016/2017.
(2) Excluding main groups with less than 1% of deaths.
** Including deaths due to *MDR-TB* and *XDR-TB*.

- While screening decreases CRC inherent mortality, it does not decrease overall mortality.

7. Means and resources

Do we have enough trained endoscopists?

UK

- Only 17.0% of colonoscopists have received supervised training for their first 100 colonoscopies and only 39.3% have attended a training course (Bowles et al. 2004)
- 2013: 1,289 trained medical gastroenterologists (Romaya C & Lockett M. 2013, GASTROENTEROLOGY WORKFORCE REPORT)

SA

- population of 57.7million
  - 3.2 million persons over 64 years
  - 36.9 million between 15 and 64 years old.
- < 500 trained colonoscopists

Currently, we simply do not have enough trained endoscopists.

8. Poor attendance

- Danish RCT: FOBT biennial screening
  - The more screening rounds individuals are enrolled into, the poorer the attendance.
  - lesser reduction in mortality from CRC. Dropped from 18% to 11% after 5 screening rounds

9. Personal responsibility

- Some may abandon healthy lifestyles if they believe that screening will pick up cancers at an early stage when it is more likely to be curable.

10. Socio-economic status

Gap between the rich and poor

Canada (1997-2001)

- 1 664 188 people, 21.2% received a colorectal investigation
- Multivariate analysis: significant association between receipt of any colorectal investigation and income ($p < 0.001$);
- People in the highest-income quintile had higher odds of receiving any colorectal investigation (adjusted odds ratio [OR] 1.38; 95% confidence interval [CI] 1.36–1.40) and of receiving colonoscopy (adjusted OR 1.50; 95% CI 1.48–1.53).

These inequities persisted even after the launch of the programs to widely educate the public

Ontario Canada study (2005 – 2011)

- Immigrants and the poor are less likely to be screened for CRC
- Residents living in low-income neighborhoods were consistently and significantly less likely to have a FOBT and be 'up-to-date' with CRC screening than long-term residents living in high-income neighborhoods (2.9-4.5%; 14.7-17.3% respectively).

11. Culture

Alex residents kill owls because they are used for 'witchcraft'

ALEXANDRA – Owls released in Alexandra as part of the City of Joburg's multi-million rand project to combat a rodent infestation are allegedly being killed by residents.

October 13, 2014

Alex township owl day a hoot

2016-06-08 13:57

Ahmed Areff, News24

news24

Johannesburg - Paintings of owls adorned the fences of five schools in Alexandra this week, to highlight the importance of these rodent-killing birds of prey.

The Township Owl Project's Kefiloe Motaung said 750 pupils from the Carter, Iphutheng, and Zenzeleni primary schools, Marlboro Gardens Combined School, and Minerva Secondary School, painted pictures of owls on recycled wooden templates and put them up on Monday.

A banner, with the each school's name and the words "Alex Owl Day", was displayed on the schools' perimeter fences.

"The learners' owl artwork was judged by a local actress, Itumeleng Bokaba, and the winning

(Supplied, Alexandra Township Owl Day)

- Screening modalities should be culturally appropriate to the target population.
- Public education

Summary

- The ideal screening method
- Money wasted on colonoscopy and consultation fees following false positive screening tests.

- A resource-constrained environment,
- Equitable distribution resources
- Wiser to spend this money on treating actual patients with CRC rather than healthy members of the public.

- First determine local data (incident rates, age etc.)
  - CRC data base (screening, stage, surveillance)
  - Finnish model

- Ensure that there will be adequate numbers of trained endoscopists to carry out safe screening colonoscopy for those that will have positive screening tests

- Screening should only be done if it is done in an organized fashion and linked to quality assurance programmes.

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Thank you