Mr Chris Wakeman

General Surgeon

University of Otago, Christchurch

Saturday, August 13, 2016

(Plenary)

12:15 - 12:40 Management of Colorectal Cancer

Bowel cancer

Chris Wakeman

Colorectal Surgeon

Christchurch

Audrey Hepburn

Queen Elizabeth The Queen Mother

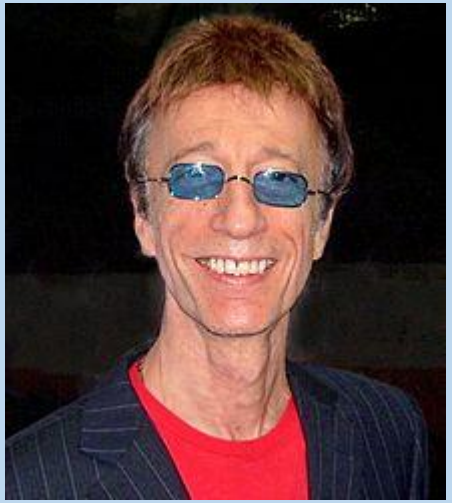
Sam Simon (Simpsons)

Elizabeth Montgomery (bewitched)

Bobby Moore

Malcolm Marshall

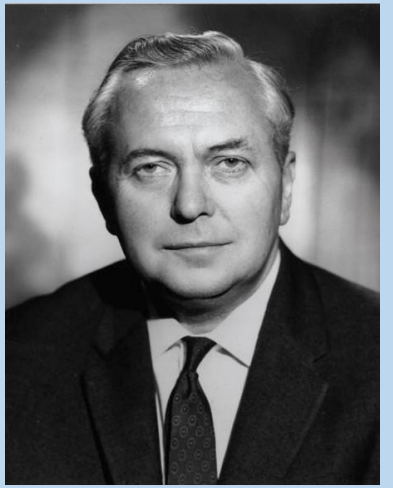
Ronald Reagan



Robin Gibb

Vince Lombardi

Charles M. Schulz

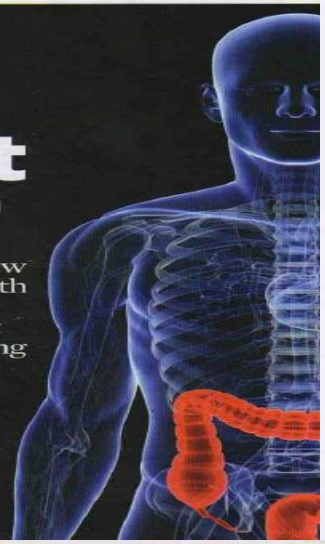


Harold Wilson

The silent killer

More than 100 New Zealanders a month die from bowel cancer. Why don't we have a screening programme?

by RUTH LAUGESEN



Are you at risk?

See your GP if you notice any of the following:

- Rectal bleeding
- Changes in bowel habits, including diarrhoea or constipation
- Feeling that your bowel doesn't empty completely
- Abdominal pain

Excessive worry is not the right response to bowel cancer symptoms. In most cases, the symptoms will have another cause. The Waitemata screening pilot is finding cancer is the cause in only about 2% of people with microscopic blood traces in the stool and other studies have found that symptoms at primary-care level are predictive of bowel cancer in only 5% of cases.

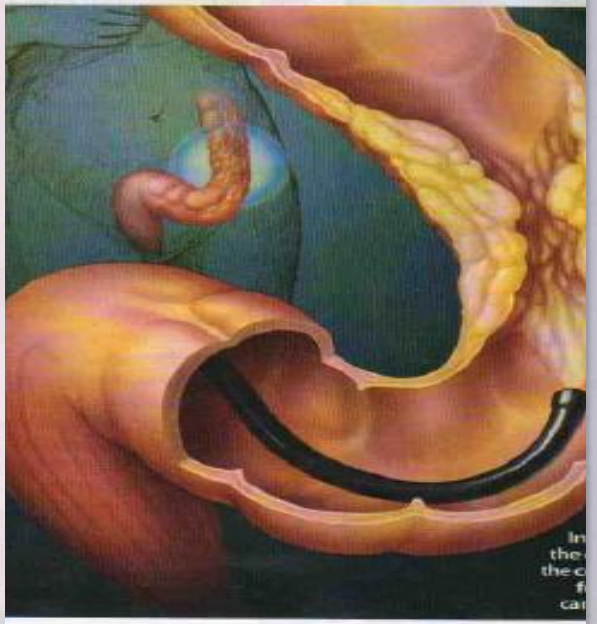
year-olds who can afford to
t peace of mind, many GPs are
ling colonoscopies because
sing risk of bowel cancer as
At 50 you have a one in 300
tting the disease; by 60 that has
in 100; and by 75 to one in 20.

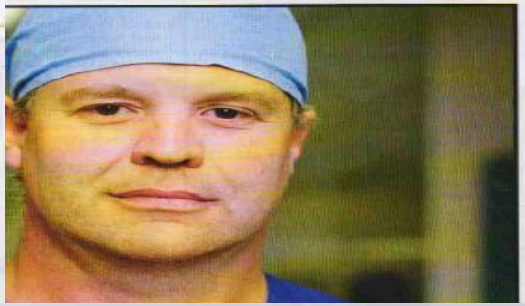
Colonoscopies are particularly recommended for those with a family history of bowel cancer.

The highly invasive procedure costs $1500-2800. It involves insertion in the anus of a flexible metal rod with a wide-angle camera lens at the end of it. Pictures are transmitted to a monitor watched by a specialist, who scans the entire length of the colon. As well as looking for tumours, the specialist can remove potentially cancerous polyps.

Many people dread colonoscopies, partly because of a requ
drink large quantities of
day before to purge the
partly because the proce
undignified and can be
Sedatives and painkillers
sedatives have an amnes
ing the patient often late
discomfort. The procedu
a risk of perforation of th
is higher in older people
illnesses.

A newer, less intrusive
flexible sigmoidoscopy,
that looks only at the rec
part of the colon. The pr
between $1200 and $20
and less uncomfortable,
doesn't require purging.
are found, a full colonosc
recommended.





Mike Hulme-Moir: Bowel cancer surgery is "a much bigger deal than having a hip replaced or knee done [or a] hysterectomy".

A malignant polyp grows and takes up room in the bowel tube, sometimes blocking it. It goes on to grow through the muscle layers of the bowel and through its wall, and if not detected in time can spread to organs close by, such as the bladder, the uterus or prostate, or through the bloodstream to the liver, or to other organs through the lymphatic system.

Some patients have tell-tale symptoms – changes in bowel habits, blood in their stool or abdominal pain. But some notice nothing until it is very late in the piece. One recent New Zealand survey found that one in 10 cases were only discovered when sufferers turned up at accident and emergency

Rachel Holdaway took six months to feel well again.

Athlete's lucky escape

After getting over early-stage bowel cancer, an Ashburton woman is working to raise awareness of the disease.

Rachel Holdaway was 41 and training for a duathlon. But instead of her usual fit, vigorous self, she was feeling bad. "It was getting to the stage where I couldn't even complete the run part of my training." She was exhausted, with legs that felt like lead.

"I also had overwhelming urges to go to the toilet; I was bleeding from the bottom. I put it down to increased exercise and haemorrhoids. I minimised my symptoms until it got to the point where I couldn't ignore them any more." After seeing her doctor, she had a colonoscopy.

She turned out to have a 4.5cm-long tumour on the wall of the rectum and was operated on towards the end of the same month, in May 2006. The cancer was not advanced and she didn't require chemotherapy.

Recovery from surgery was slow, however. Her rectum was removed and a new one constructed from the colon. To allow that to heal, the large bowel was temporarily bypassed by making an opening in the stomach and bringing the end of the small intestine to the surface, a procedure called an ileostomy. This was then connected to an external bag that collected waste.

At first Holdaway found the bag "totally repulsive", and couldn't even look at it. But within a short time she became used to it and comfortable changing it. After eight weeks the ileostomy was reversed, "and they plumbed me all back up".

"Initially, I did find it difficult to talk about it. But I'm over it now, and I like to be open about it because it's just another part of the body like the heart or whatever."

Holdaway, whose experience led her to set up a patient advocacy group for bowel cancer, Beat Bowel Cancer Aotearoa, says it took six months to feel well again. She quit her job as a pharmacy technician and now works on the family cropping farm near Ashburton, combining that with her advocacy work. She has been healthy since. "I feel I'm very lucky."

"Initially I did find it difficult to talk about it. But I'm over it now and I like to be open about it."

occurs before your 25th birthday.

"It could be some early exposures change the risks of developing adenomatous polyps in the bowel. And it may be that there are some aspects of adult diet that influence whether those adenomas develop into a full-blown cancer." Factors in childhood might include diet, or they might be related to the combination of bacterial flora present in the gut.

EARLIER THE BETTER

Hulme-Moir says one of the heartening features of the screening programme is that he now sees more cases of early-stage bowel cancer, for which there is a 90% chance of successful treatment. "As a bowel cancer surgeon, I want to cure patients, and I know if we get them early we can cure them," he says. Some tumours are so small they can be cut out at the colonoscopy stage.

New Zealand has a particularly atrocious record internationally in early detection of bowel cancer. A 2009 study that compared New Zealand with Australia, the UK, the US and Hong Kong found we had the lowest proportion of surgically curable, early-stage cancer. In this country one in five cases has metastasised, which is often considered a death sentence, by the time it is diagnosed.

The Waitemata screening trial, which began in October 2011, will run for four years at a cost of $26 million. Some 137,000 people in the Waitemata DHB area will be offered the faecal occult blood test, which is done using a stool sample. Fears people would not take part have been allayed, as more than half of those offered the test have taken it up – a high turnout by world standards. By September, almost 23,000 samples had been returned, with 1400 positive for microscopic traces of blood. Of those, more than 900 had a colonoscopy to look for signs of cancer.

Colonoscopies are one reason most of us never want to have to think about bowel cancer. As University of Auckland oncology professor Michael Findlay puts it, screening procedures for breast and cervical cancer are bad enough, but "to be told the screening process contains the potential for a 1m-long steel tube [to be inserted] up your bum, most people don't go for that".

Findlay says anyone advised by his or her GP to get a colonoscopy should consider having it done privately.

The procedure, which is carried out under sedation and involves insertion of a flexible metal rod with a camera on the end, delivers impressive results. The operator can not only look for tumours, but also remove any precancerous polyps or any that are in the early stages of malignancy, lowering risks for the future. (As a bonus, the patient gets pictures of his or her insides to take home.)

Figures from the screening programme show polyps were removed from 700 of the 900 people colonoscoped, a much higher rate than expected. A total of 35 cancers were detected and treated, corresponding to about 2.2% of those with a positive blood test. Although the latest figures have yet to be released, the number of cases of bowel cancer detected through the screening programme is now over 50, says Hulme-Moir.

Clinicians working in the field are impatient for national bowel cancer screening to go ahead. Beat Bowel Cancer Aotearoa is even arguing that the need for screening is so urgent it should proceed before the Waitemata pilot programme finishes.

How many lives might be saved? Overseas trials suggest screening can reduce bowel cancer deaths by 15%. But according to Otago's Cox, in practice the number of lives saved would be smaller because of the difference between trials and the real world. He calculates actual lives saved each year would be 6.8% of those who die, or about 86 people. The estimated cost of a national screening programme is $60 million. Put crudely, that's about $700,000 a life.

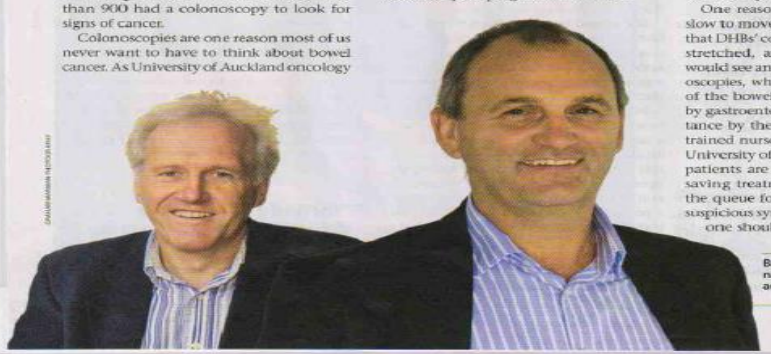
Would 86 lives saved a year be worthwhile? One comparison is the national breast-screening programme, BreastScreen Aotearoa, which offers screening at a cost of $56 million. On Cox's estimates, this screening programme is preventing 5.3-7.5% of breast cancer deaths a year, representing 35-49 women's lives, or half as many lives as a bowel screening programme.

GOVERNMENT COMMITMENT WANTED

Beat Bowel Cancer's Holdaway considers Cox's estimates make a strong case for bowel screening. "His figures just highlight how incredible and outrageous it is that we don't have a commitment from this Government to a national roll-out of a bowel-cancer screening programme. We call on the Government to commit to this roll-out in the upcoming Budget."

Cox favours a different kind of national bowel screening, using a flexible sigmoidoscope to view the rectum and a short part of the bowel, the area where two-thirds of the cancers are found. These would be offered once in a lifetime, not every two years as the faecal occult blood test is. The UK is to begin offering the test at age 55 as part of national screening. Cox has calculated 120 lives a year in New Zealand would be saved by doing something similar.

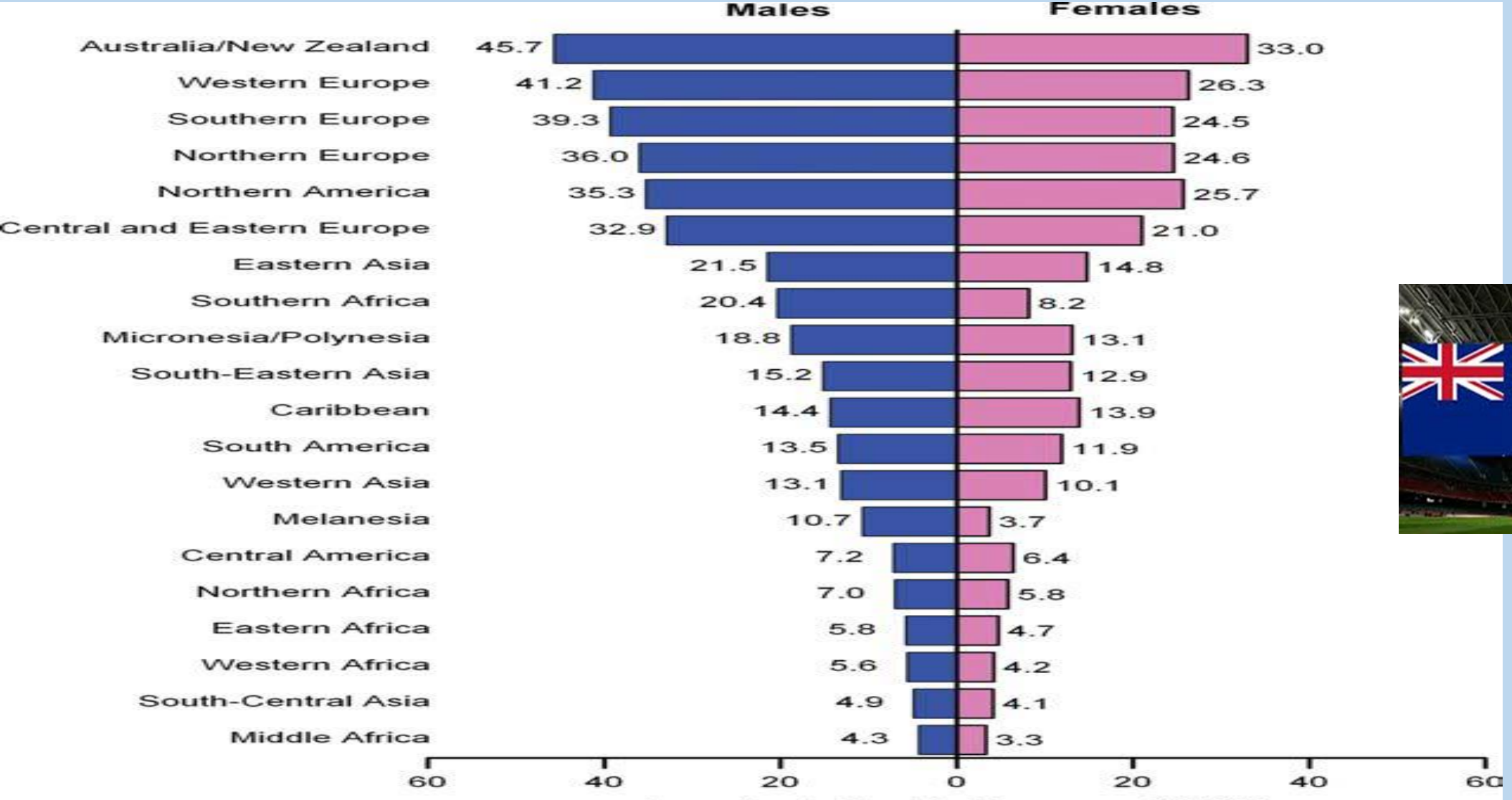
One reason the Government has been slow to move on a screening programme is that DHBs' colonoscopy services are already stretched, and a screening programme would see an explosion in demand. Colonoscopies, which carry a risk of perforation of the bowel, are traditionally performed by gastroenterologists, and there is a reluctance by the profession to allow specially trained nurses to carry out the procedure. University of Auckland's Findlay says some patients are already missing out on life-saving treatment because of a logjam in the queue for colonoscopies to check out suspicious symptoms. He says ideally someone should get a colonoscopy within a

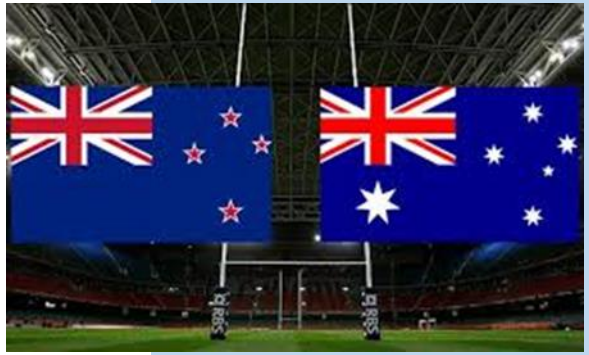


Brian Cox and Michael Findlay: national bowel-screening advocates.

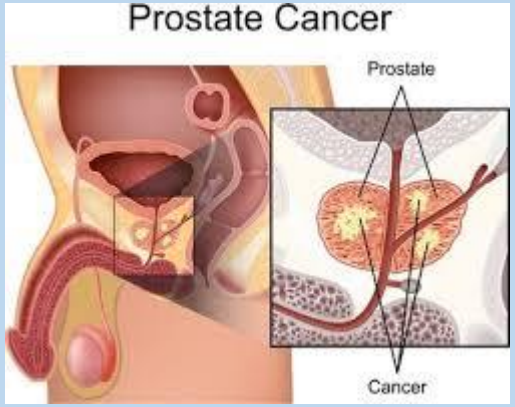
Age-Standardized Colorectal Cancer Incidence Rates by Sex and World Area.

Global Cancer Statistics A CANCER J CLIN 2011;61:69–90

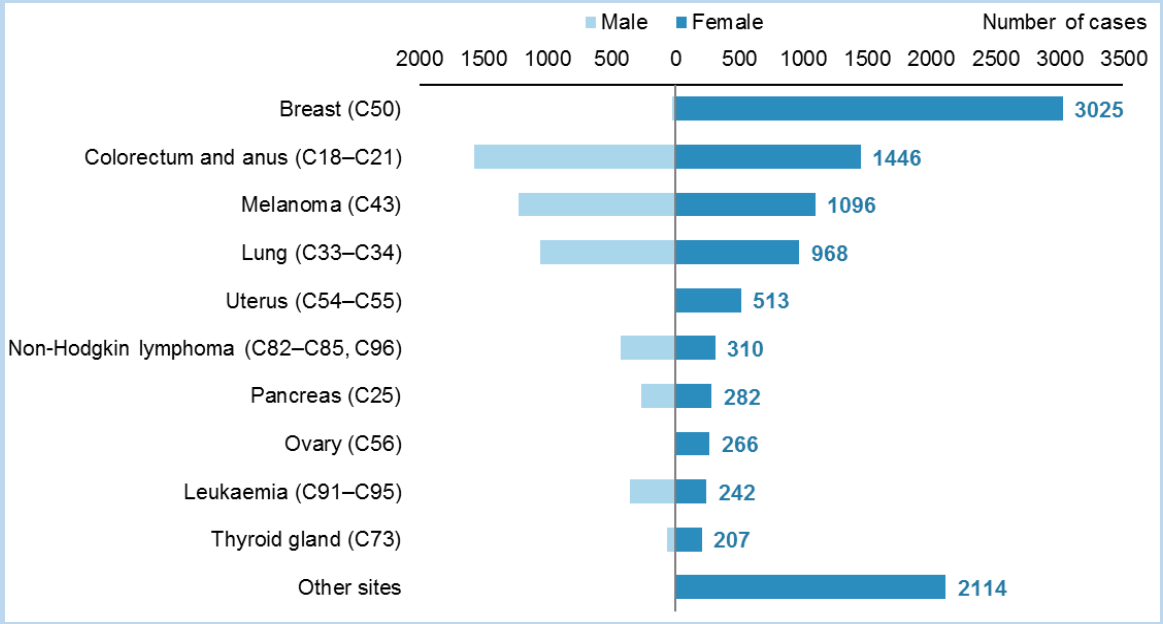




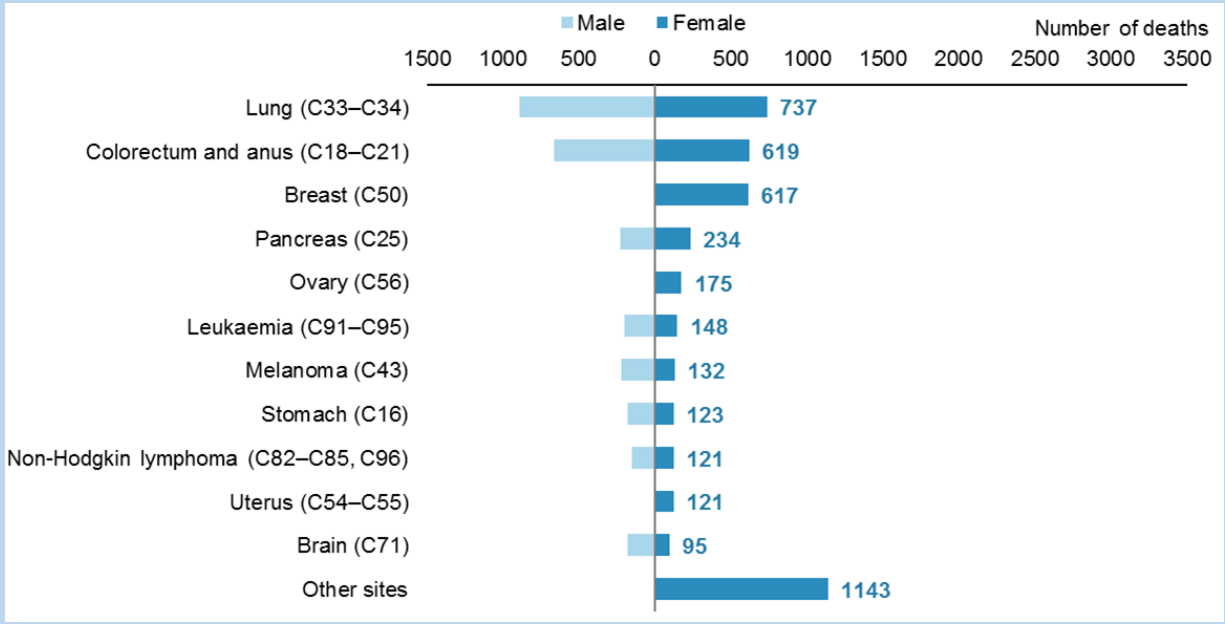
Bowel cancer kills as many Kiwi lives every year as breast and prostate cancer combined



The 10 most common cancers in females, 2012



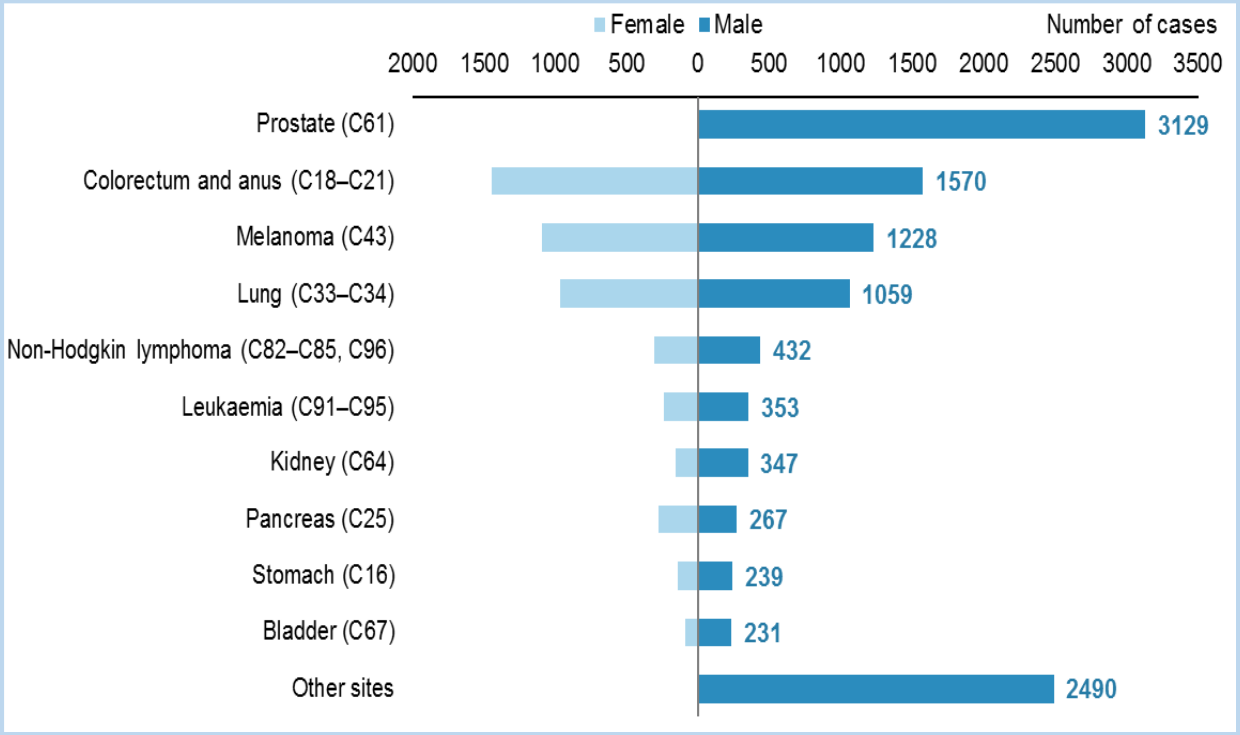
incidence



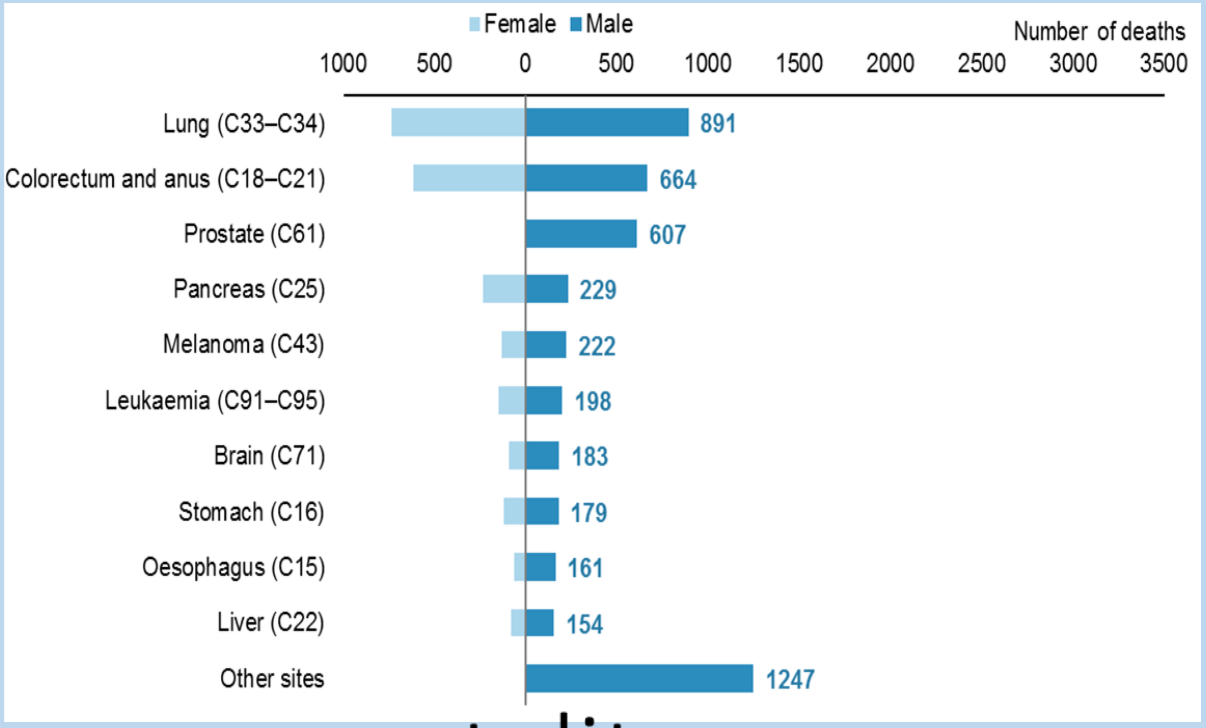
mortality

Source: New Zealand Cancer Registry

The 10 most common cancers in males, 2012



incidence



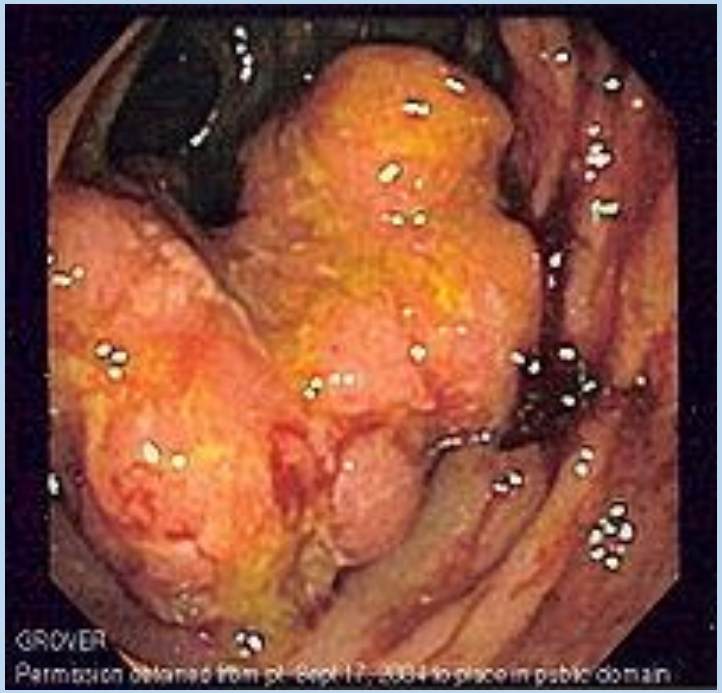
mortality

Source: New Zealand Cancer Registry

What is the Average Risk for individuals in NZ?

- **55 yrs**:
  - Overall risk 0.6%

- **75 yrs**
  - Overall risk 5.6%
  - Men: 1 in 18
  - Women 1 in 23



What happening with the incidence

<50

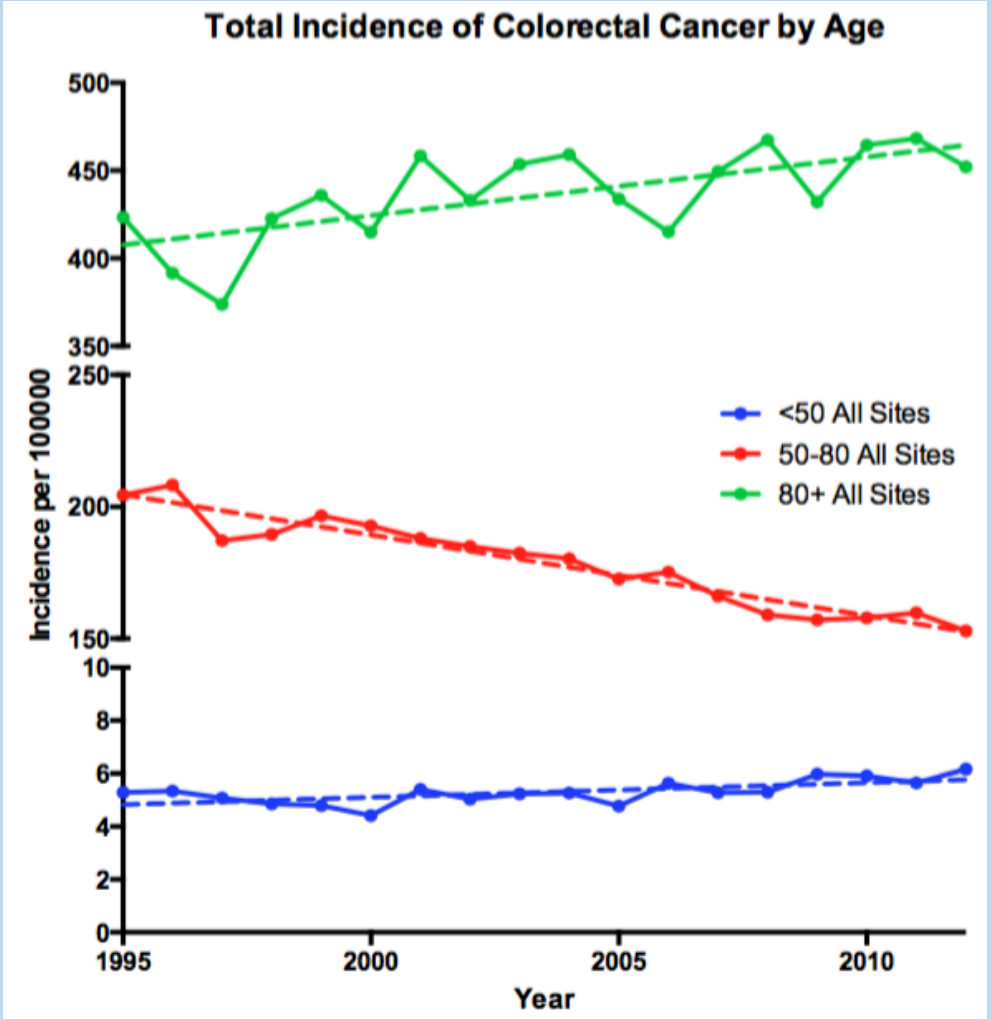
- Incidence increasing – supports hypothesis
  - 0.05531 (0.02141, 0.08920) *p = 0.0032*

50-80

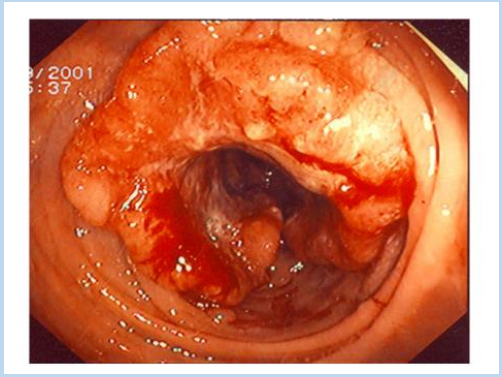
- Incidence decreasing
  - -3.066 (-3.520, -2.612) *p <0.0001*

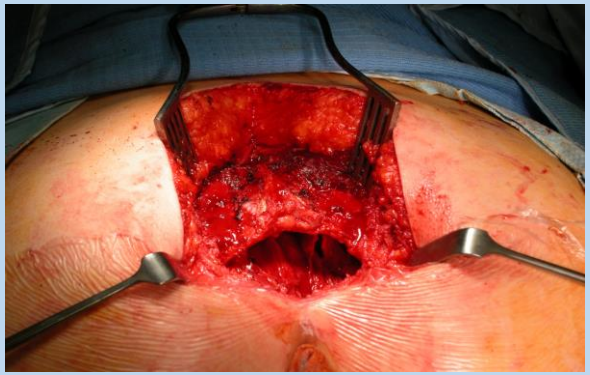
80+

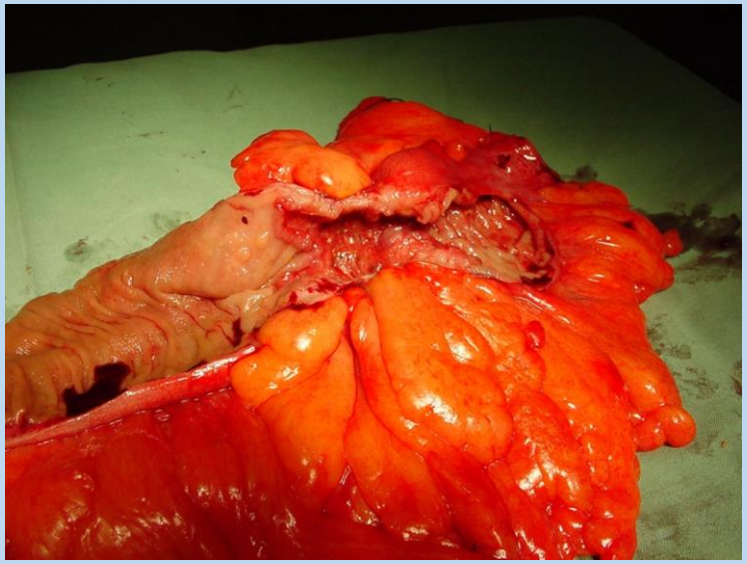
- Incidence increasing
  - 3.342 (1.431, 5.252) *p = 0.0019*

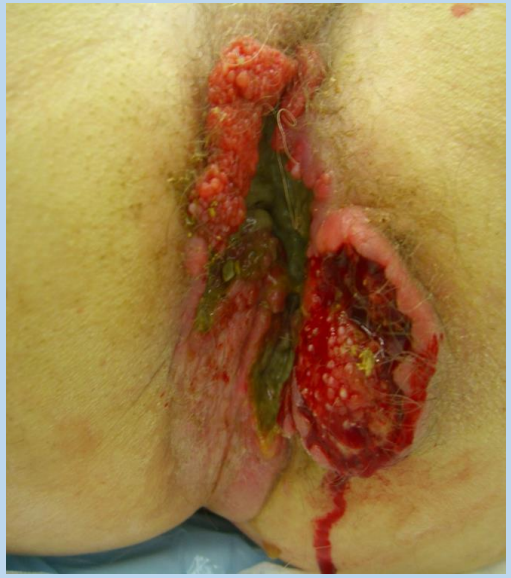


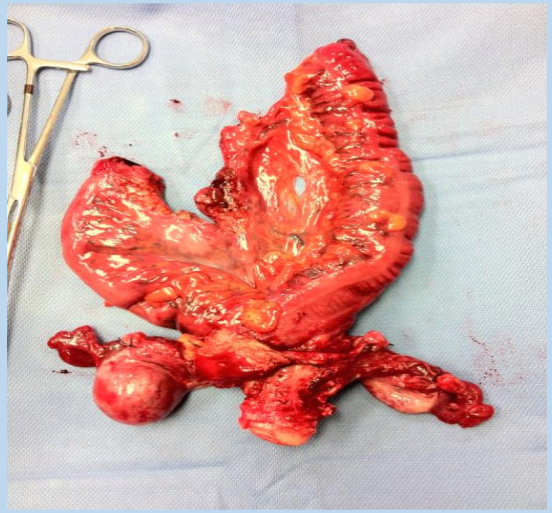
Five times as many Kiwis die as a result of Bowel Cancer than road traffic accidents







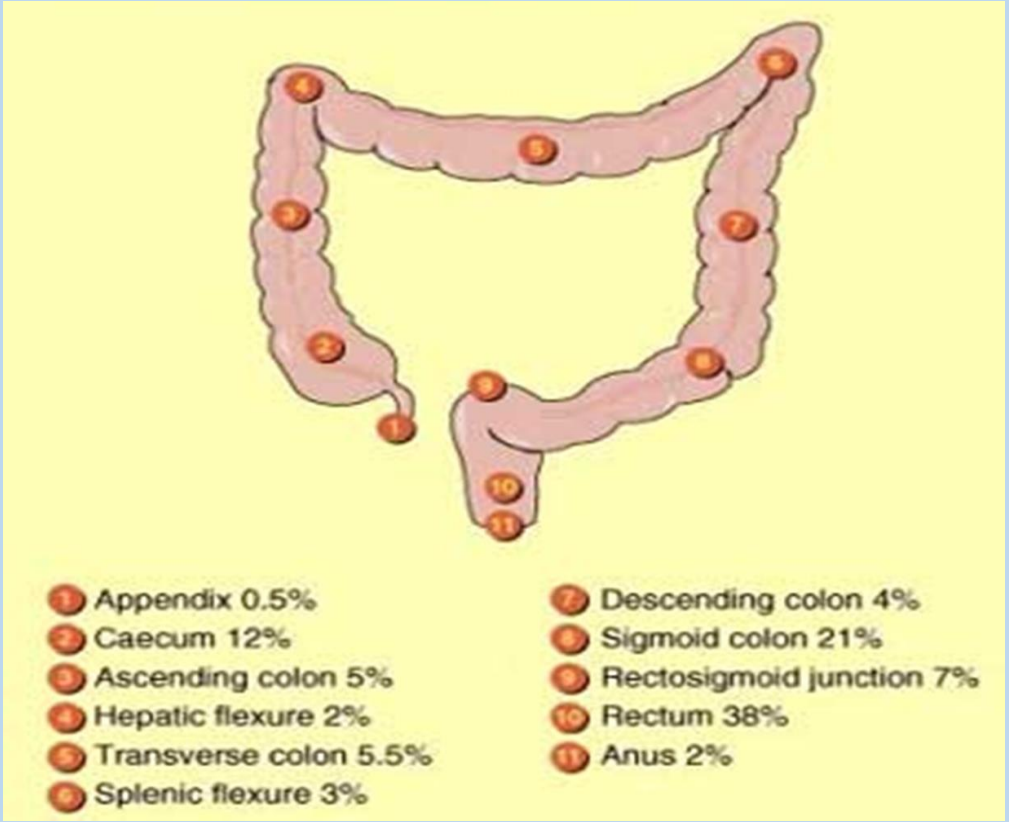




Colorectal Cancer

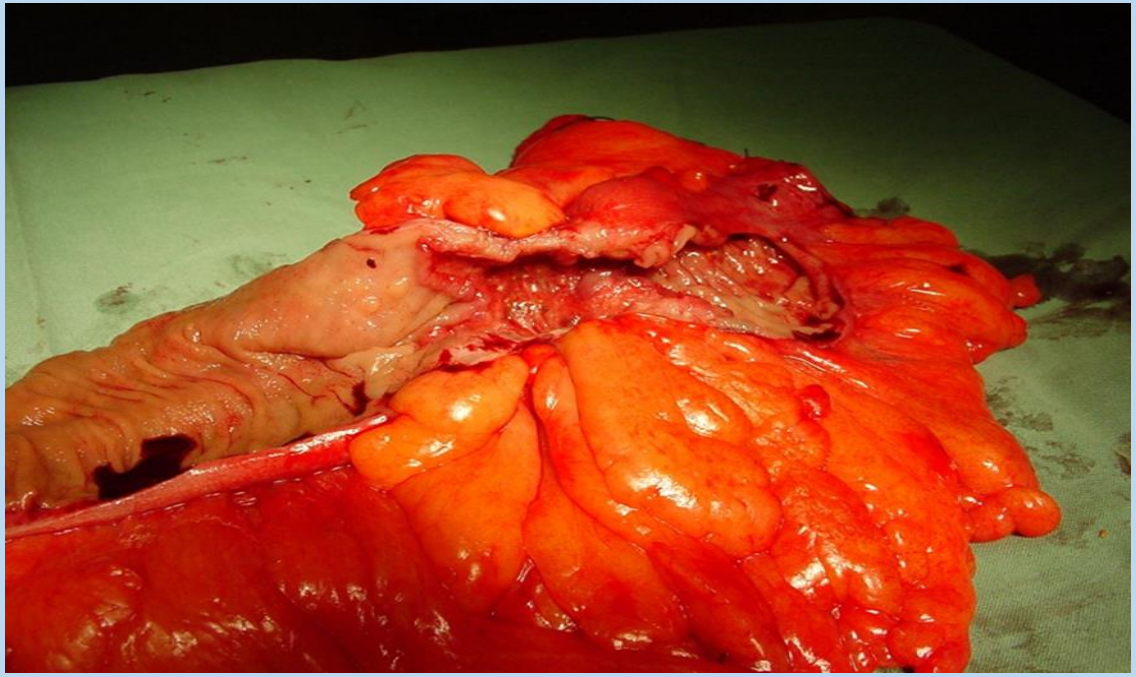
Symptoms

- Change in bowel habit
  - closer to the anus the more symptoms
  - change in frequency or consistency of stool
- Rectal bleeding
  - overt or occult
  - bright red, purple, black, not apparent
  - occult-anaemia
- Mucus
- Pain; rectal or abdominal
  - Uncommon
  - Implies obstruction or growth into other organs
  - Back pain-retroperitoneal extension
- Weight loss/fatigue
- Symptoms of metastatic disease
  - lung, brain, liver



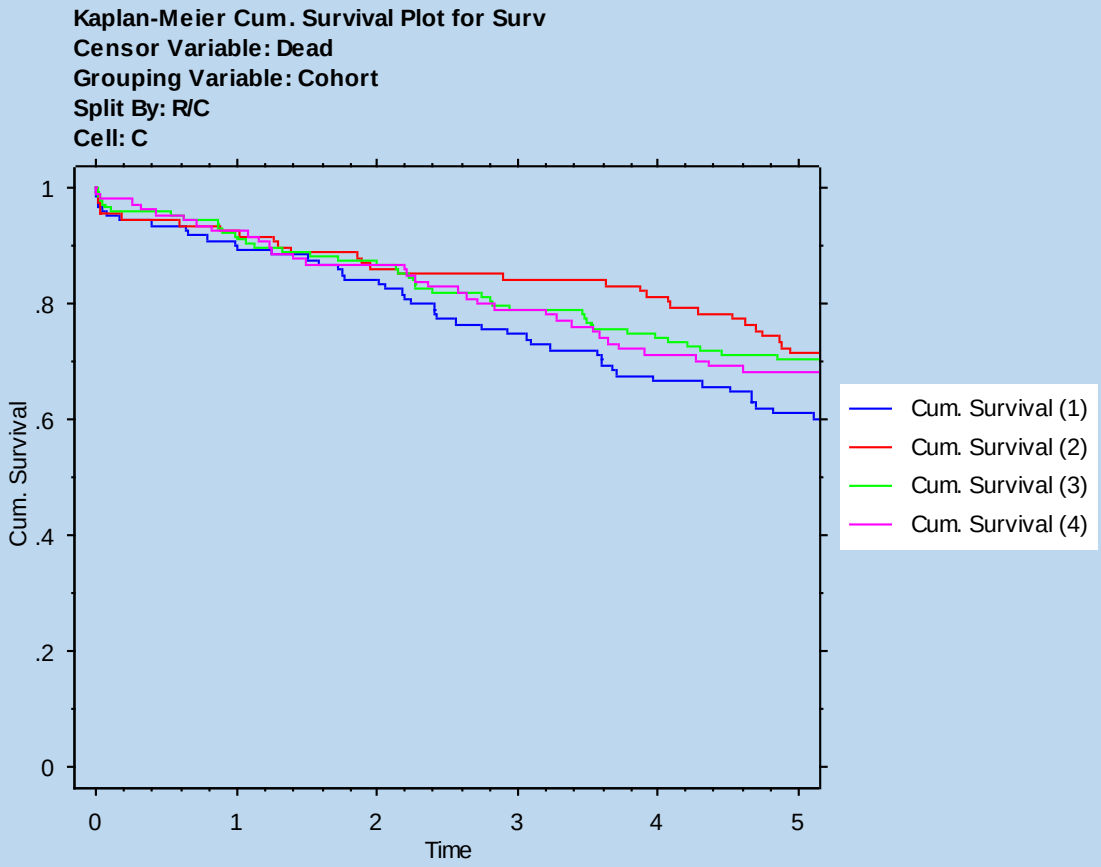
What determines outcome

- Stage of disease
- Presentation
- Quality of surgery
- Adjunctive therapy

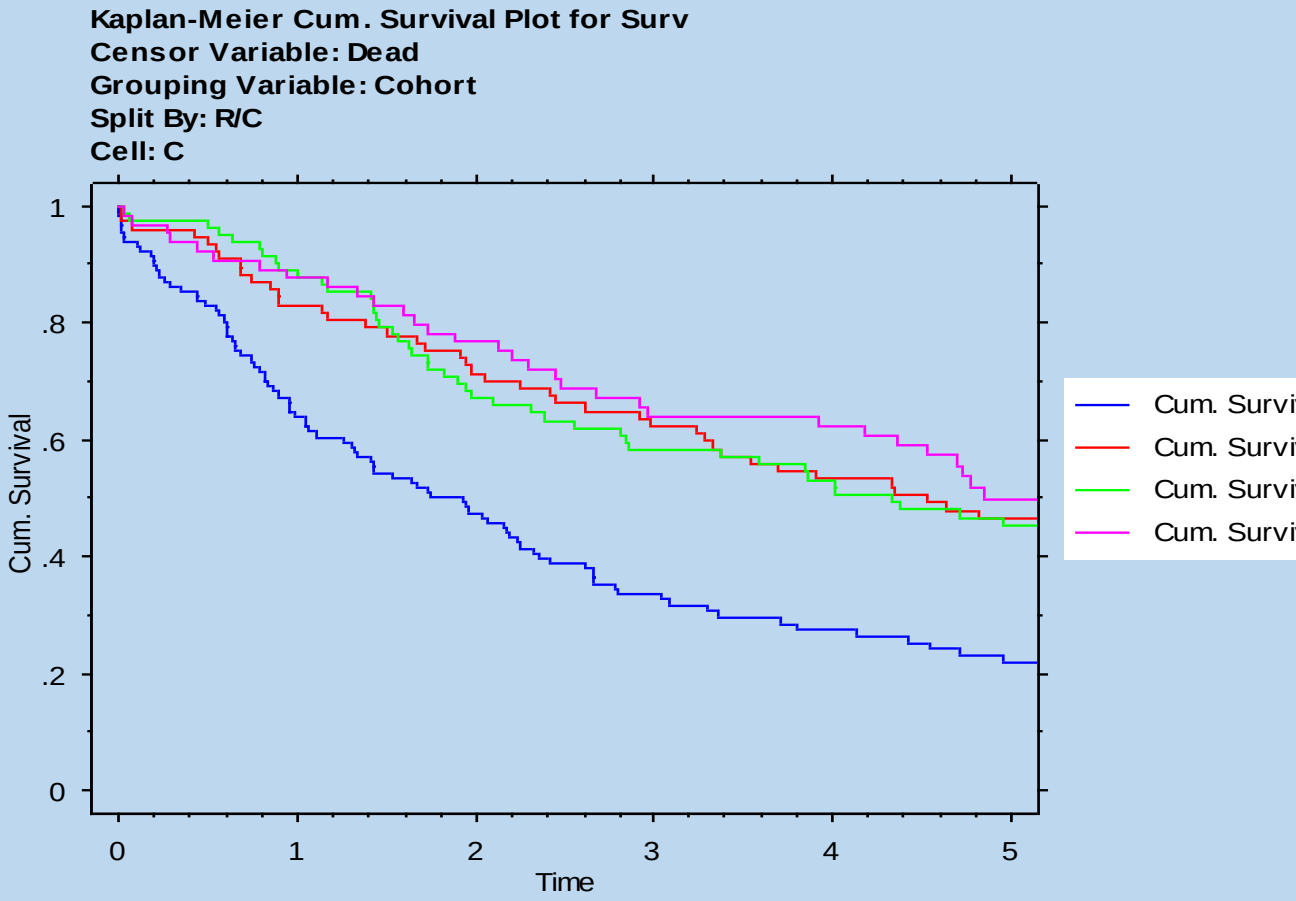


- It is the cumulative effect of small gains that lead to improvement

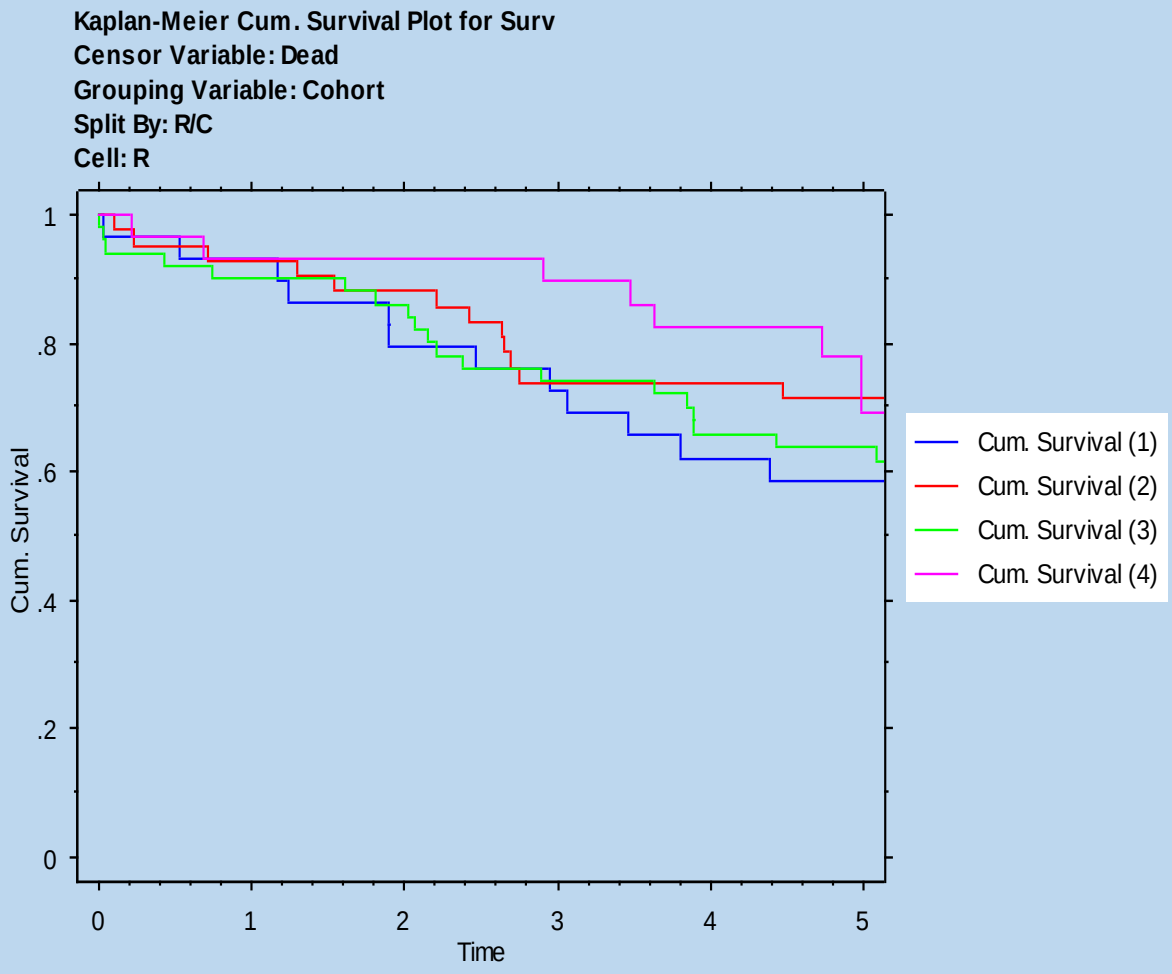
Colon Cancer stage 1 and 2



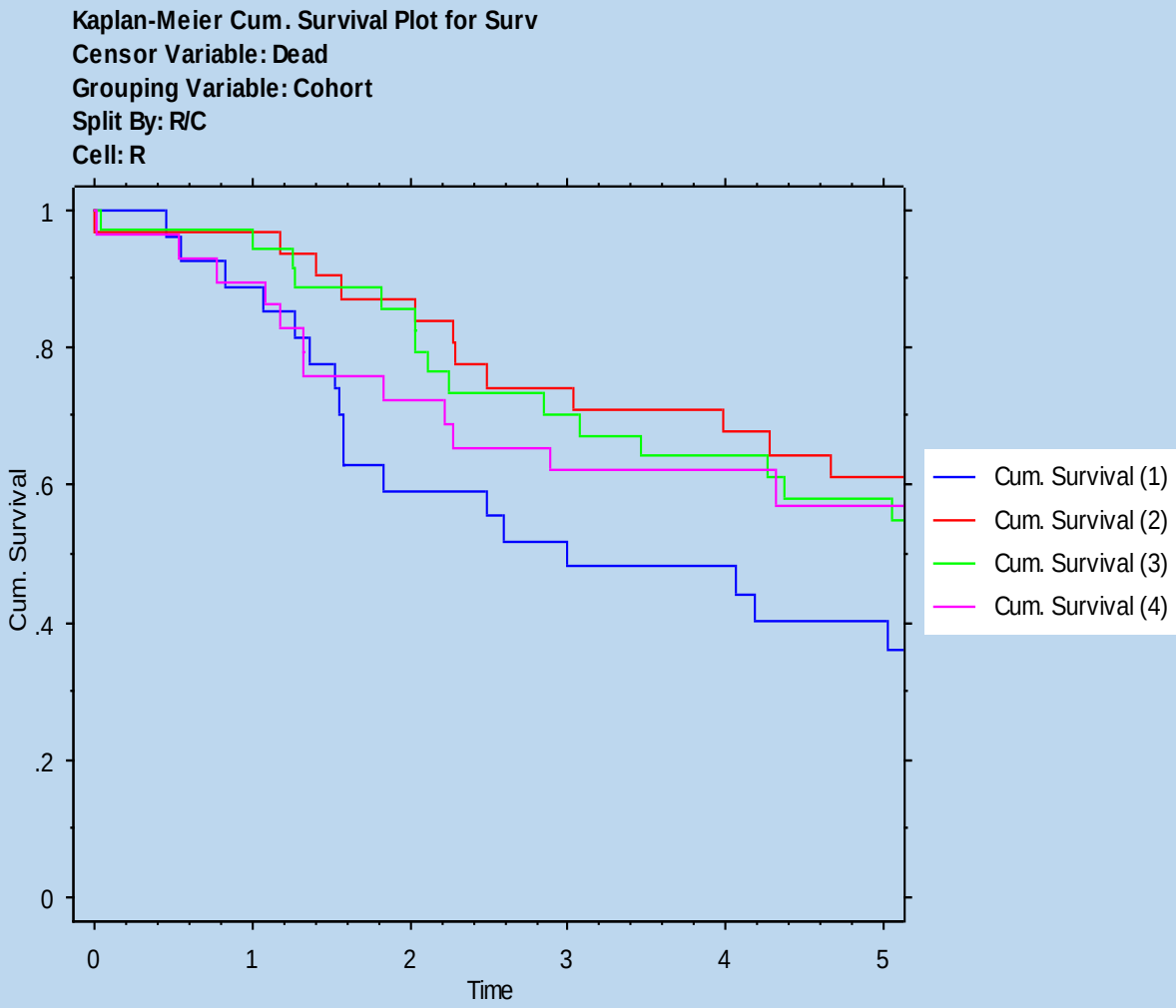
STAGE 3



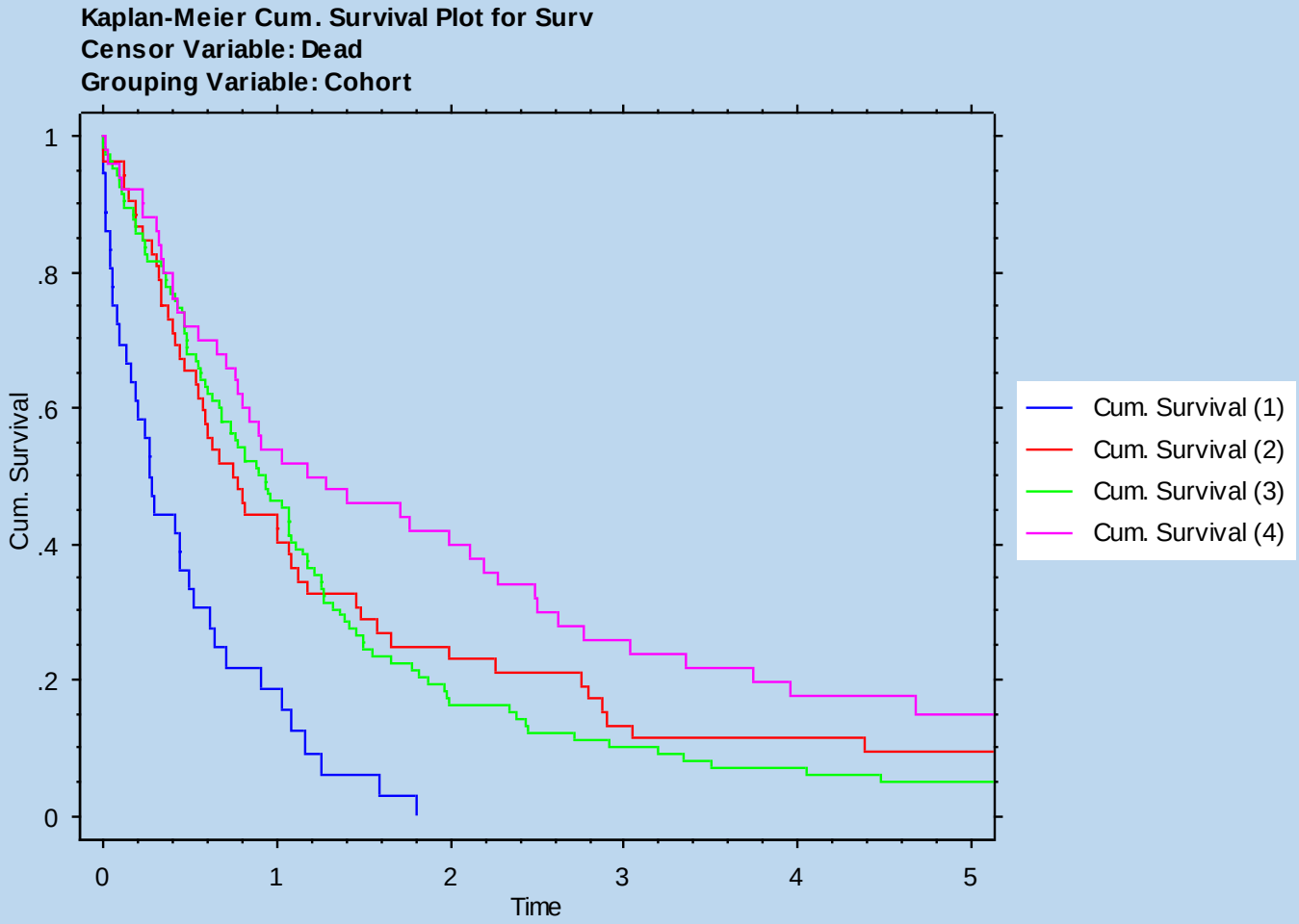
RECTAL CANCER STAGE 1 AND 2



STAGE 3

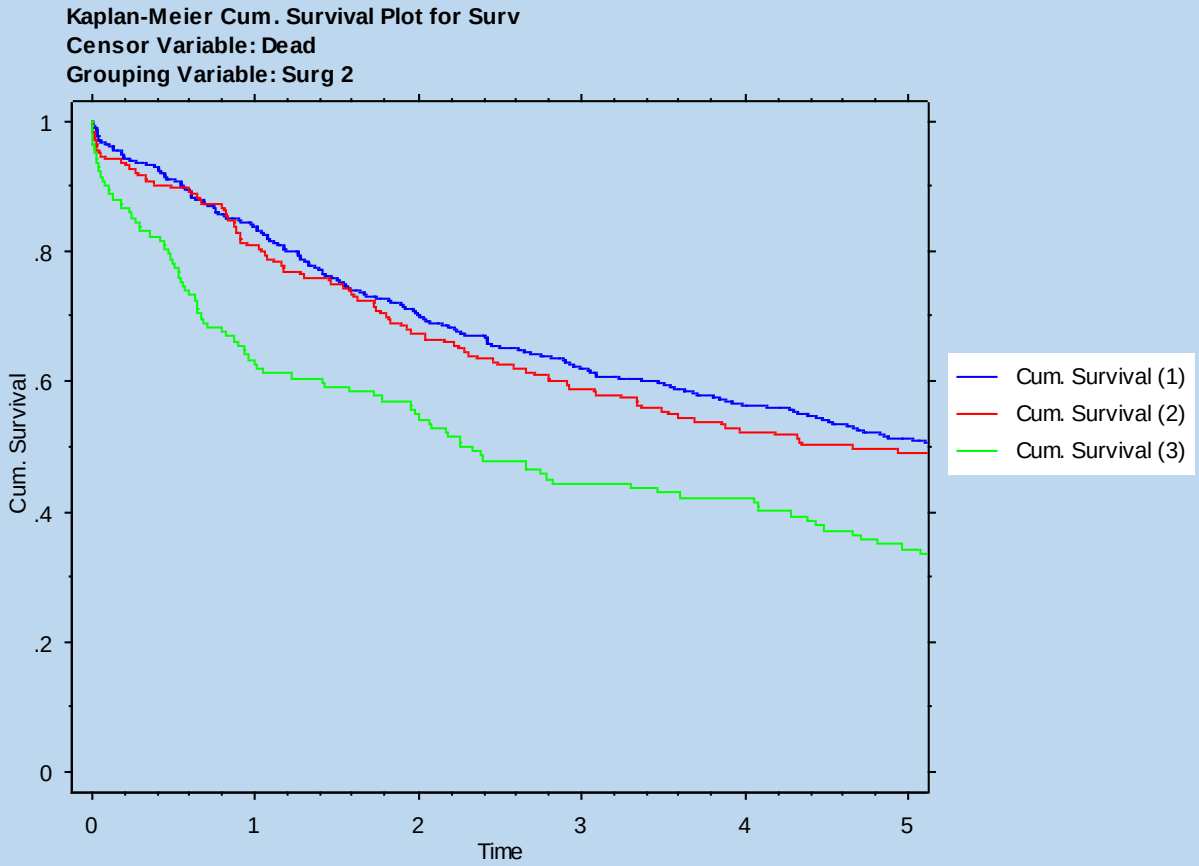


STAGE 4 (both colon and rectum)

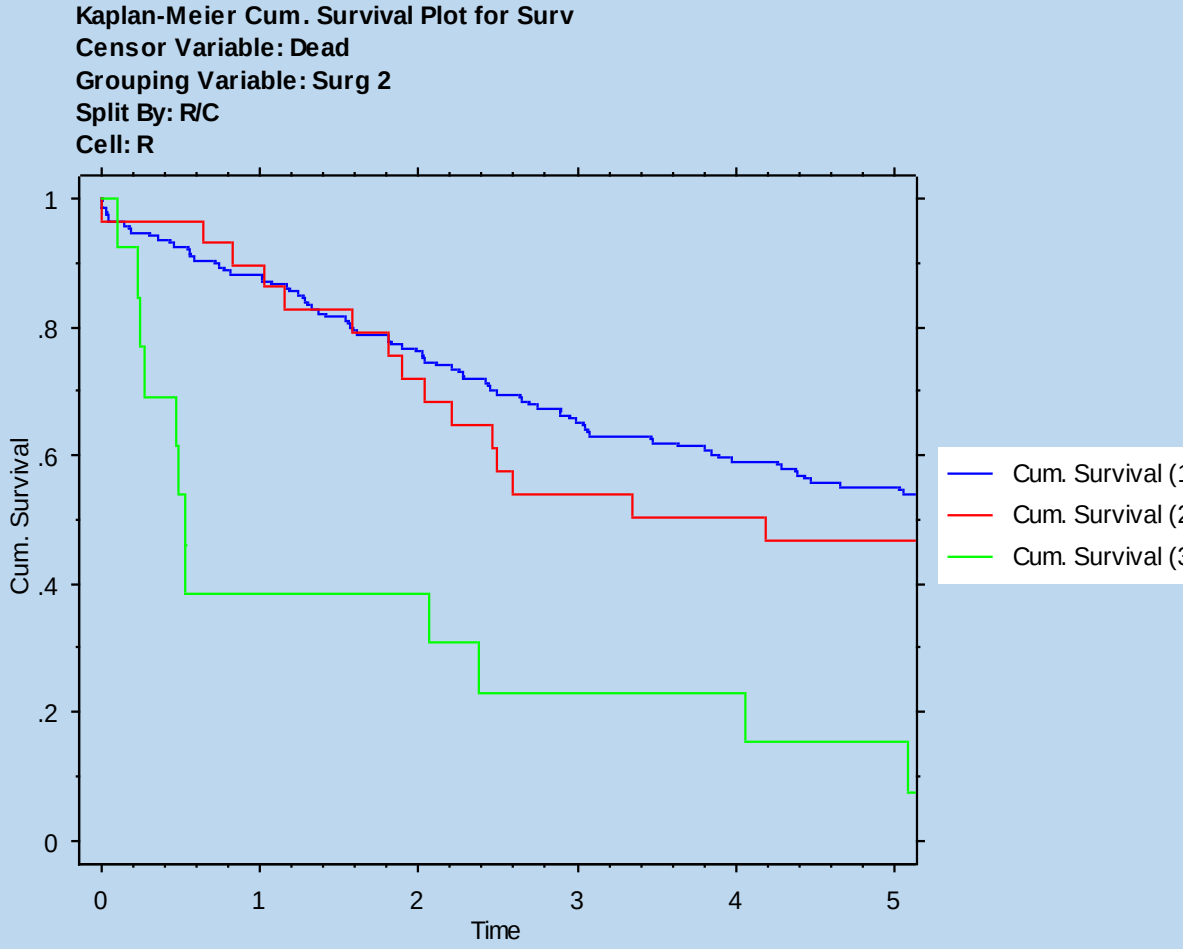


TYPE OF SURGEON

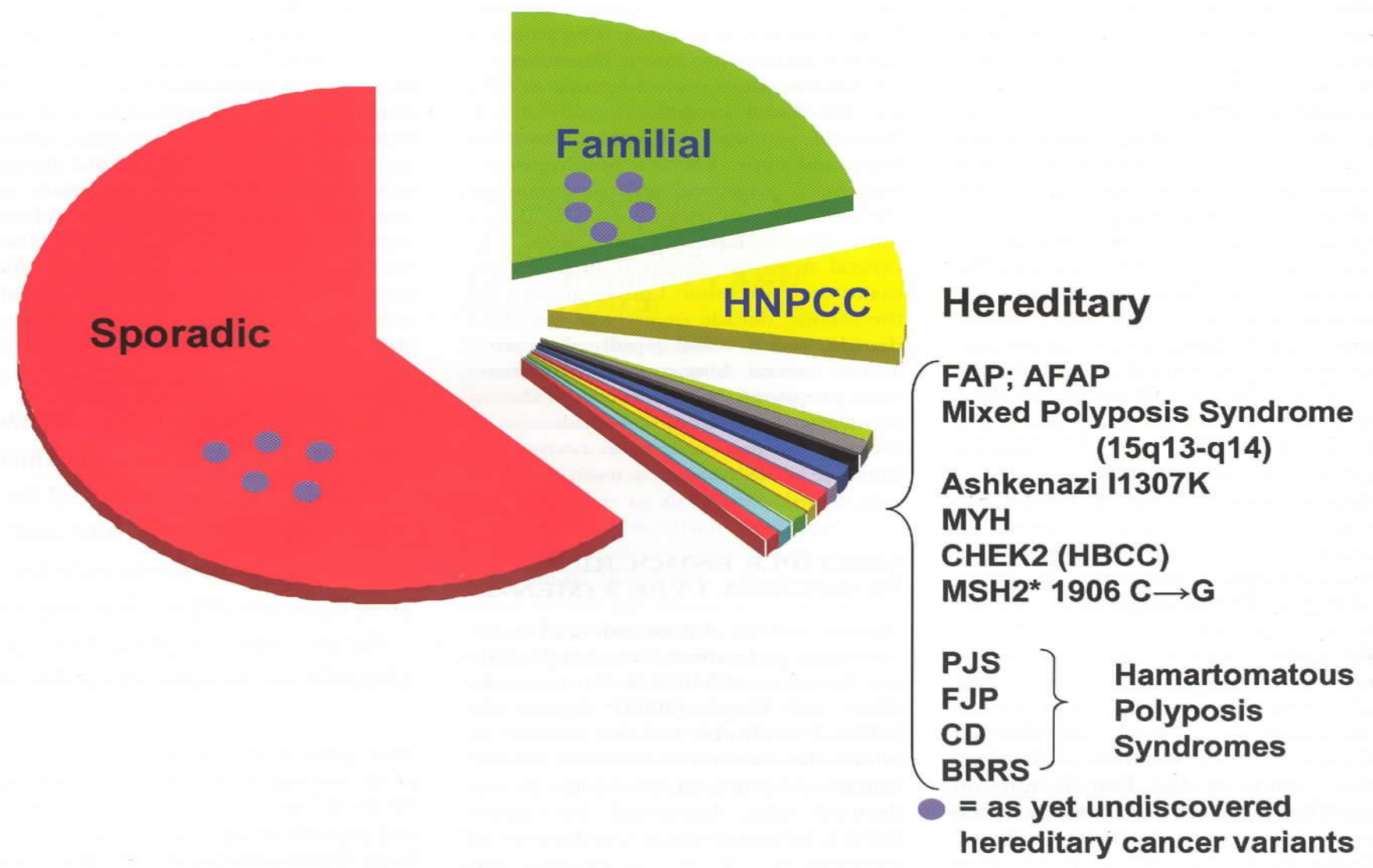
Colon



Rectum



Colorectal Cancer



Am J Med genetics Vol 129C Aug 15th 2004

Hereditary Non Polyposis Colorectal Cancer HNPCC

- First described by Dr Scott Warthin
- Published family pedigree that meets HNPCC criteria in 1913
- His seamstress predicted her death from gynaecological or CRC…. and was correct

- Henry Lynch followed up on this and other Nebraskan families in 1960's
- Condition termed HNPCC - to distinguish it from FAP with multiple polyps

Lynch Syndrome - Genetics

- Autosomal dominant familial cancer syndrome
  - 50:50 chance of passing it on
- Caused by germline mutation in DNA mismatch repair (MMR) genes
  - Tumours have microsatellite instability (MSI)
  - Loss of protein expression of the 4 genes can be shown with IHC (immunohistochemistry)

- MLH1 and MSH2 – 70- 80% - ‘classic form’
- MSH6 - 5-10% –’attenuated’ later onset
- PMS2 – 2-5% - ‘attenuated’ - reduced penetrance

Families previously called HNPCC now divided up

- **Lynch Syndrome families** – where a mutation has been found in the family by genetic testing

- Families where criteria are met and special tests suggest the involvement of the MMR genes but genetic testing has not found a mutation- **Presumed Lynch Syndrome.**

- Families where Amsterdam criteria are met and special tests DO NOT suggest the involvement of the MMR genes – **Familial Colorectal Cancer Syndrome X**

- Those who meet criteria but no testing possible- **currently still HNPCC**

Lynch Syndrome : management

Colorectal Cancer

- Intensive colonoscopic surveillance
  - 1-2 yrly from 25 years.
  - 43% reduction in incidence of CRC
  - Significant decrease in mortality from CRC (detected at earlier stage)
- Surgery for treatment of CRC
  - Segmental or subtotal colectomy
  - Balance of metachronous CRC risk with quality of life

Surveillance for extra-colonic tumours

- Urinary Tract tumours– value unknown
  - Urine cytology may be undertaken 1-2yearly from 35yrs
- Endometrial Cancer – value unknown
  - Annual surveillance by examination, transvaginal ultrasound and aspiration biopsy
  - from age 35yrs may be beneficial
  - Hysterectomy may be an option

Aspirin and bowel cancer in Lynch Syndrome

- Long-term effect of aspirin on cancer risk in carriers of hereditary colorectal cancer: an analysis from the CAPP2 randomised controlled trial

- 600 mg aspirin per day for a mean of 25 months substantially reduced cancer incidence after 55.7 months in carriers of hereditary colorectal cancer.

- Further studies are needed to establish the optimum dose and duration of aspirin treatment.

Burn et al Lancet ;378 December 2011

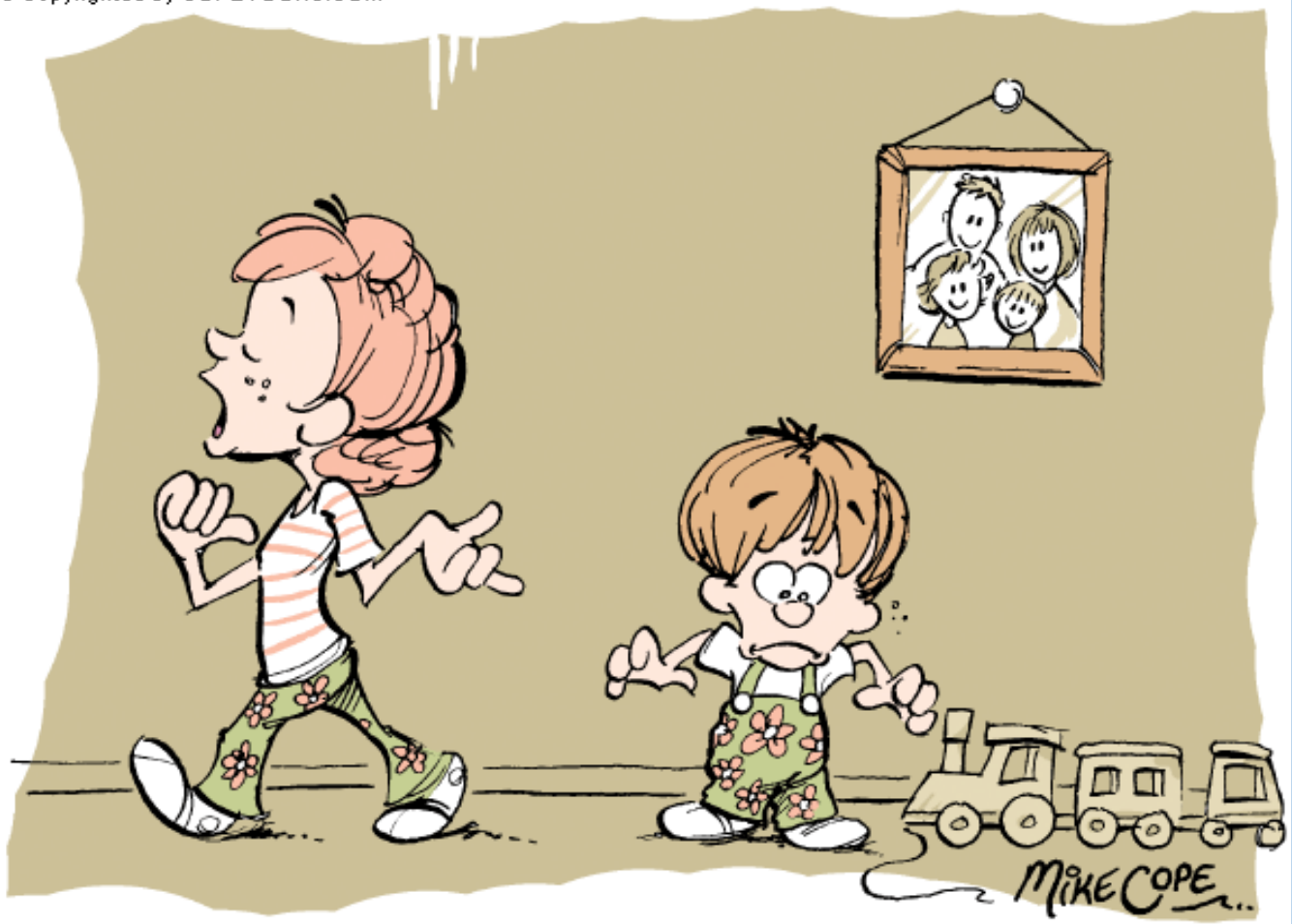
FAP Inheritance

- APC gene on Chromosome 5
- 20 % have no family history
- In 10% cases unable to identify APC gene mutation
- Penetrance is virtually 100%
- Onset of polyposis is in teenage years.
- Most patients are asymptomatic
- Age of onset for colorectal cancer is late 30’s - early 40’s


FERTILITY
associates
a better understanding

PGD

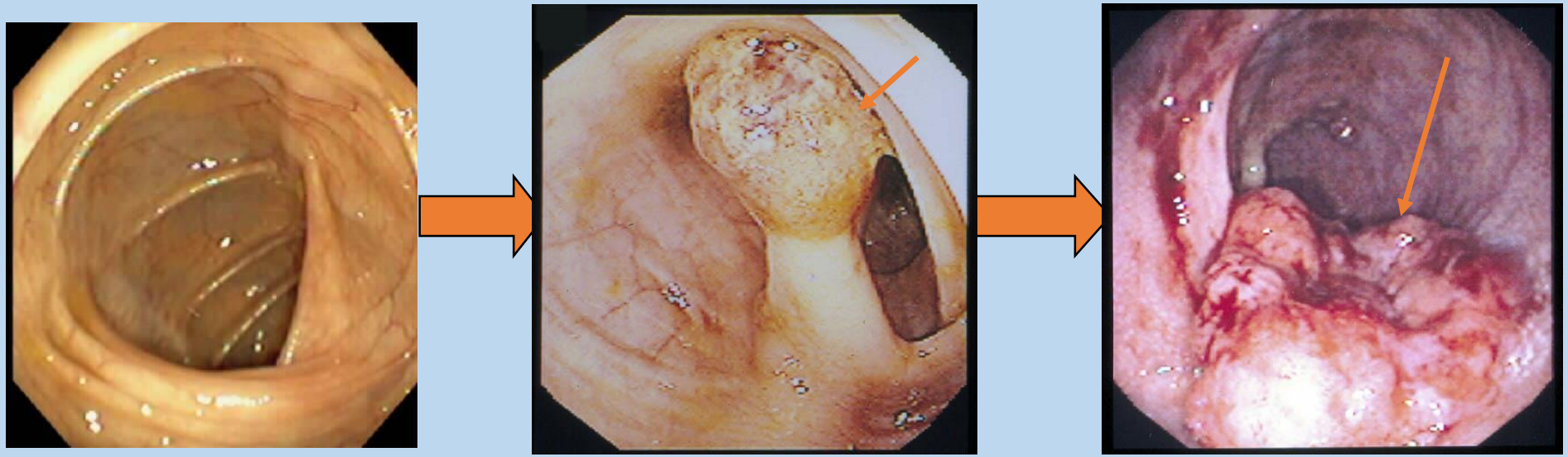
- Preimplantation genetic diagnosis
- Testing a few cells from a day 3 or 5 embryo
- Blood test/CVS/amniocentesis – testing hundreds of cells
- Feasability testing
- Genetic advice



"It's not my fault I got all the good genes.
Nobody told me you'd be coming."

Something must cause bowel cancer or is it just random event

Adenoma to Carcinoma Pathway

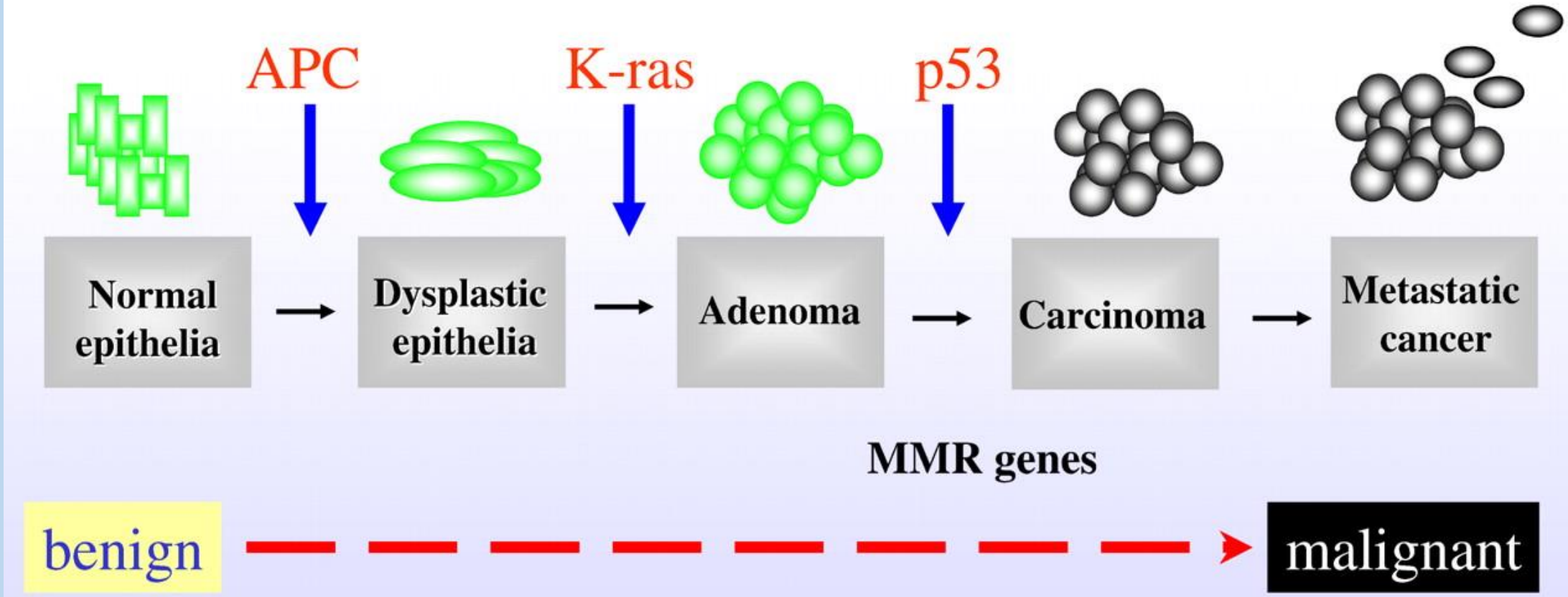


Normal

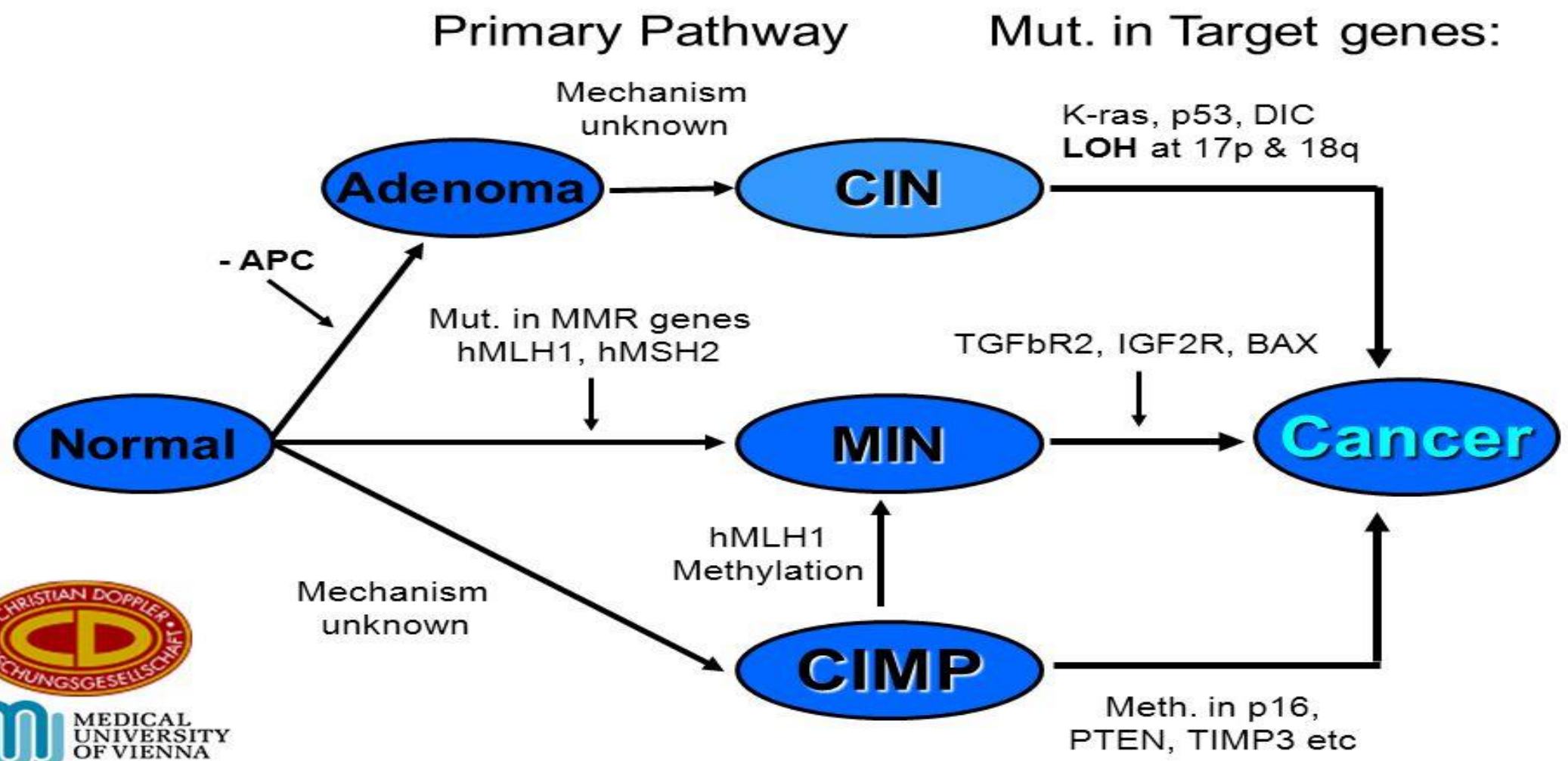
Adenoma

Cancer

- Most cancers develop from adenomatous polyps


APC
K-ras
p53
Normal epithelia
Dysplastic epithelia
Adenoma
Carcinoma
Metastatic cancer
MMR genes
benign
malignant

Multiple Pathways to Colorectal Cancer



CHRISTIAN DOPPLER FORSCHUNGSGESELLSCHAFT

MEDICAL UNIVERSITY OF VIENNA

We think that sporadic CRC is caused by a chronic low grade infection

Keenan and Frizelle *Infectious Agents and Cancer* 2014, **9**:31
http://www.infectagentscancer.com/content/9/1/31

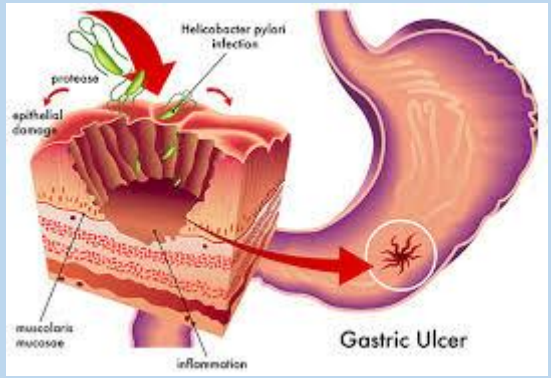
INFECTIOUS AGENTS AND CANCER

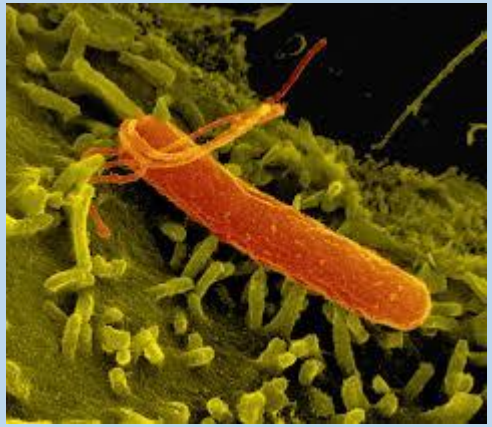
LETTER TO THE EDITOR Open Access

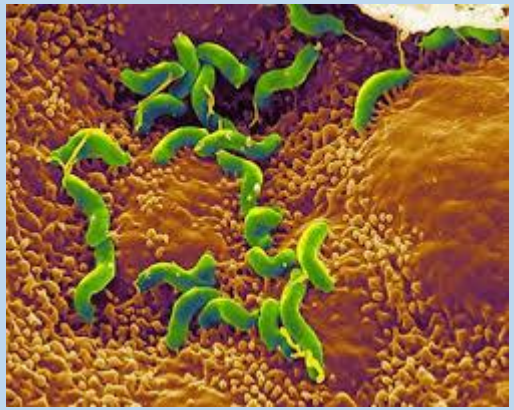
Bacteria flying under the radar: linking a bacterial infection to colon carcinogenesis

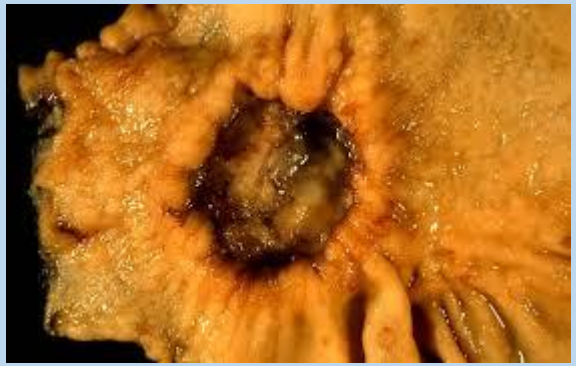
Jacqueline I Keenan* and Frank A Frizelle

Bacteria causing gastric cancer; H Pylori









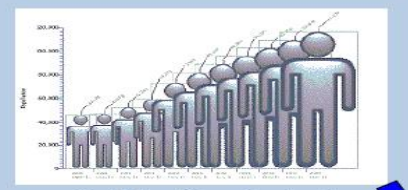
Environment has some effect
Migrant studies

- Migrants adapt to country of residence
- Japan to USA
- Polish to Australia
- Chinese to Australia
- Maintaining the cuisine if country of origin reduces this effect

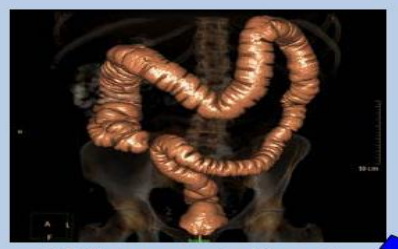
Some risks you can reduce

- Diet
- Exercise
- Weight
- Smoking
- Alcohol

Can we find CRC sooner



Statistics New Zealand
Population Projection



CT Colonography Capacity

BowelScreening
Check Yourself Out
Waitemata District Health Board
Best Care for Everyone
MINISTRY OF HEALTH
MANATŪ HAUORA

Parameters from Waitemata DHB
Pilot Project

Workforce Capacity Projection
by HWNZ

Literature Review

DHB Specific Capacity
and Projection

The National Bowel Screening Programme Model

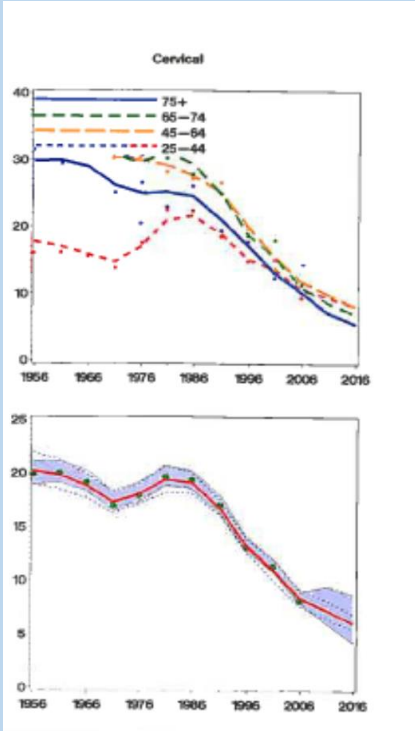
BowelScreening
Check Yourself Out

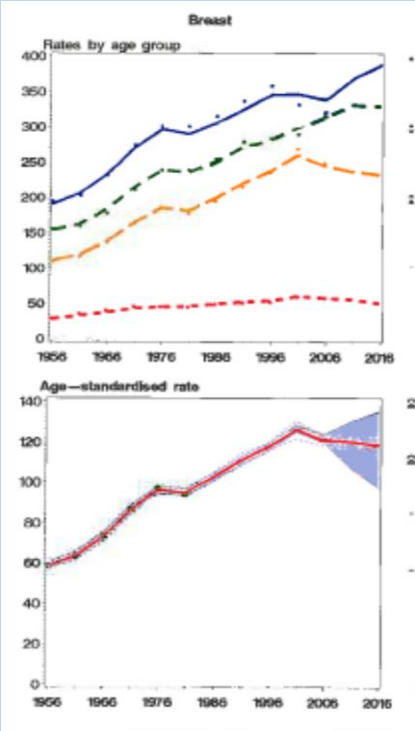
Screen or not to screen

- Wait for patients to get symptoms or screen

- At present screen for
  - Breast Cancer
  - Cervical Cancer

  - Screening as about as effective for CRC as it is for these





Colorectal cancer screening

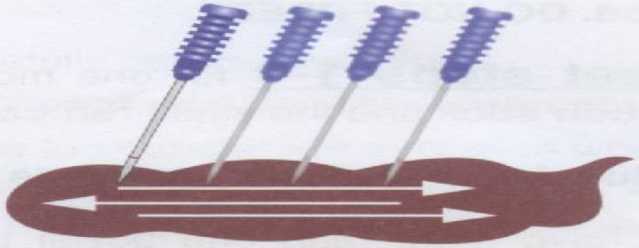
- For screening to work
  - Precursor lesion
  - Tool to find this
  - Low morbidity
  - Cost effective

Collection Method:

The collection method is simple:

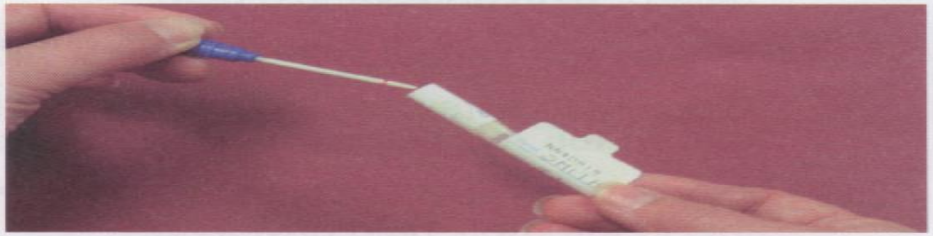
1. Empty your bladder, then flush the toilet.
2. Place the **collection sheet, printed side up**, on the surface of the water in the toilet bowl.
3. Pass the bowel movement onto the sheet.
4. To collect the test sample use the small **blue collection stick** and the small **blue collection tube**.

a) Insert the tip of the small **blue collection stick** into the faeces up to the red line then drag the tip along the length of the faeces several times (see diagram).



Collect the test sample immediately as the sheet will disintegrate within five minutes.
The sheet is biodegradable and can be flushed away.

b) Insert the small **blue collection stick** into the small **blue collection tube** through the white end (in a single action).
Ensure that the collection stick fits tightly.



Please DO NOT attempt to fill the collection tube with faeces, as only a small amount on the collection stick is required for the test.

For assistance, call the Dorevitch Pathology FOBT Communications Officer on **1300 738 365** (local call charge) between 9am - 5pm EST Monday - Friday

Bowel Screening Pilot results

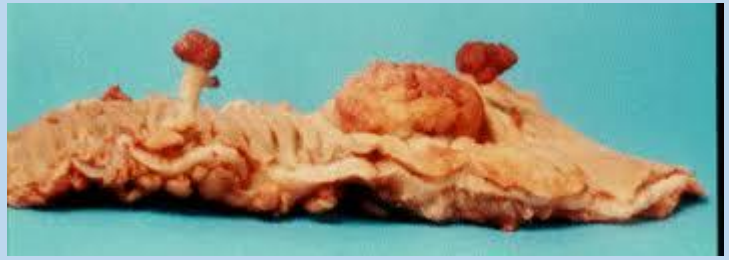
- Round 1- 121,798 people were invited to take part and 69,176 people returned a correctly completed kit.

- The New Zealand participation rate for Round 1 of 56.8 percent was higher than the internationally acceptable minimum participation rate of 45.0 percent for first screening rounds.

- Round 2 -115,776 people were invited and 61,771 people returned a correctly completed kit.

Bowel Screening Pilot results

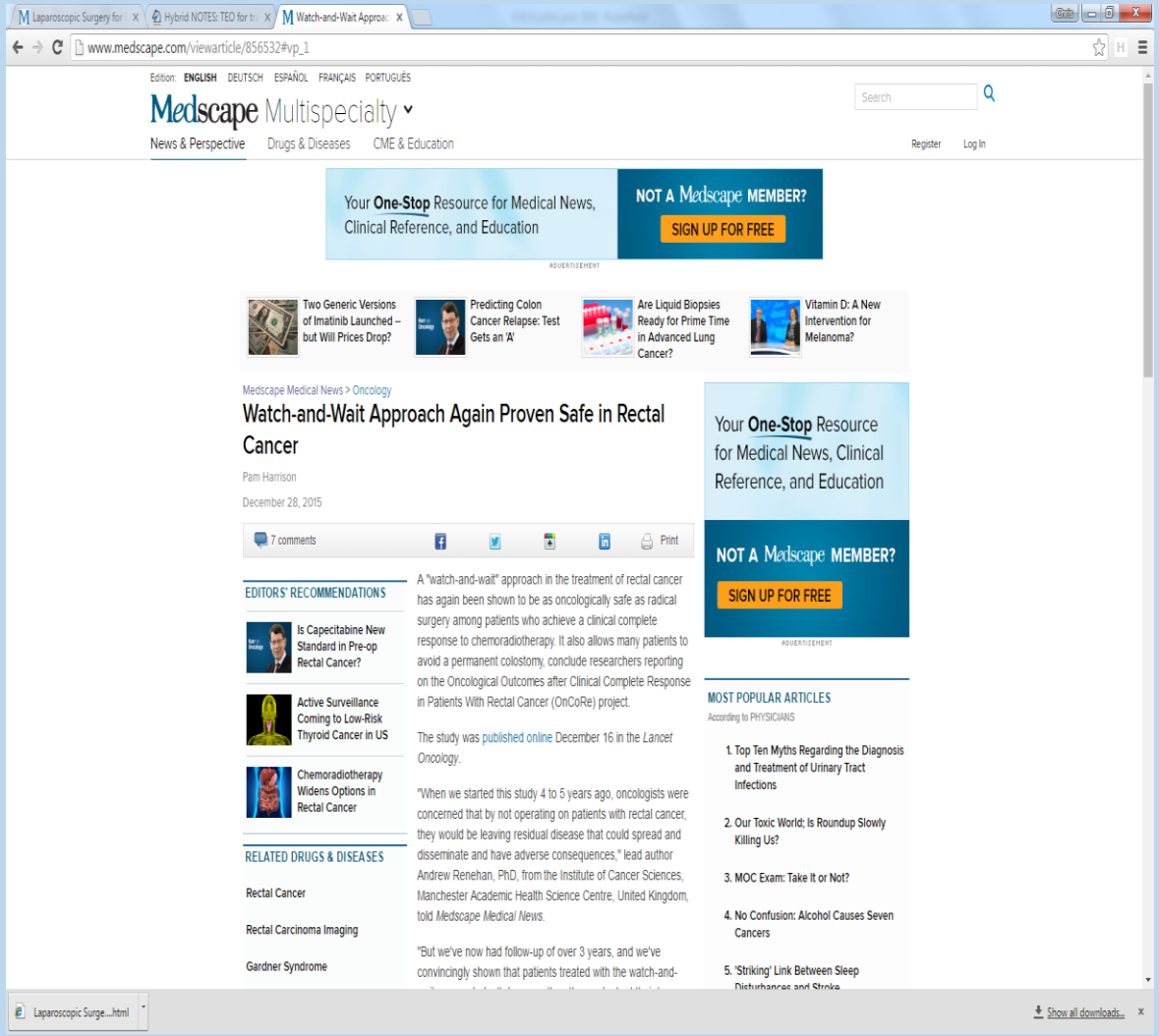
- 7800 patients had colonoscopies
- 316 patients were found to have a CRC (some more than one)
- 30+ other lesions found that need operation
- Many polyps removed (65%+)



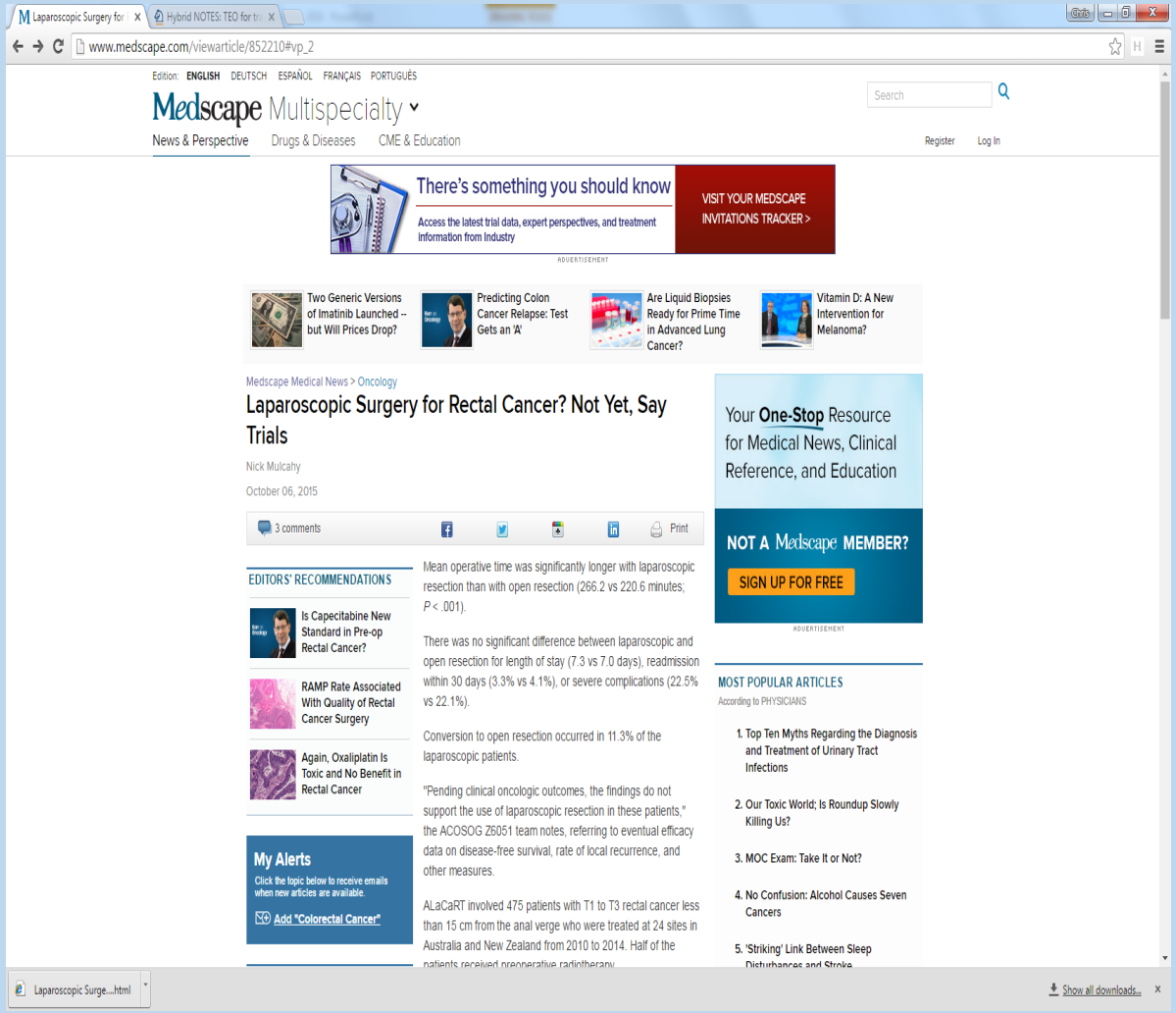

Colorectal Cancer is 95% preventable with screening. Unless you cover it up and pretend it isn't there.
The Colorectal Cancer Screening Initiative Foundation

What is new?

- A "watch-and-wait" approach in the treatment of rectal cancer has again been shown to be as oncologically safe as radical surgery among patients who achieve a clinical complete response to chemoradiotherapy. It also allows many patients to avoid a permanent colostomy, conclude researchers reporting on the Oncological Outcomes after Clinical Complete Response in Patients With Rectal Cancer (OnCoRe) project.
- The study was published online December 16 in the *Lancet Oncology*.

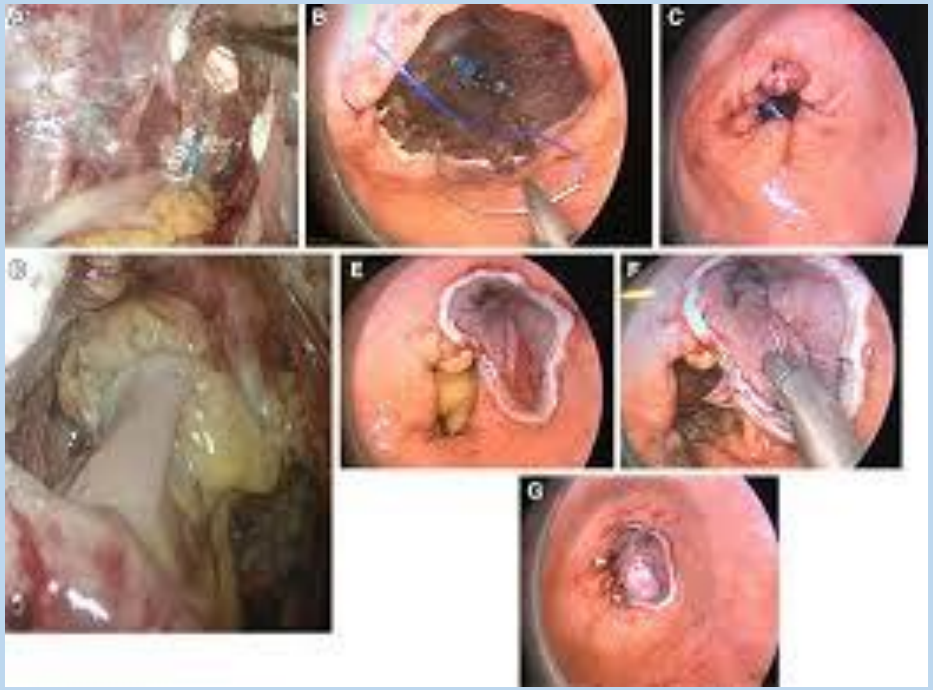


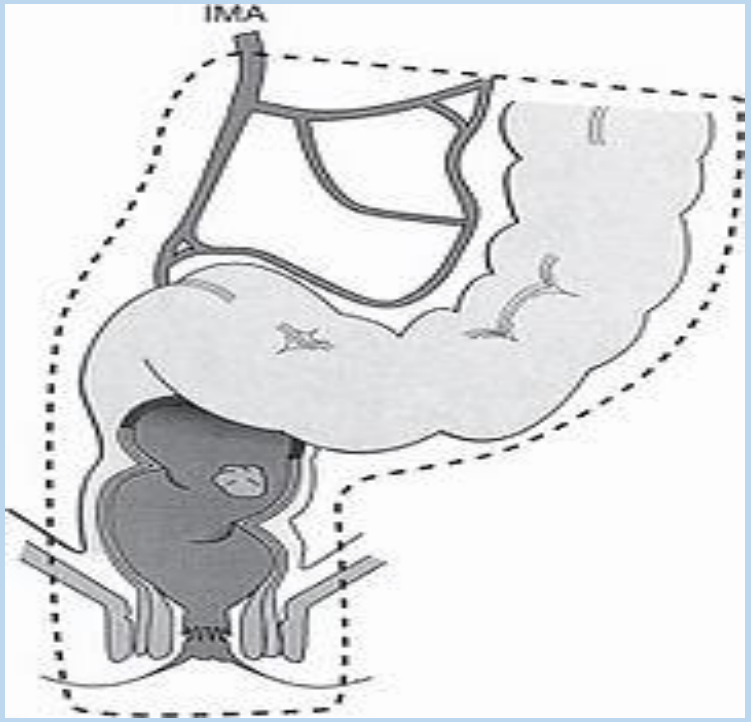
Laparoscopic rectal cancer



- The "revolutionary change" brought about by laparoscopic surgery for gastrointestinal tract cancers might stop at the rectum, according to two major randomized clinical trials that compared the minimally invasive surgery with traditional open resection.
- The studies were published in the October 6 issue of *JAMA*.
- Both trials — the ACOSOG Z6051 trial conducted in North America and the ALaCaRT trial conducted in Oceania — failed to establish the noninferiority of laparoscopic rectal cancer surgery.

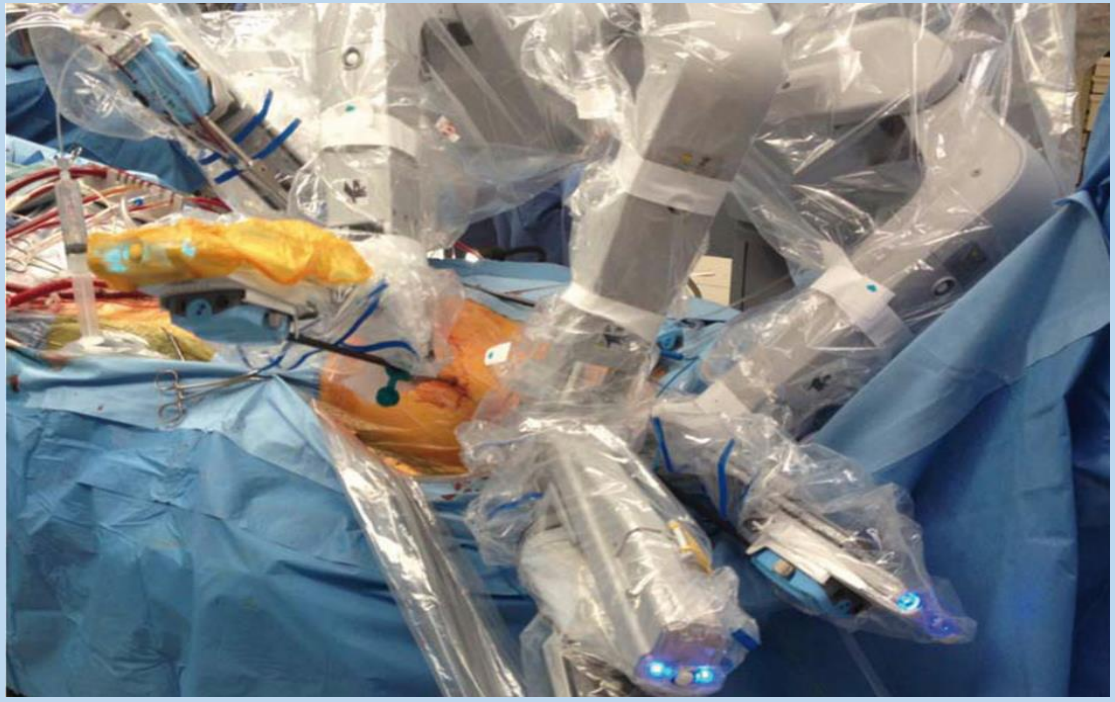
Trans anal TME





Whats new

Robotic surgery

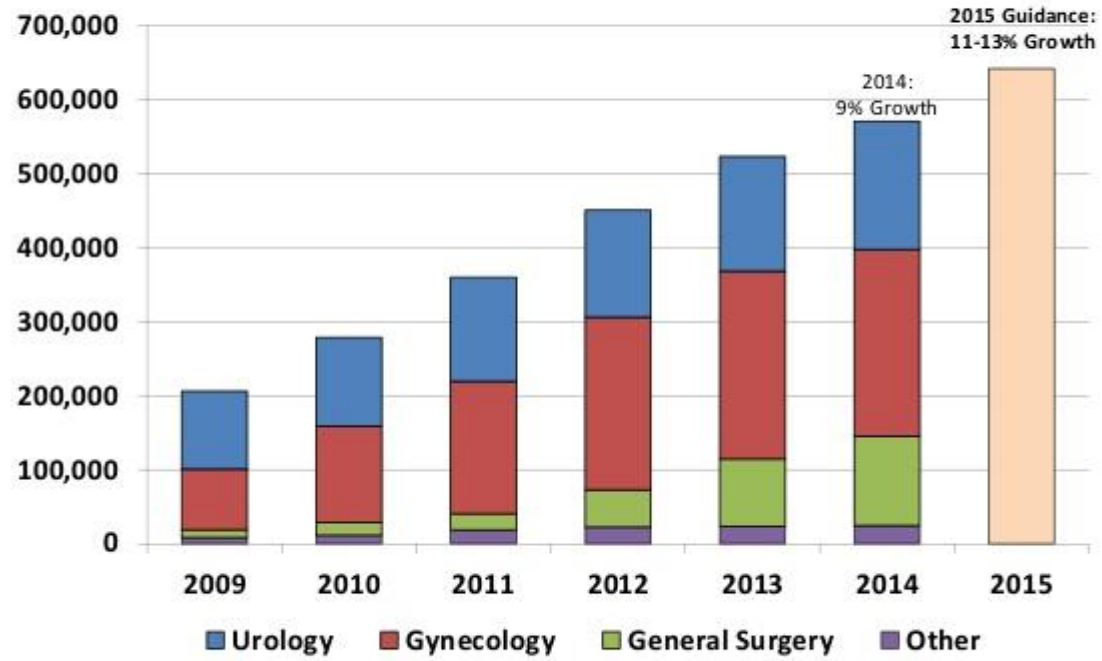


Installs by Country and Region

Intuitive sells directly to customers in the US, Korea, and the European countries indicated above. Sales are through distributor partners in all other areas of the world including, Canada, Latin America, the Middle East, Asia and Australia.

INTUITIVE SURGICAL

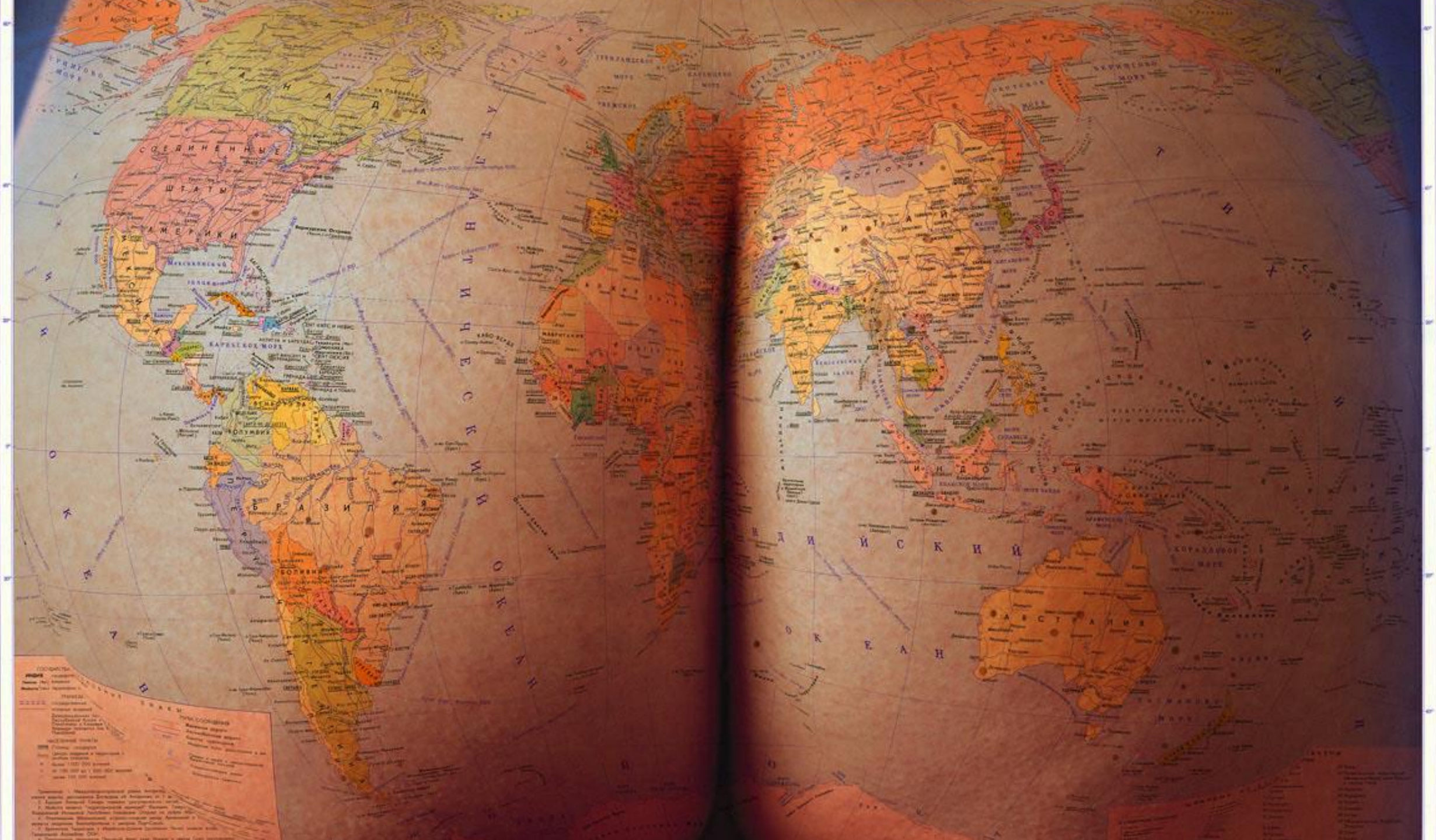
Annual Worldwide Procedures



Company estimates

da Vinci Surgery

- **3rd MOST** Diagnosed cancer in New Zealand.
- **3,300** People are diagnosed with bowel cancer every year in New Zealand.
- **1,300** New Zealanders die each year as a result of Bowel Cancer.


Канада
Соединенные Штаты Америки
Мексиканский
Карибское море
Колумбия
Бразилия
Боливия
Атлантический океан
Тихий океан
Индийский океан
Индонезия
Австралия