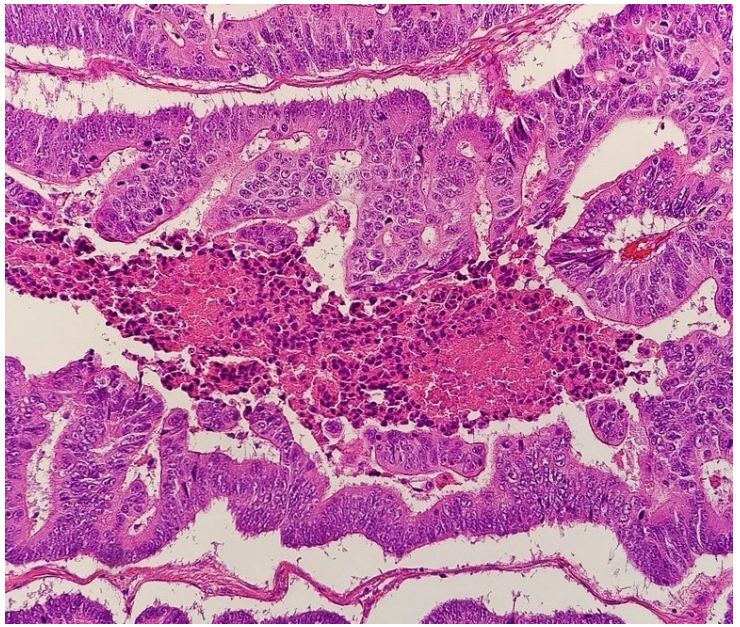
Cancers of the bowel and digestive system.

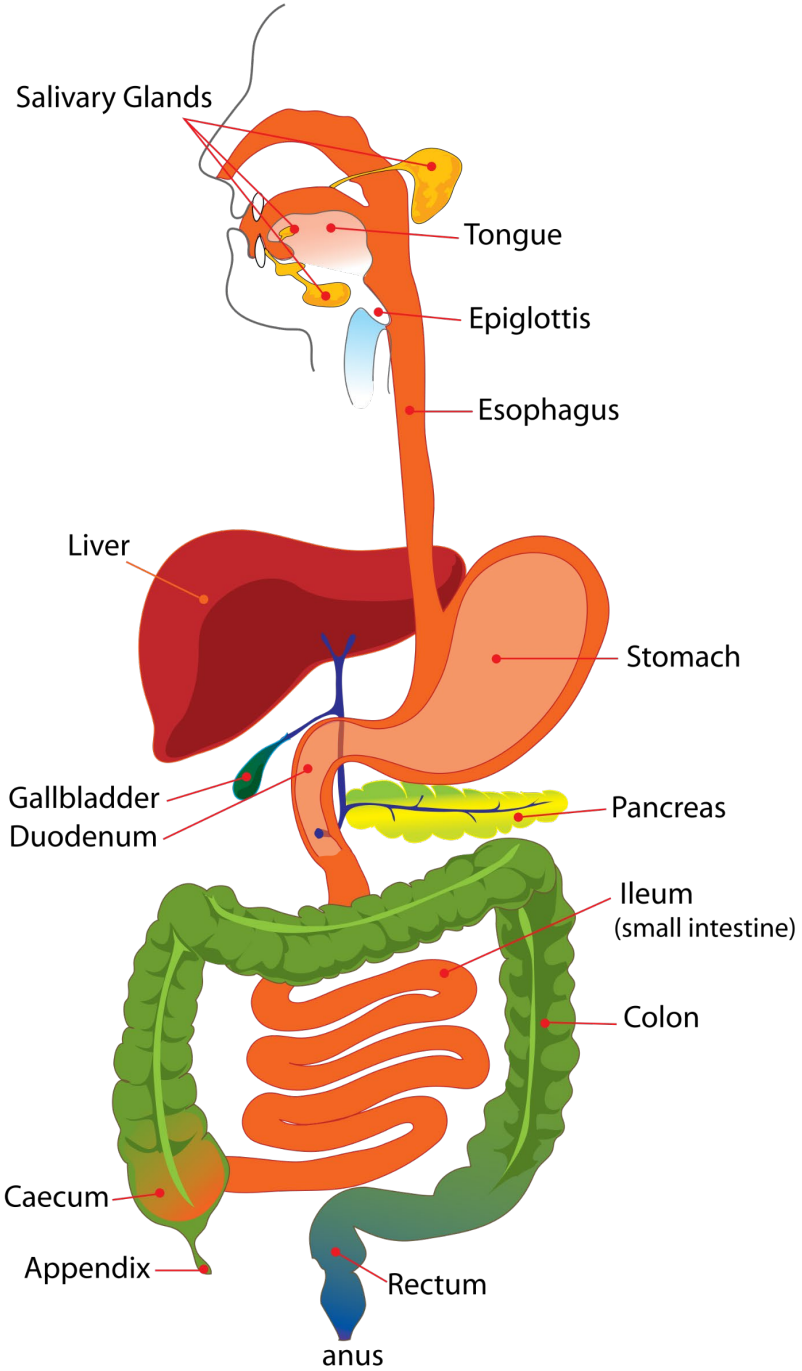


Christopher Whitty

Gresham College 2020.

The digestive tract- a refresher.

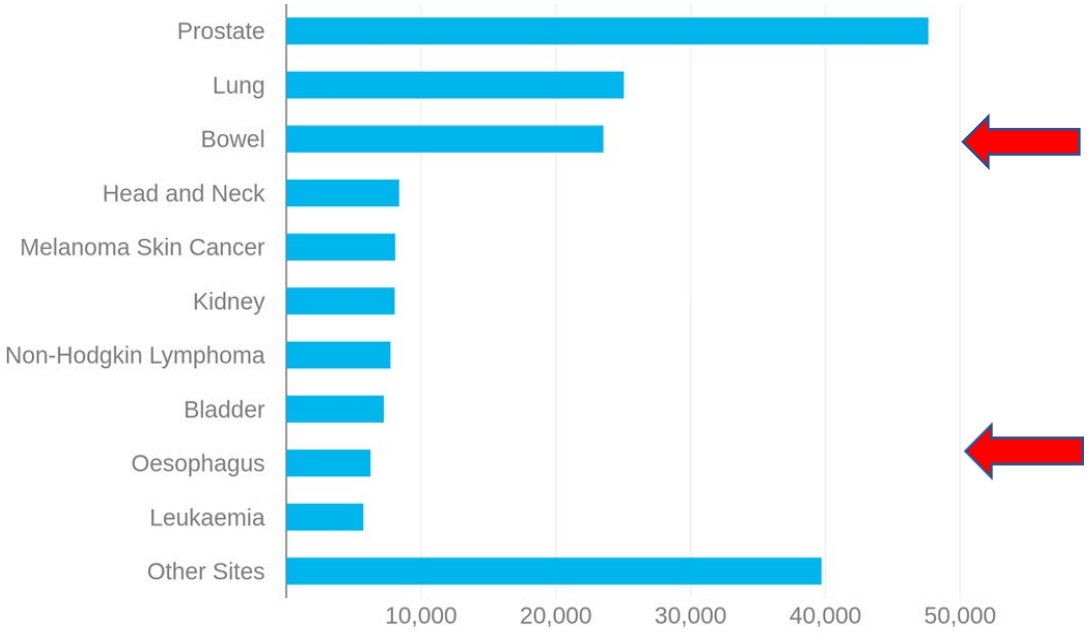
- The oesophagus- gets food from the mouth to the stomach.
- The stomach- acid and enzymes break down food.
- Pancreas- powerful digestive enzymes and insulin.
- Small bowel absorbs nutrients.
- Colon absorbs water.
- Sigmoid, rectum regulate defaecation.

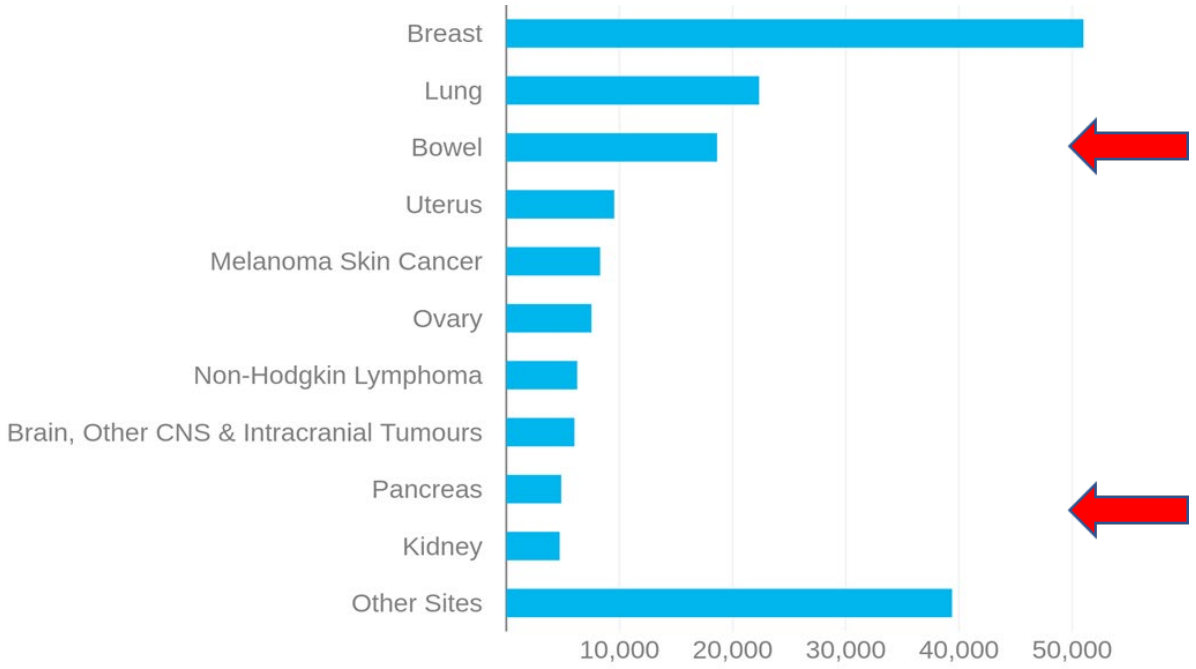


Leysi24/Wiki

Bowel and digestive tract cancer cases. Male (L) and female (R).

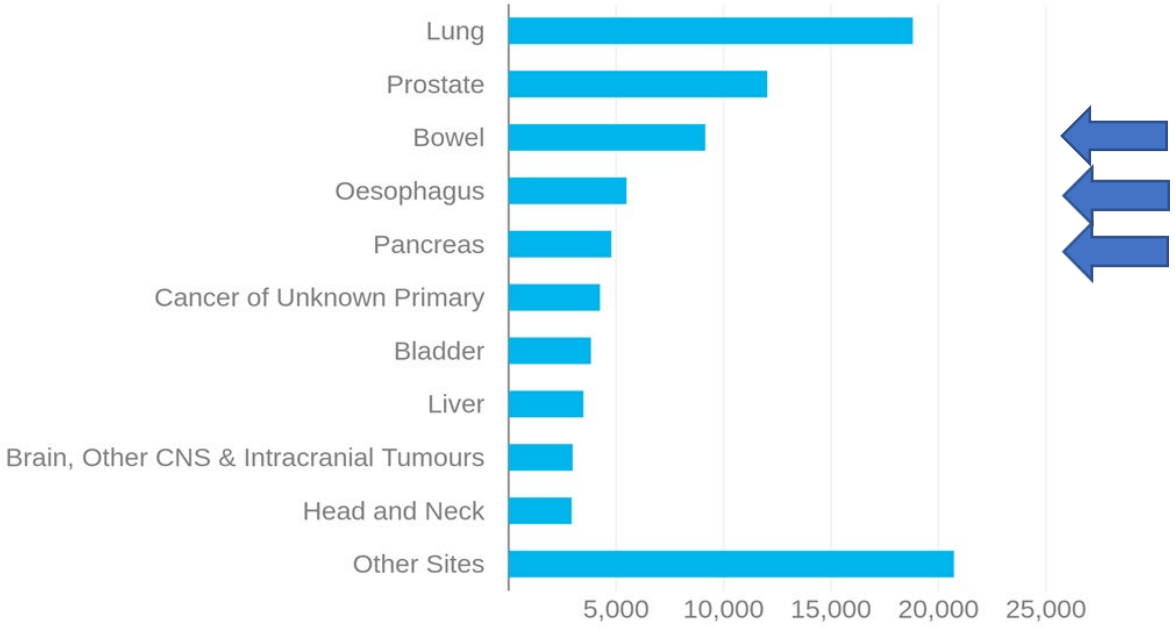
Bowel cancer around 23,500 cases a year in men, 18,600 in women. CRUK.



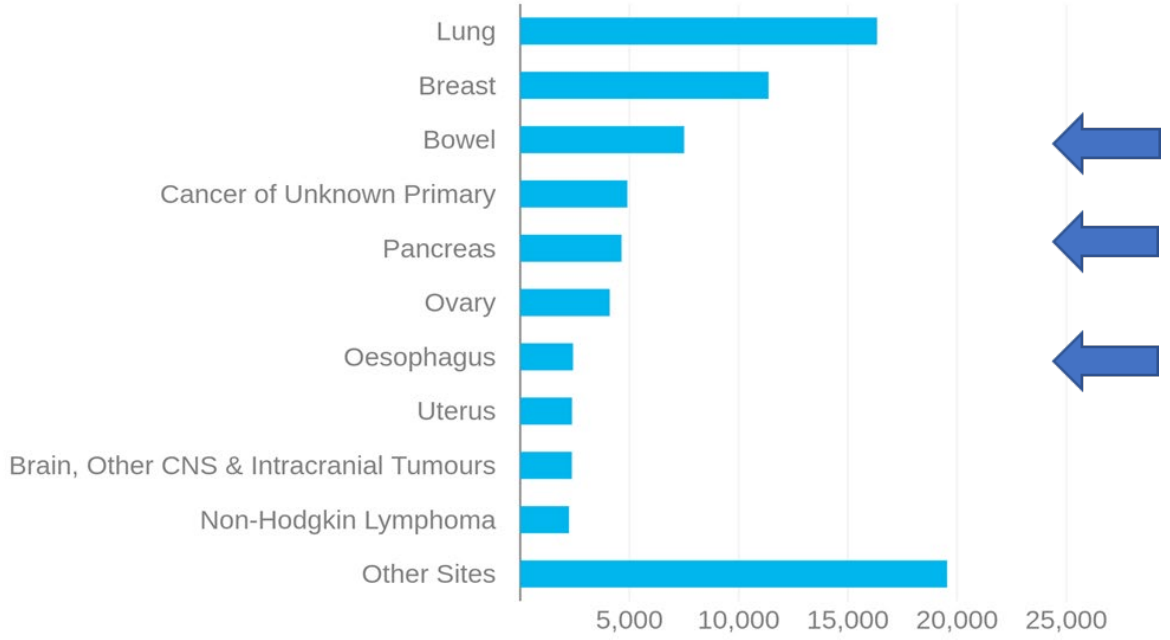


Cancers of the digestive tract the most common causes of mortality other than lung, breast, prostate, ovarian cancers.

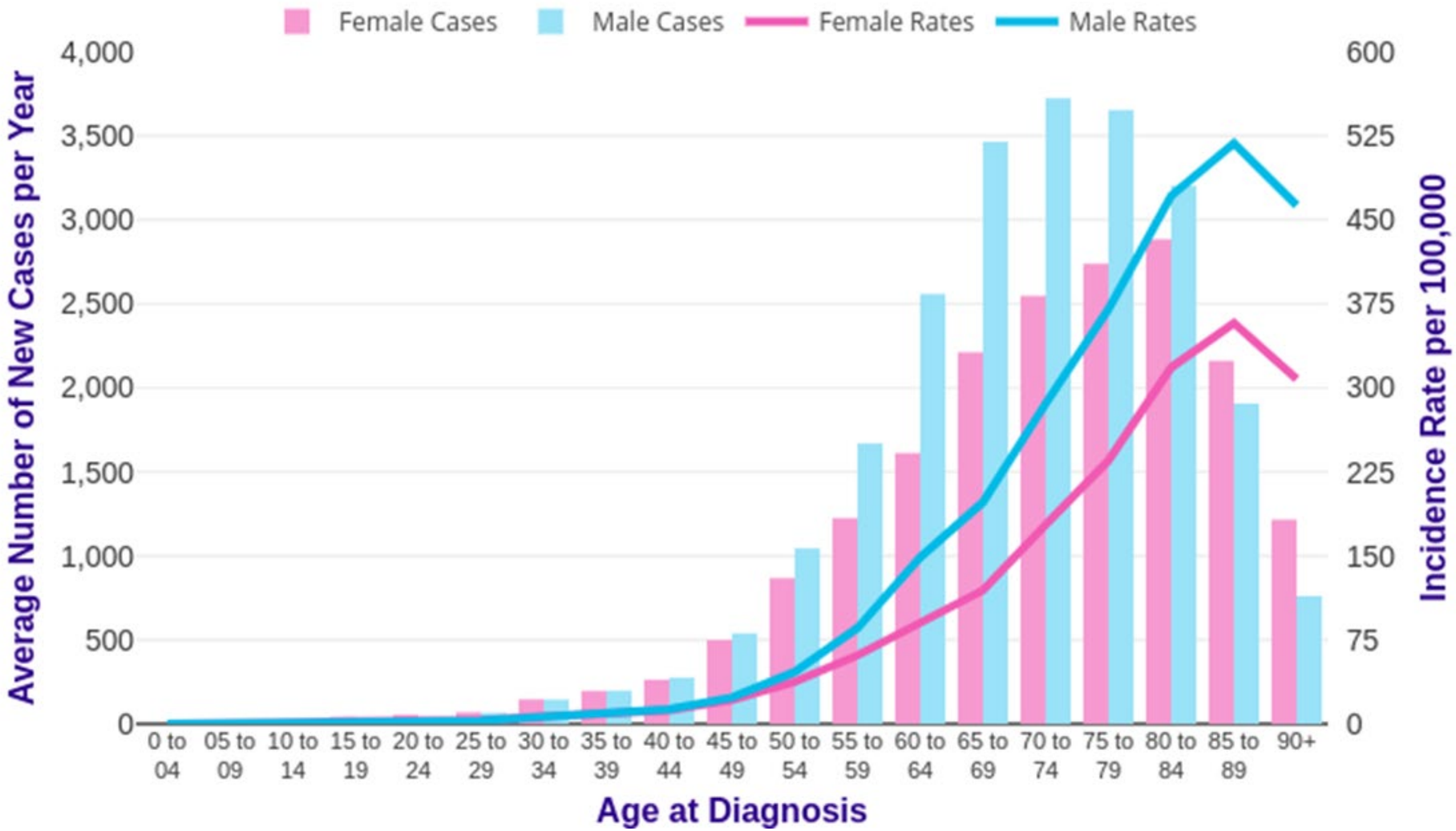
Men: UK in 2017



Women: in UK, 2017



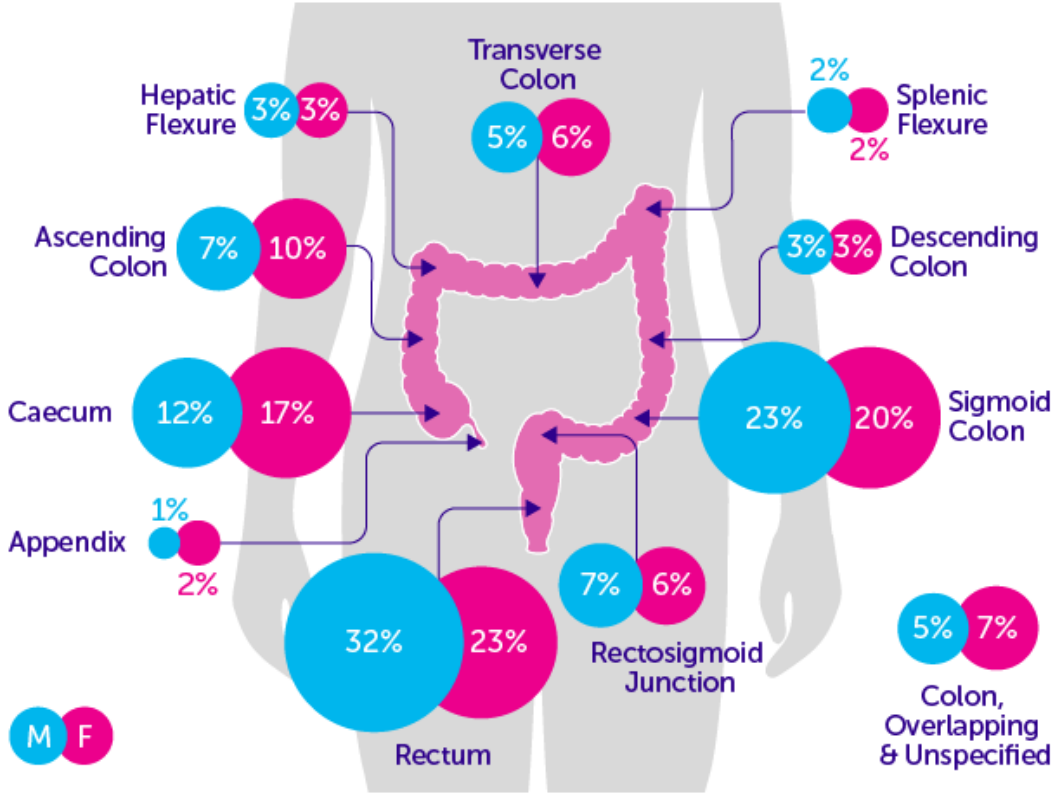
Bowel cancer is rare before 50. More common in men.



CRUK

Most bowel cancer mainly at the start and end of the large bowel.

- Rectum and sigmoid account for about half of bowel cancers.
- Caecum, where the small bowel meets the large bowel, the next most common.

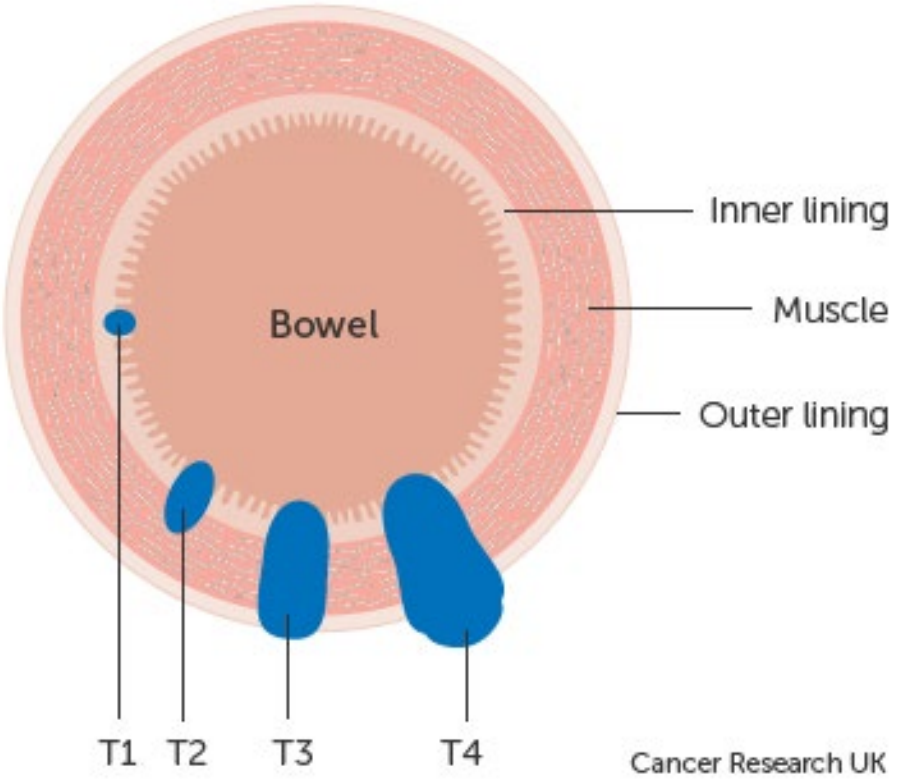


Stage, grade and type.

- Stage- size and how far it has spread.
- TNM: tumour, nodes, metastases.
- Duke's stage.

- Grade- how abnormal cells are.

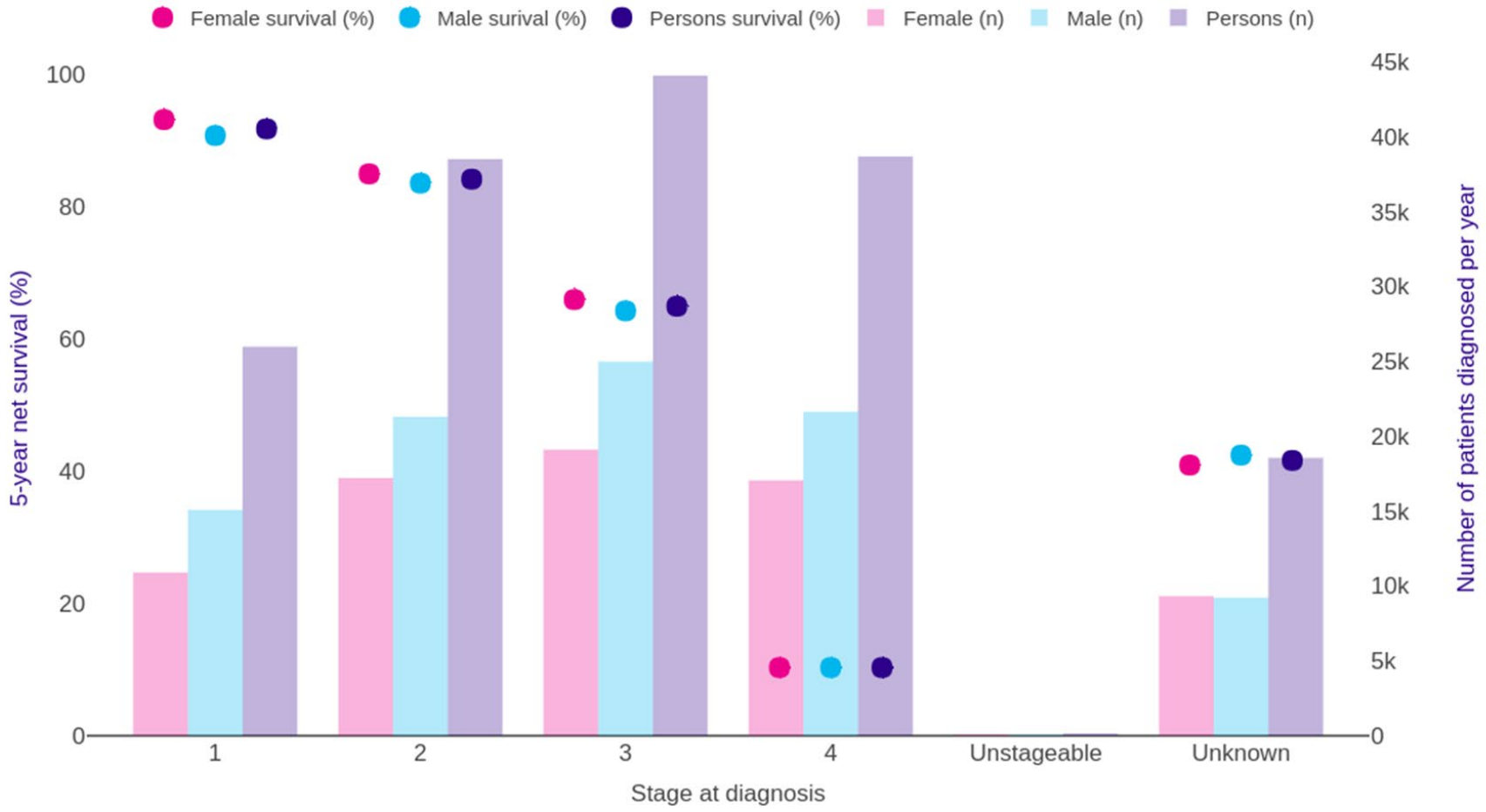
- Type- which cell type the cancer comes from. Most are adenocarcinoma from mucus cells.



TNM- T.

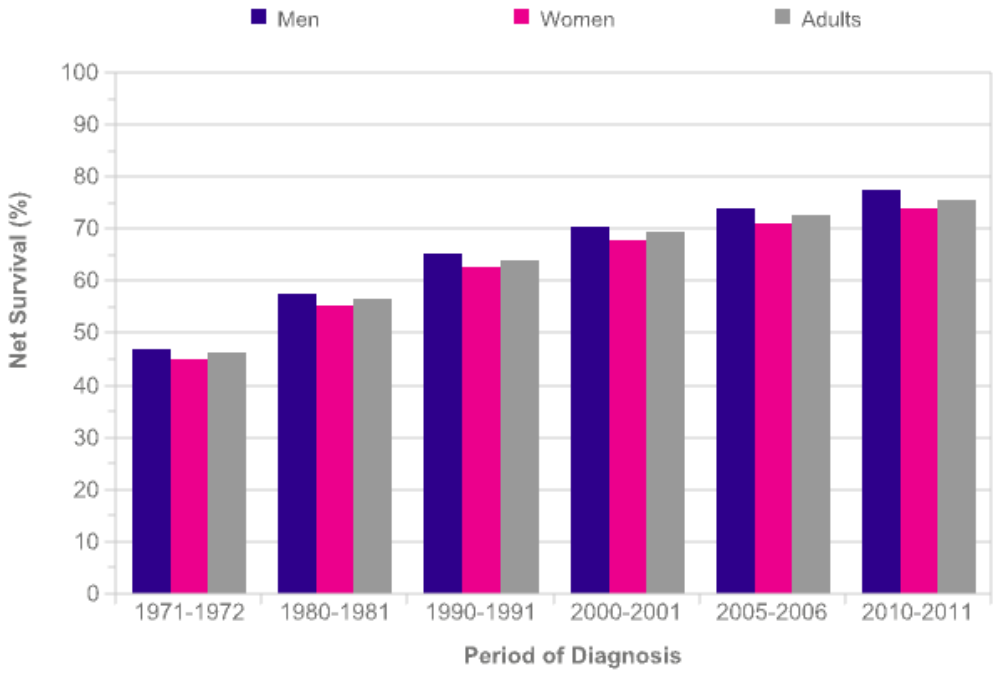
Bowel cancer 5 year survival by stage: male and female.

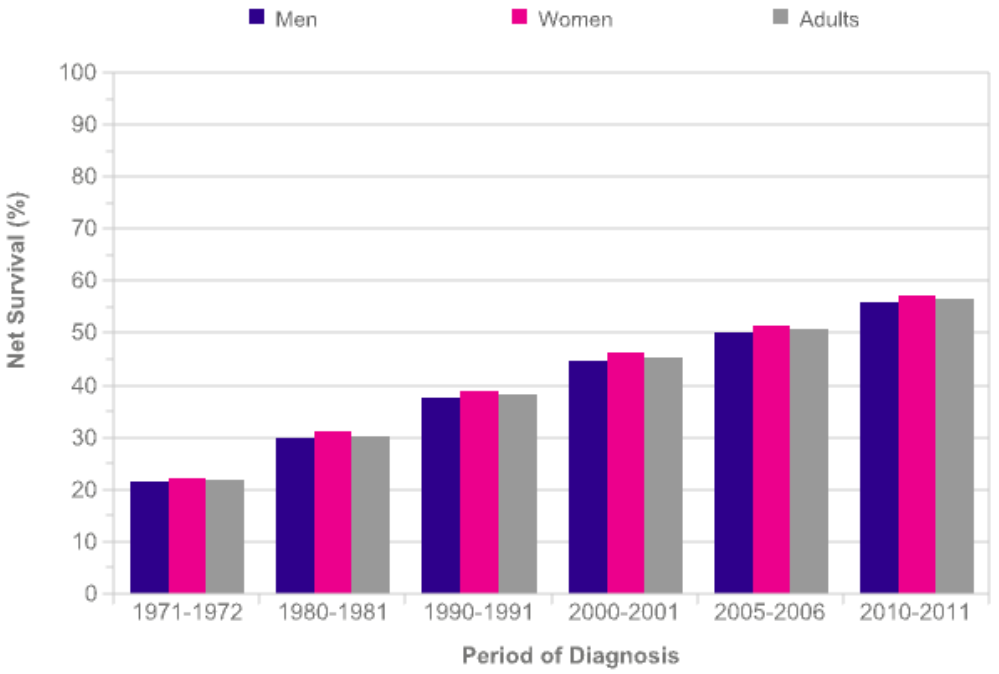
5-year survival 92% Stage 1, 83% Stage 2, 64% Stage 3, 10% Stage 4.



CRUK

Survival has improved over time- doubled in the last 40 years.
1 year survival now around 80%, most people survive more than 10 years (R).

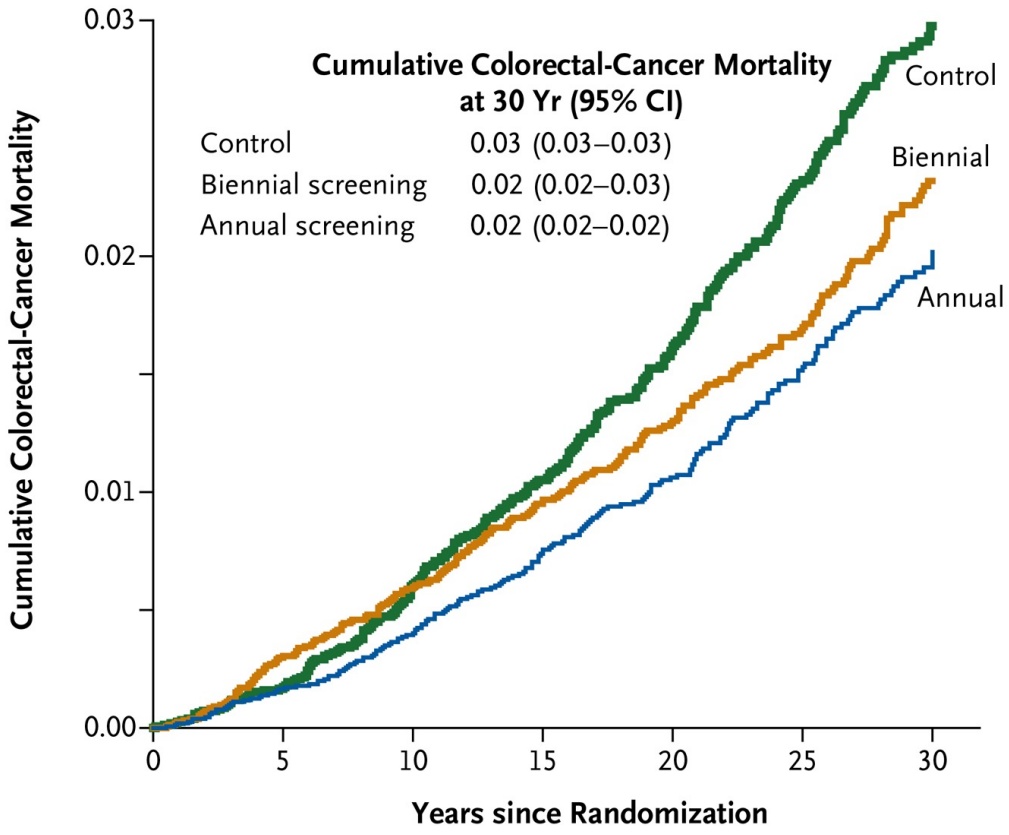




CRUK

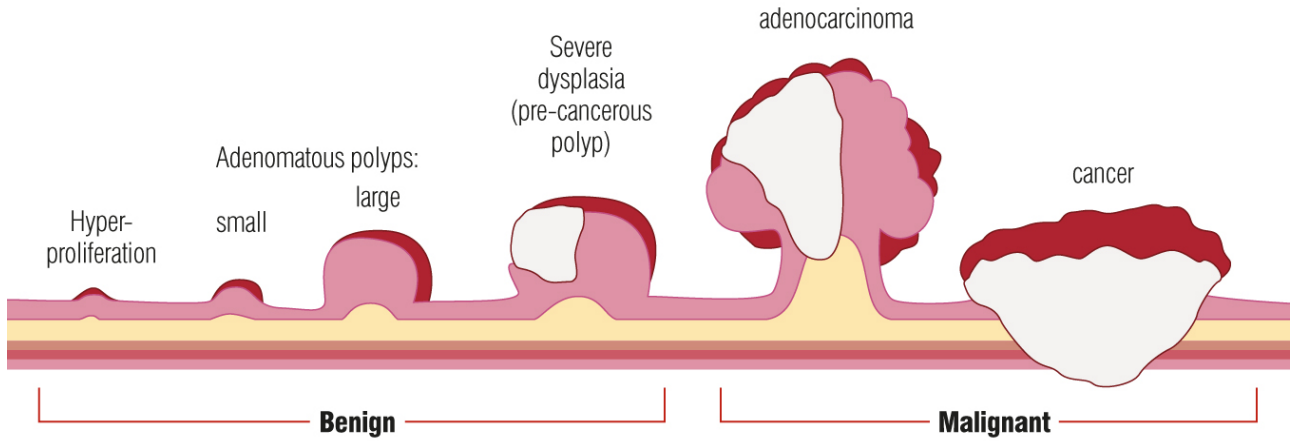
Key is to get it early. Screening.

- FIT (faecal immunochemical test) for blood in stool. Currently age 60-74. Uses antibodies that specifically recognise human haemoglobin.
- Uptake around 67% in England.
- Nottingham trial randomised 152,850 individuals FOB. At 19.5 years there was a 13% reduction in colorectal cancer deaths. *Scholefield et al Gut 2011.*
- US study (R) 46,551 randomised. RR with biennial FOB screening 0.78. *Shaukat et al NEJM 2013.*



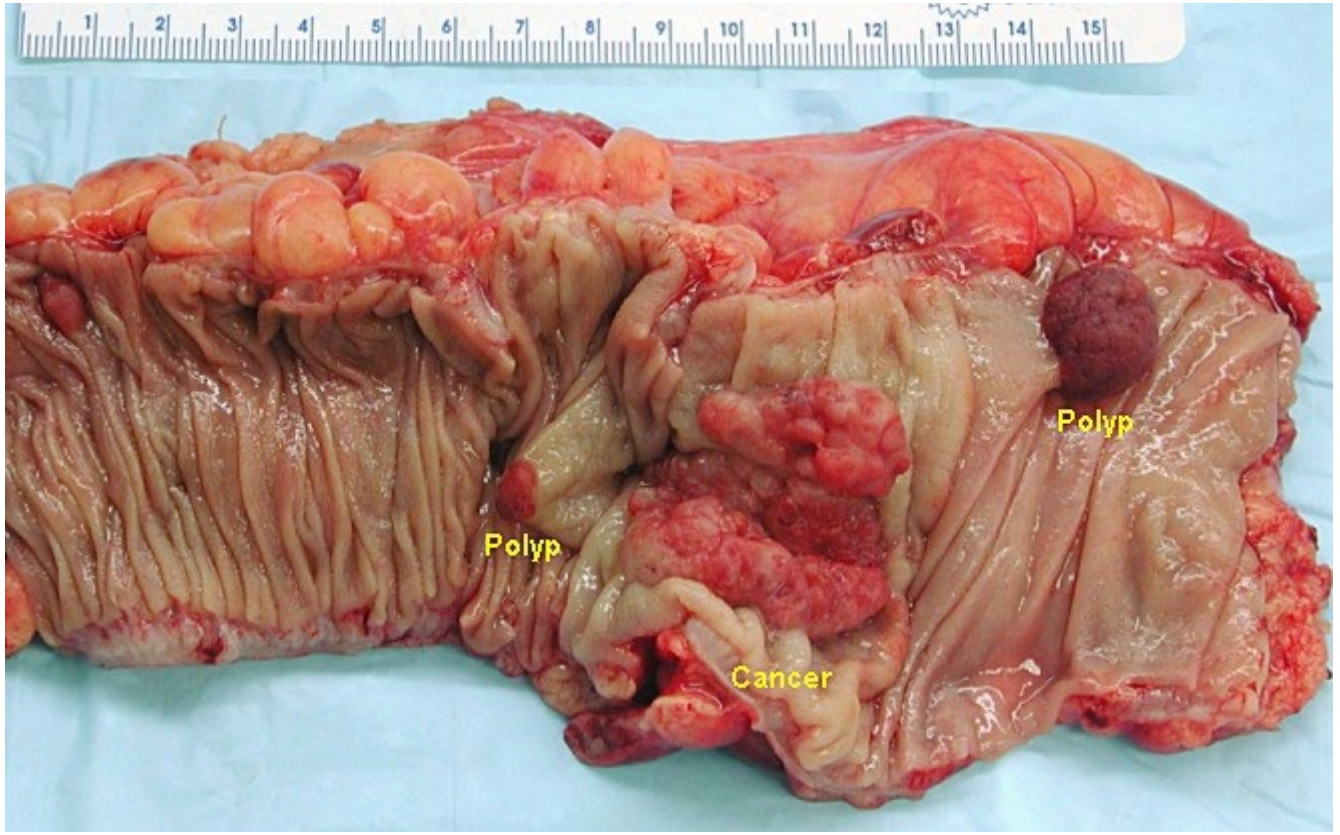
Natural history of tumour.

- Cancers (carcinomas) currently thought to arise by stages.
- Takes years.
- 80–90% of colorectal tumours follow loss of activity of the Adenomatous polyposis coli (APC) gene, a tumour suppressor gene.



GutsUK

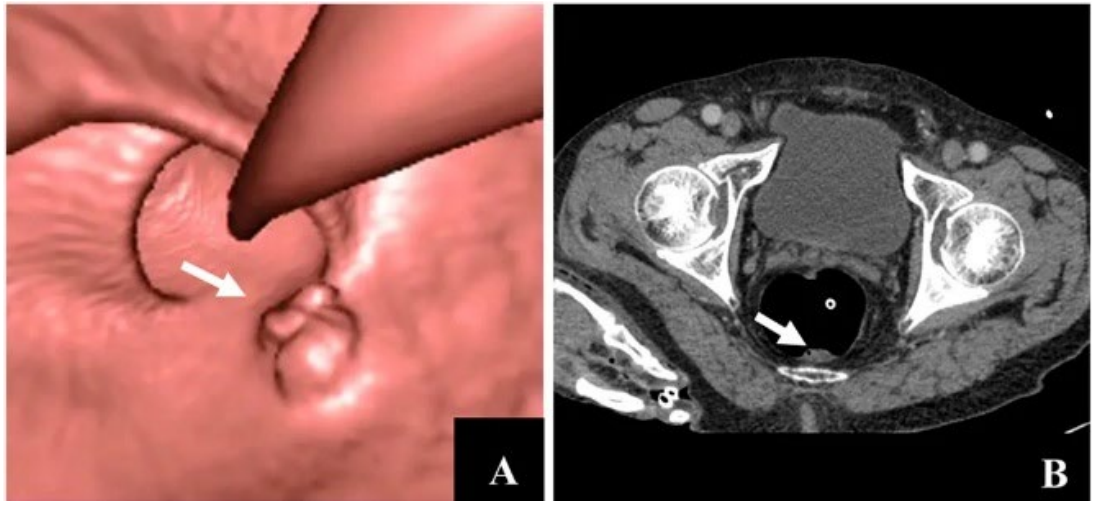
Polyps and a tumour.



Emmanuelm/wiki

Symptoms include:

- Blood in stool, or bleeding.
- Change in bowel habit.
- Feeling need to strain in back passage even after open bowels.
- Loosing weight.
- New breathlessness due to anaemia.



- Colonoscopy/sigmoidoscopy or
- CT colonography.

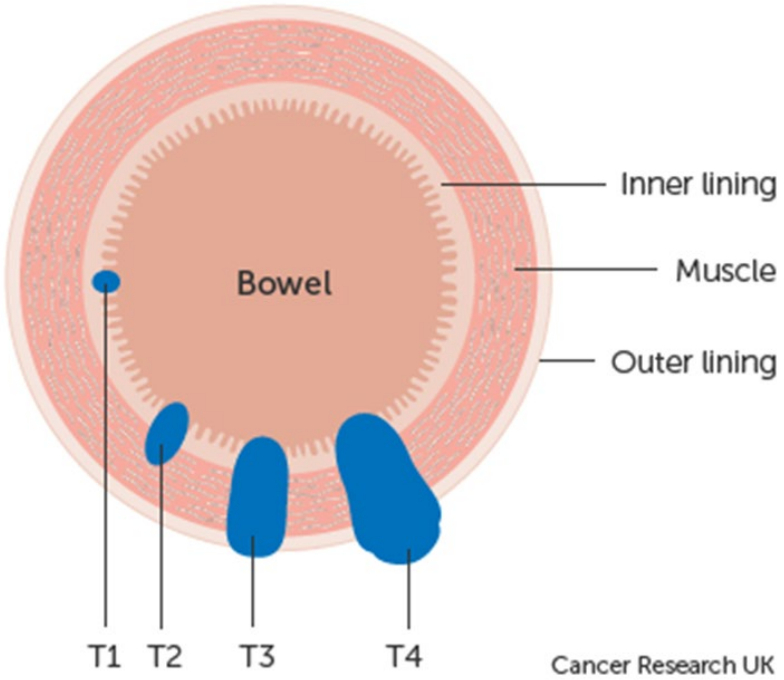
Kai Sun et al Wiki. Rectal mass.

Emergency bowel obstruction or major symptoms.

Cases courtesy of: Prof Craig Hacking, Radiopaedia.

Dr Hani Makky ALSALAM, Radiopaedia.

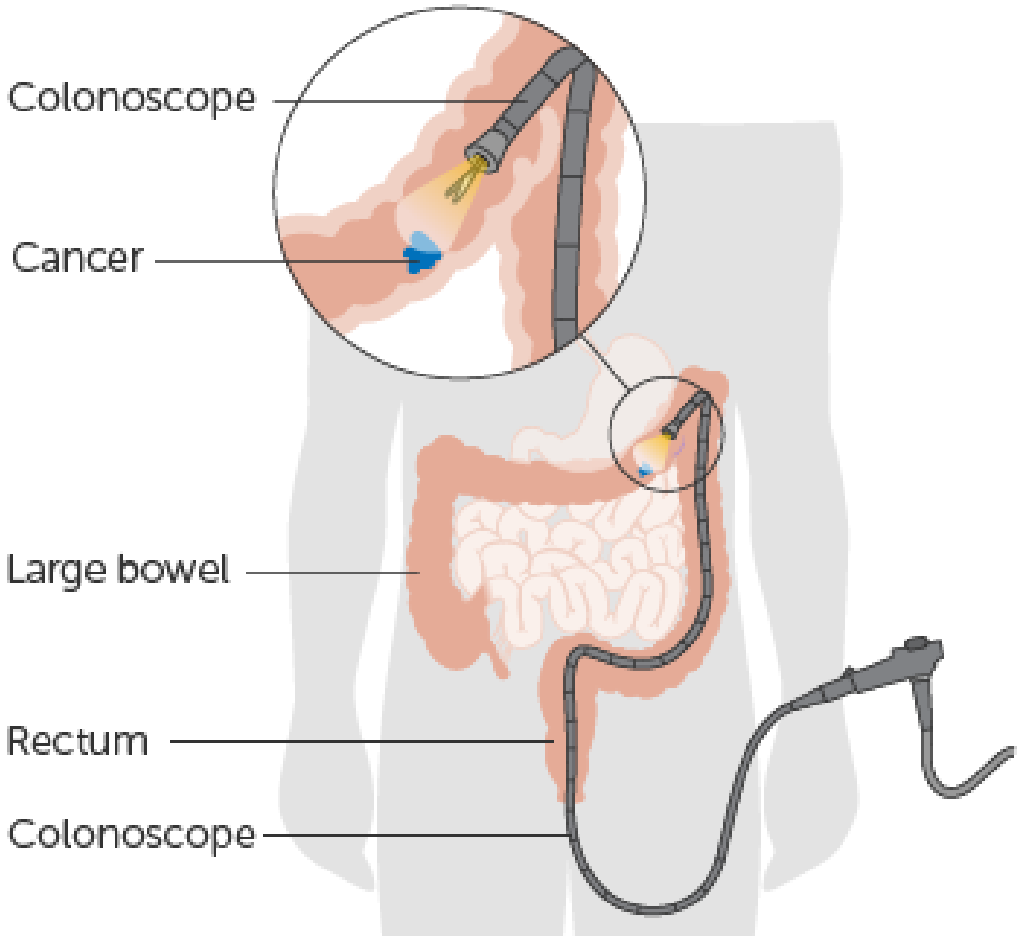
Removing the tumour (surgery) the mainstay of treatment in early stage bowel cancer.

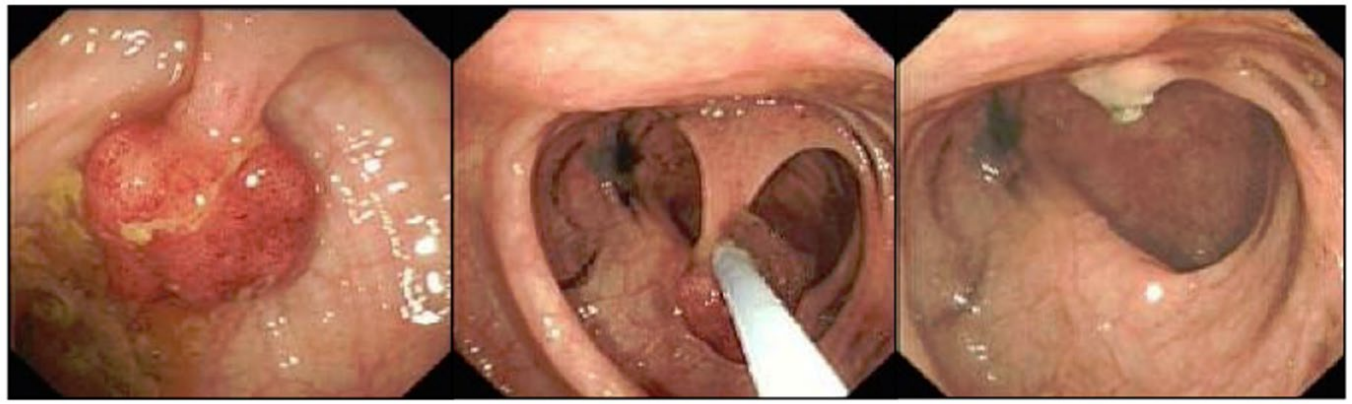


	Surgery	Radio-therapy	Chemo-therapy
Stage 1	93%	1%	3%
Stage 2	90%	2%	19%
Stage 3	87%	5%	58%
Stage 4	33%	6%	47%

CRUK, data from 2014

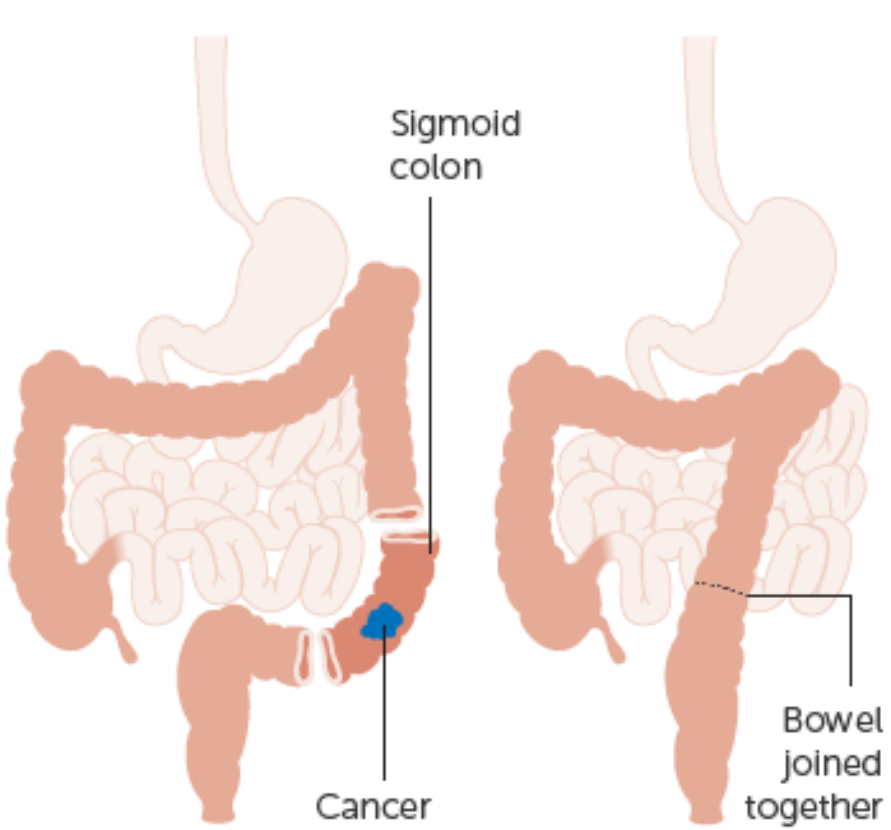
Surgery for early (Stage 1) cancer. Remove cancer and lining.

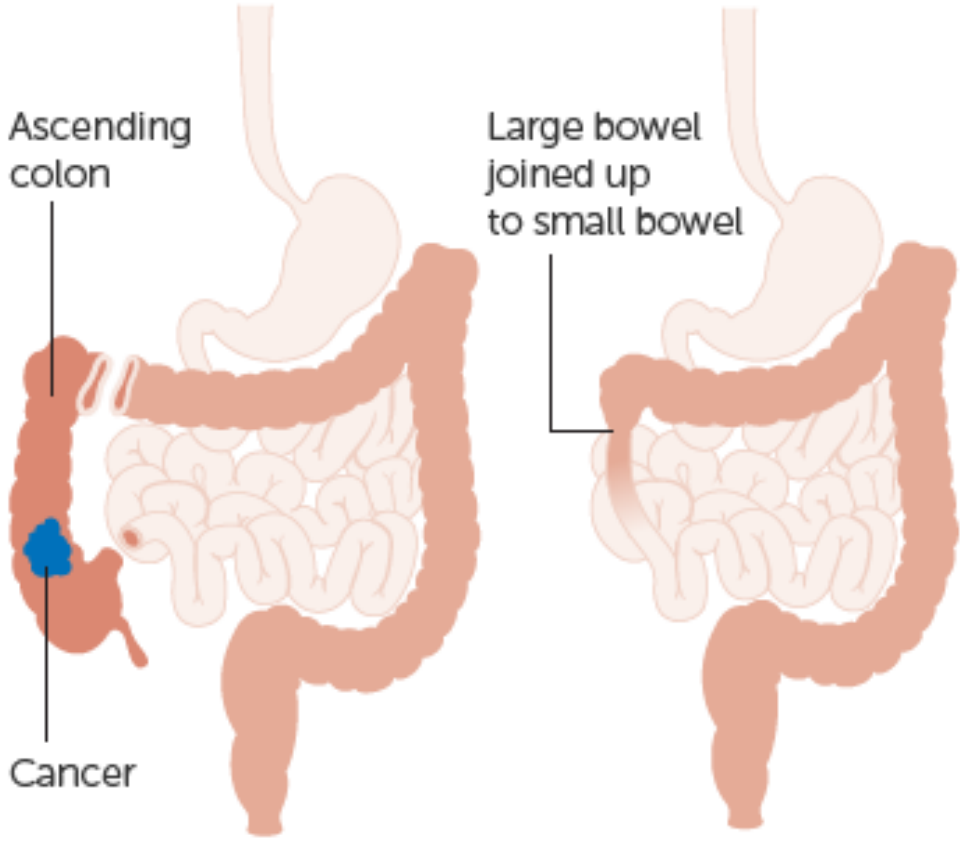




CRUK/Wiki

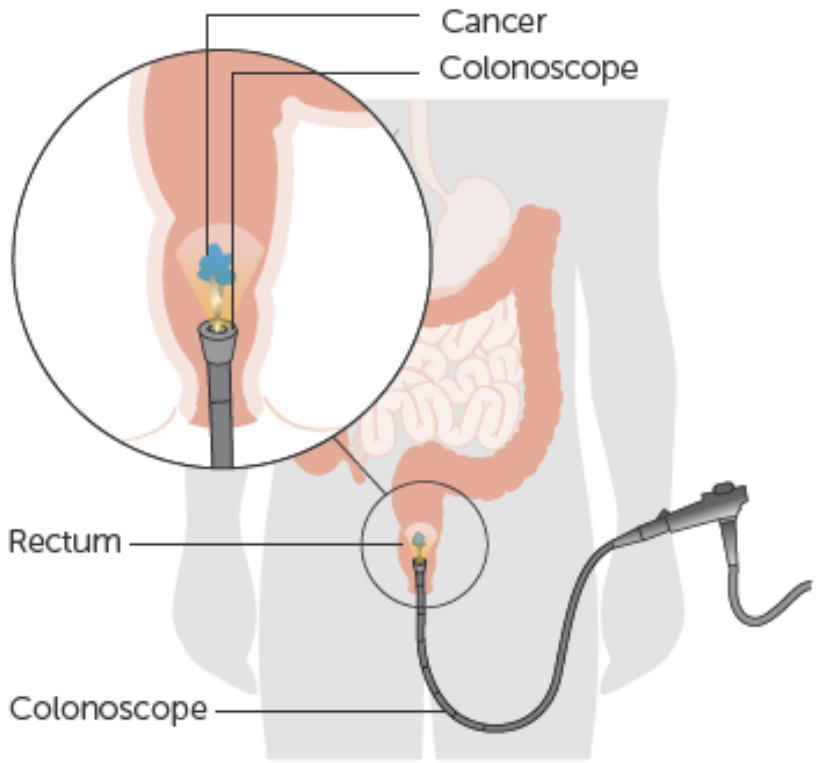
A section of the bowel may be removed, and then re-joined. Sigmoid (L), ascending colon hemicolectomy (R).



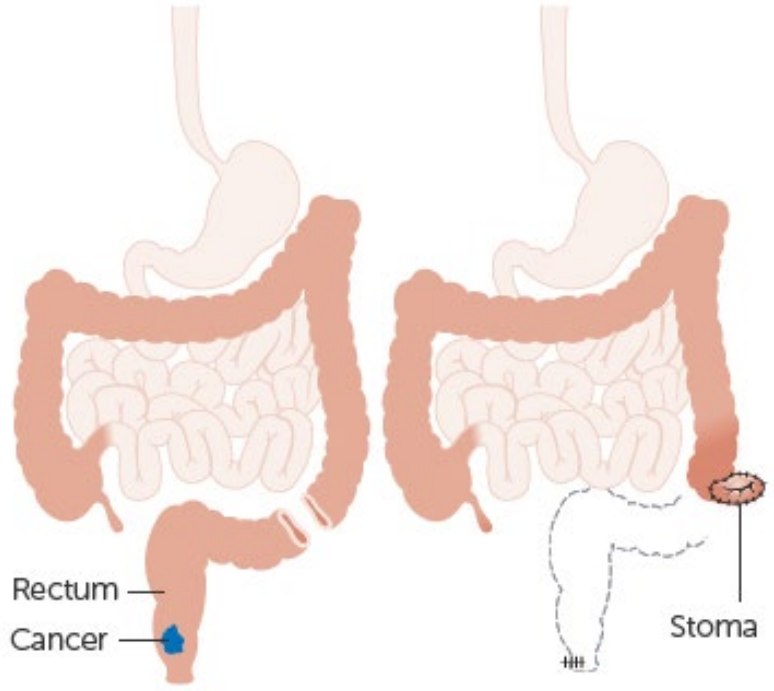


CRUK

Surgery for rectal cancer.
Depends on stage and site; lower more likely to have a stoma.



Trans anal endoscopic microsurgery

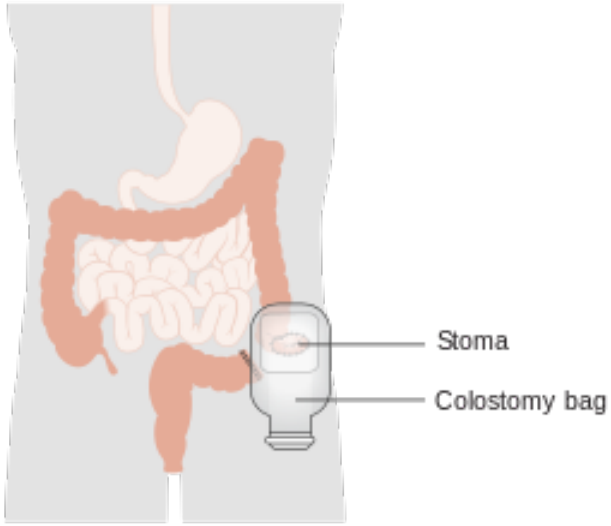


Total mesorectal excision

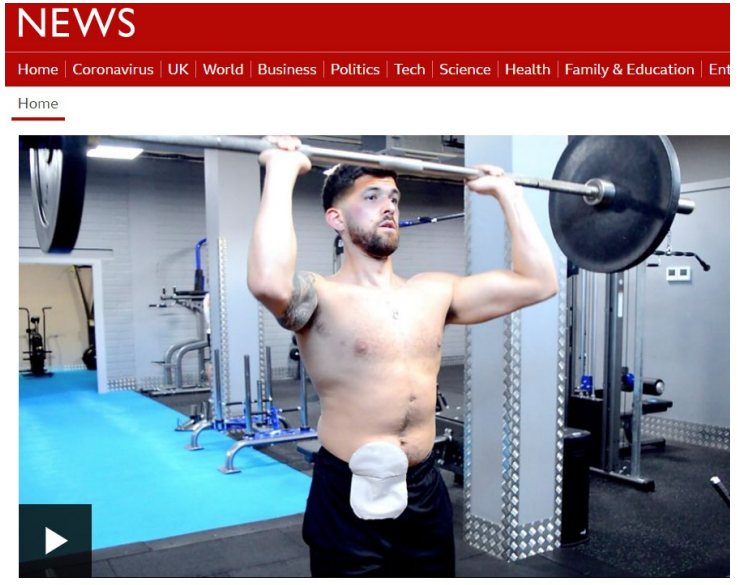
CRUK

In some cases the best option is a stoma- a bag to collect waste.

- Colostomy or ileostomy.
- Usually this is temporary in colon cancer.
- More likely to be permanent in rectal cancer.



What is it like to live in a house share with a stoma?



Stoma bag 'has given me my life back'

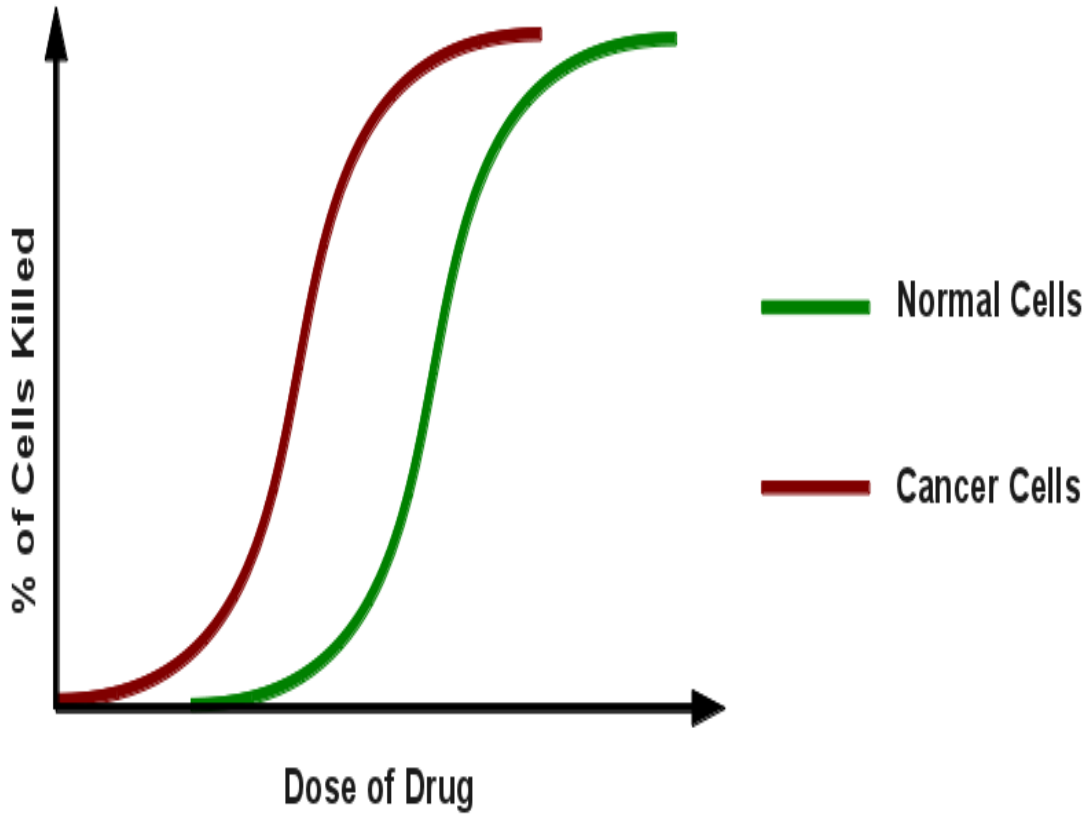
Surgery is continually advancing.

- Open surgery- the oldest.
- Endoscopic surgery.
- Laparoscopic (keyhole) surgery.
- Robot-assisted surgery.

Samuel Bendet

Cytotoxic chemotherapy mechanisms.

- The basic mechanisms of conventional chemotherapy.
- Kill any cell that is dividing- cancer cells more sensitive and slower to recover.
- Good effect depends on the cancer. Rapidly dividing = more effective.



Chemotherapy.

Examples of chemotherapy for more advanced bowel cancer.

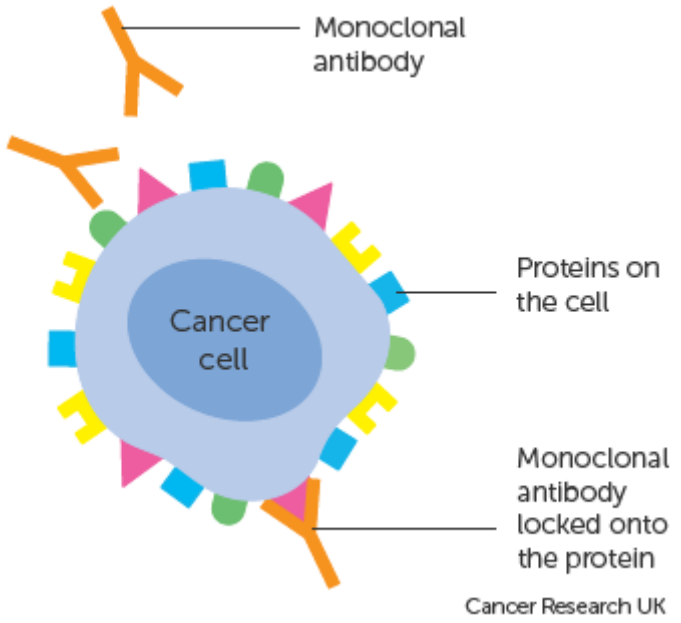
- FOLFOX- folinic acid, flourocil (5FU), oxaliplatin.
- XELOX- oxaliplatin, capecitabine (5FU prodrug).
- Irinotecan- from the bark of the Camptotheca tree (Tibet and S China).

Common side effects fatigue, feeling and being sick, diarrhoea, tingling/numbness.

Targeted therapies- currently experimental.

Examples:

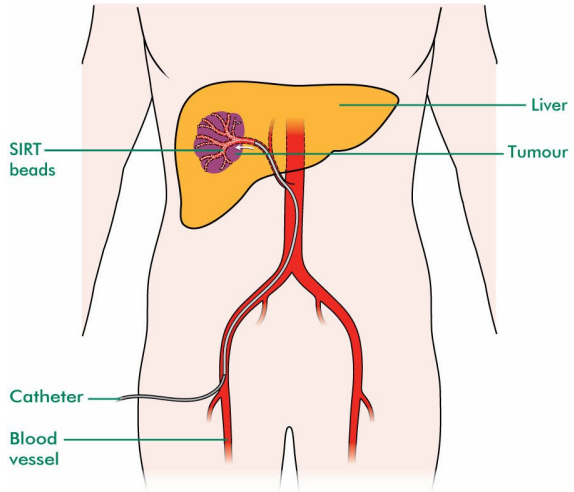
- Cetuximab, panitumumab and bevacizumab. Antibodies which target the cancer cells.
- Cetuximab, panitumumab block epidermal growth factor receptors (EGFR) on bowel cancer cells.
- Bevacizumab reduces blood vessel growth (anti angiogenesis).



Radiotherapy.

- Colon cancer that has spread, and sometimes rectal cancer that has not spread.
- External beam radiotherapy.
- Internal radiotherapy: High dose rate brachytherapy (HDR) and contact X-ray radiotherapy (Papillon).
- Stereotactic radiotherapy for liver metastases- very precise external radiotherapy.
- Selective internal radiation therapy (SIRT) for liver metastases. Tiny radioactive beads into the artery to the liver.

Cancer Research UK

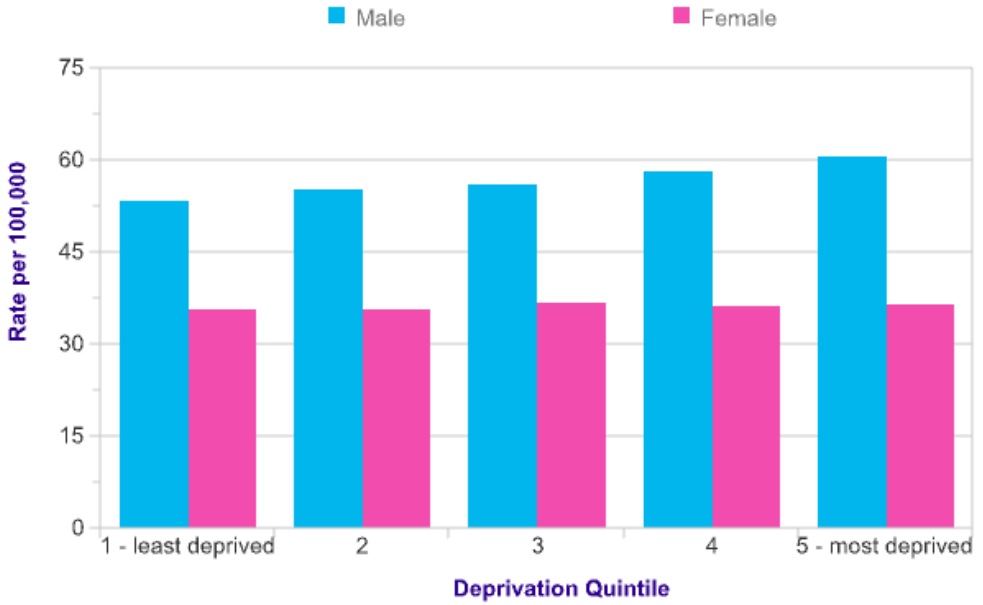


CRUK/Macmillan Cancer Support

Over half of bowel cancer is potentially preventable.

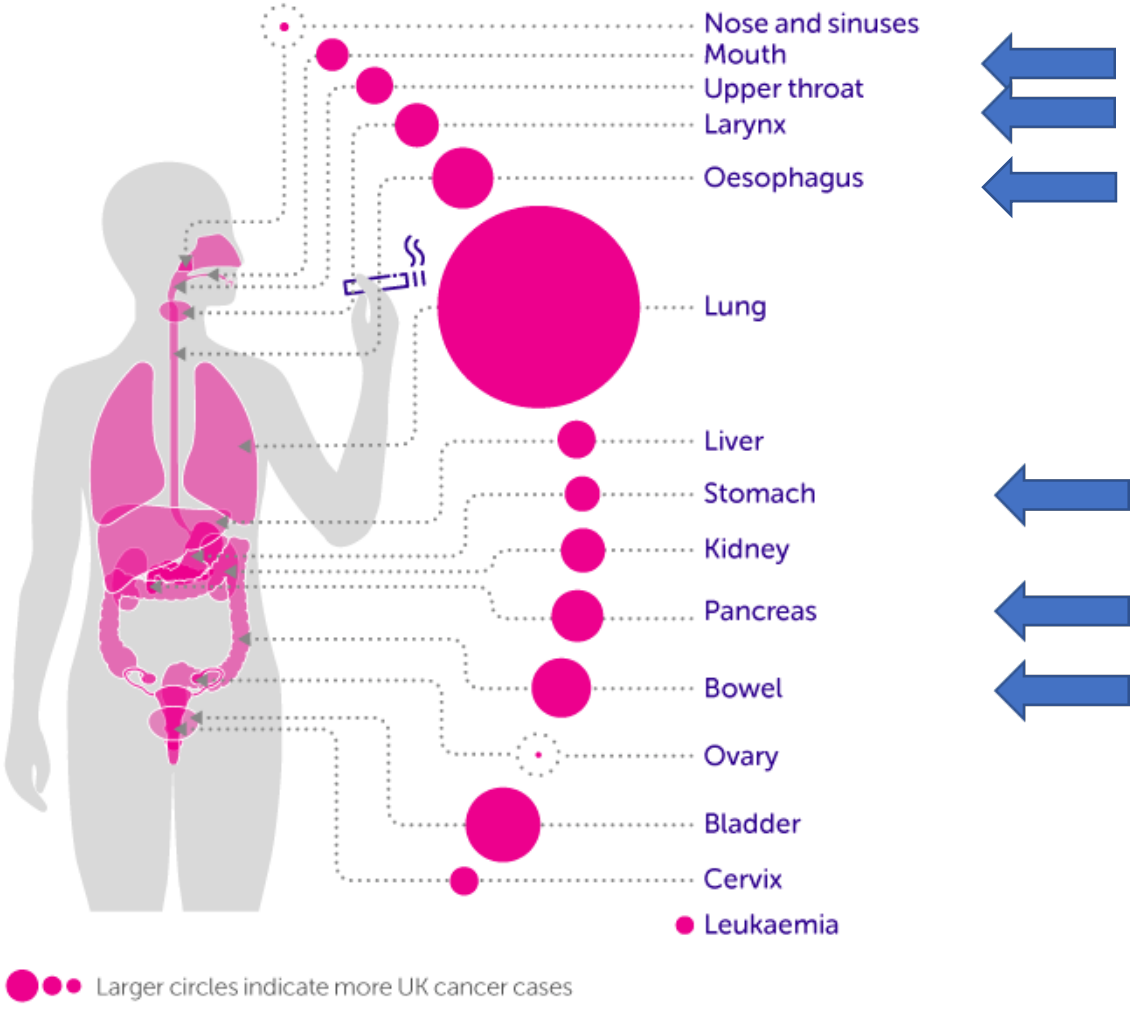
Modifiable risk factors (estimates).

- Too little fibre in diet 30%.
- Processed meat 13%.
- Obesity 11%.
- Tobacco 7%.
- Alcohol 6%.
- Exercise.



CRUK/Wiki

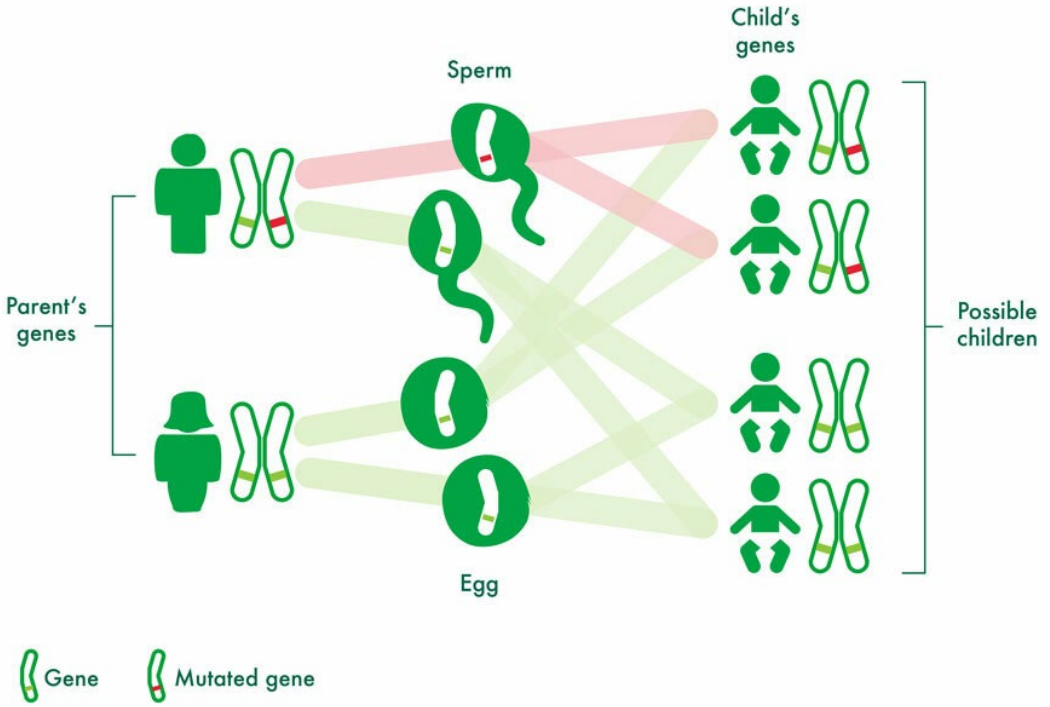
Smoking contributes to many cancers of the digestive tract.



CRUK; Vincent Van Gogh

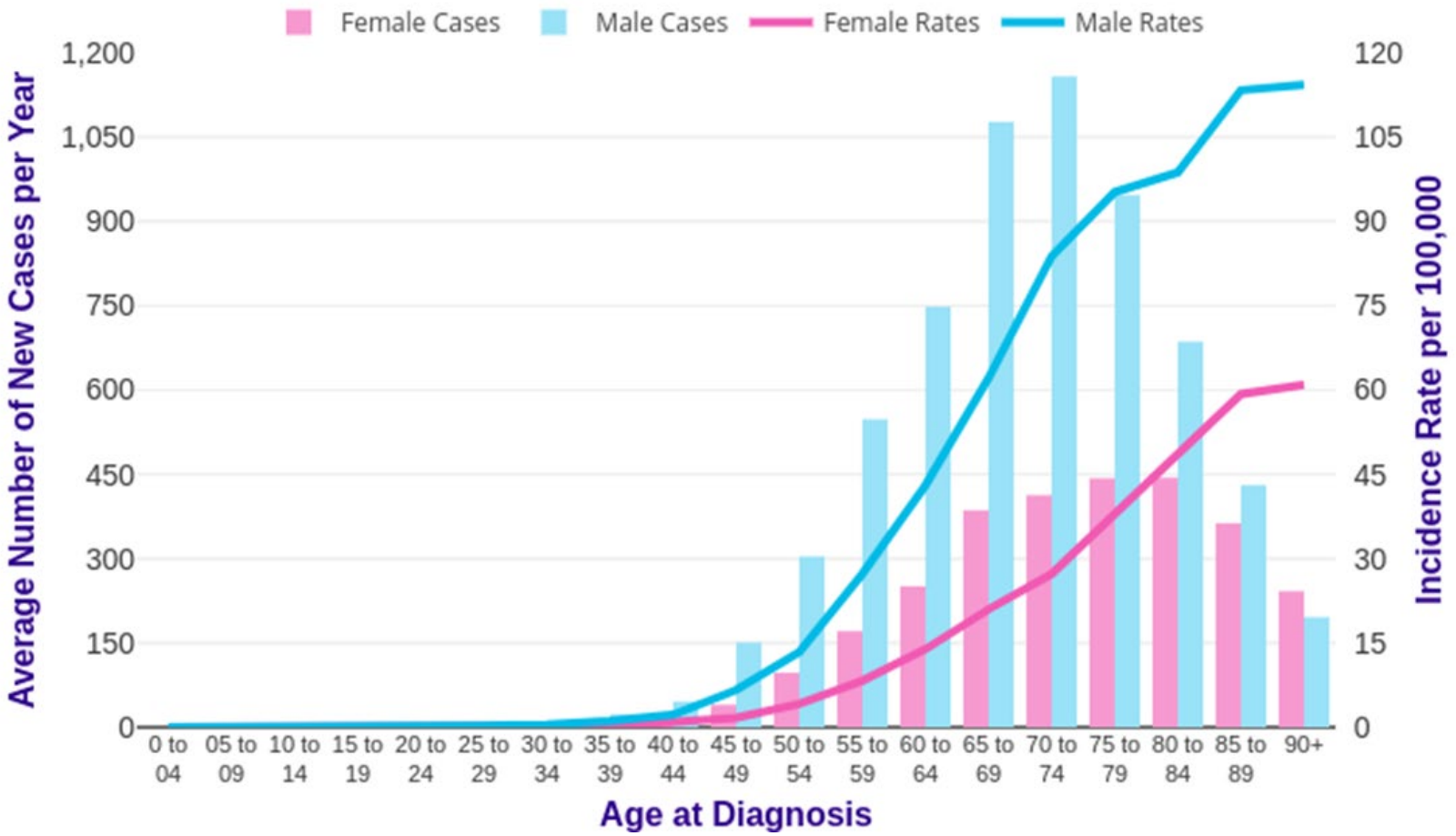
In some cases bowel cancer has a familial link.

- If close relatives (siblings, parent, child) have bowel cancer under 50 greater risk.
- If several have bowel cancer also greater risk.
- Some rare genetic conditions:
- Lynch syndrome (HNPCC). 50% chance passing on.
- Familial adenomatous polyposis FAP.
- In these cases more intensive screening needed.



Macmillan cancer support.

Oesophageal cancer. More common in men then women, very rare before 50.



Oesophageal cancer. Usually picked up due to symptoms- which are often late disease.

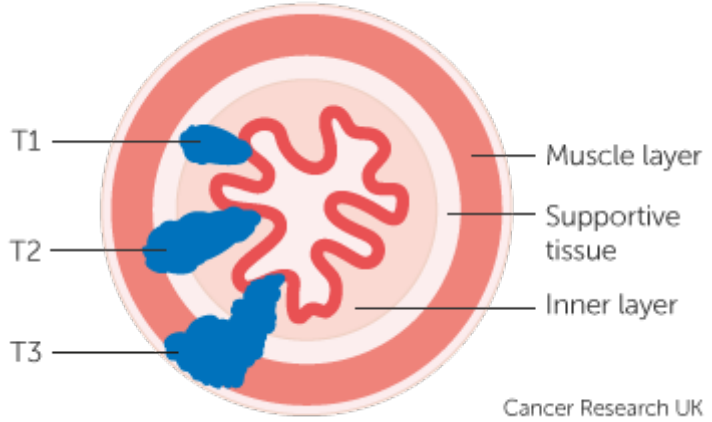
- Difficulty swallowing.
- Indigestion and heartburn that will not go away.
- Weight loss.
- Pain in throat behind breastbone.

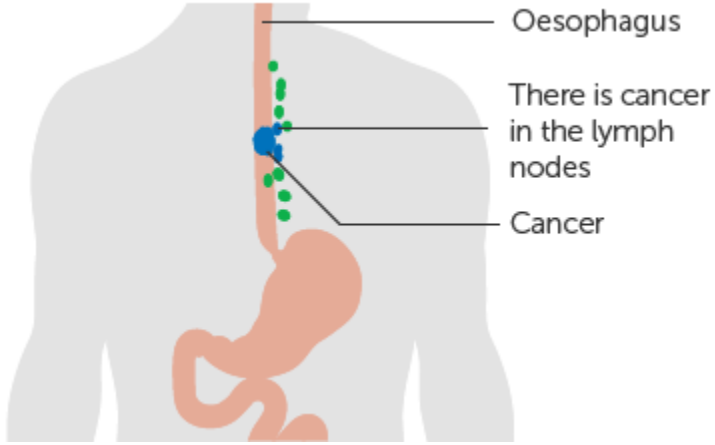
- Normally investigated by endoscopy.
- Will have CT or other imaging if a cancer found.

Drs Bahman Rasuli and Bob Tran Radiopaedia.

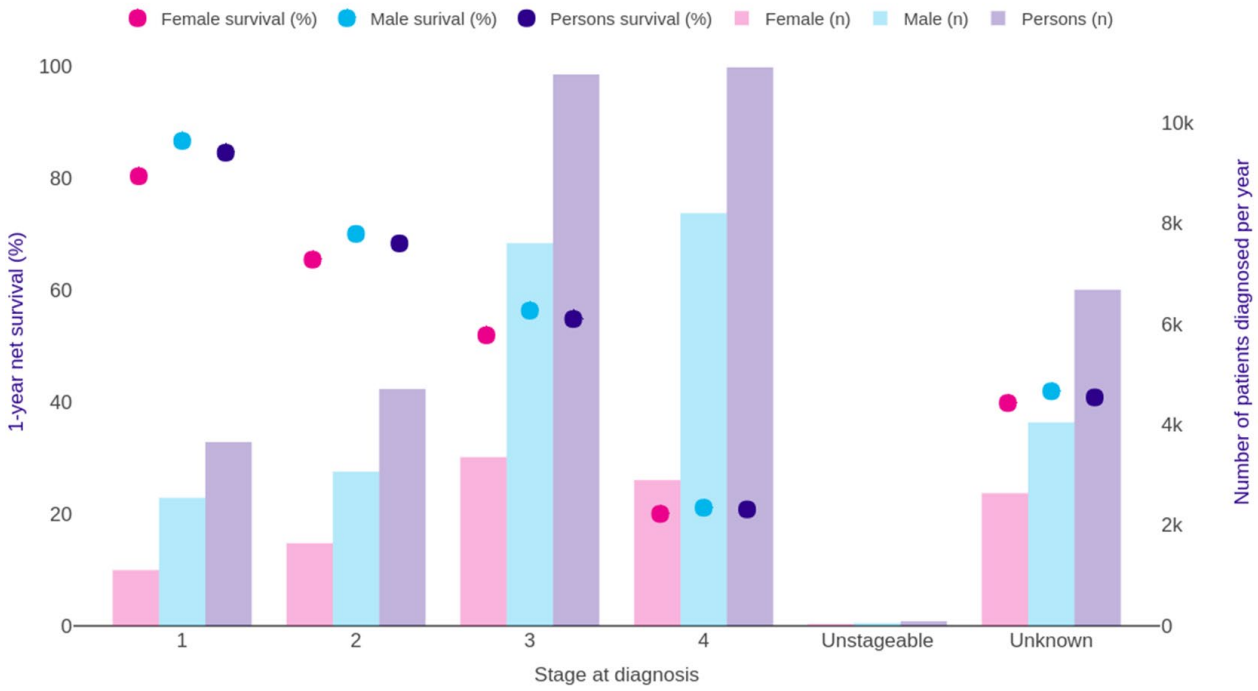
Staging and type of oesophageal cancer.

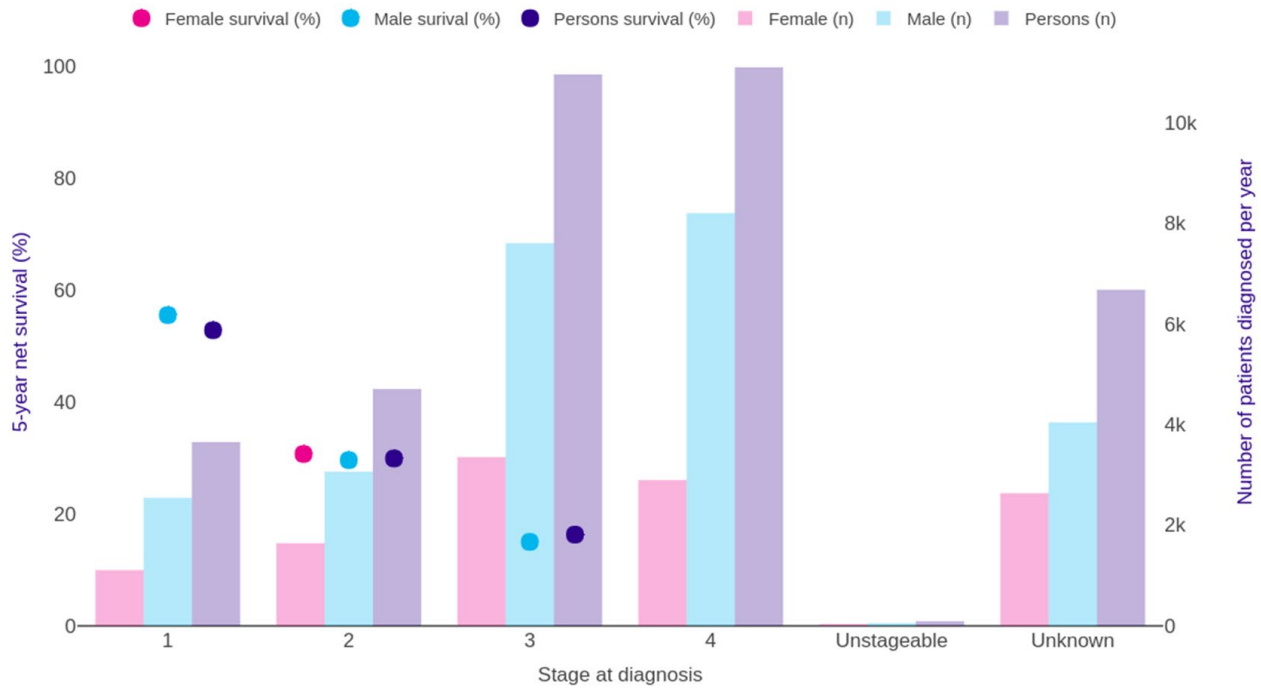
- Relatively complex, but lower stages better prognosis, more limited treatment.
- TNM: tumour, nodes, metastases.
- Stage 0, 1, 2, 3, 4.
- Type can be squamous cell (from lining- most common) or adenocarcinoma (from glands).





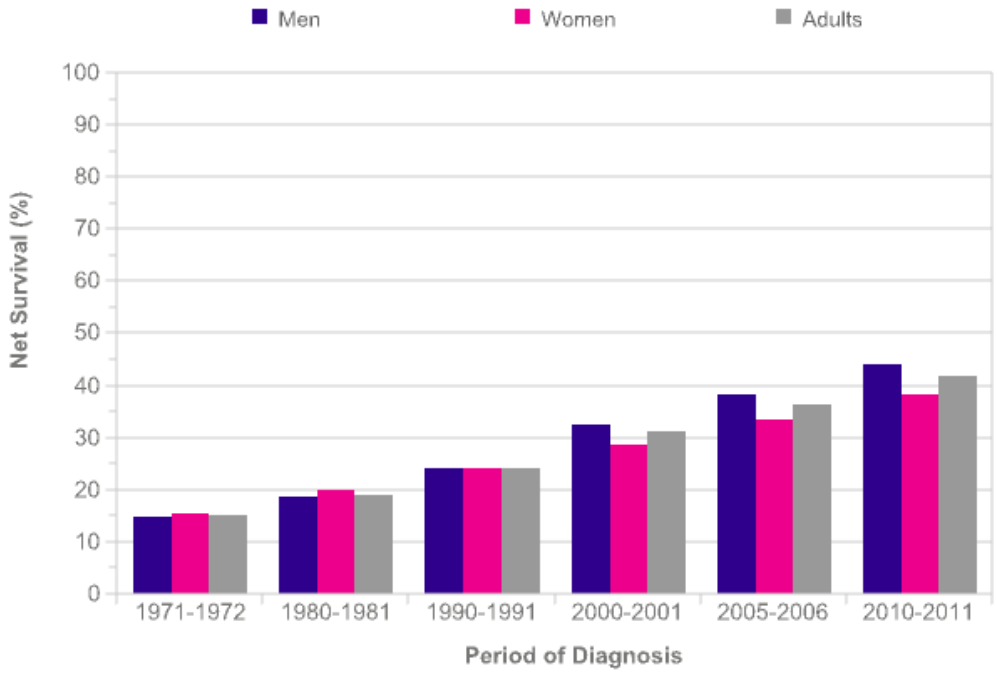
1 (L) and 5 year survival by stage for oesophageal cancer. CRUK.





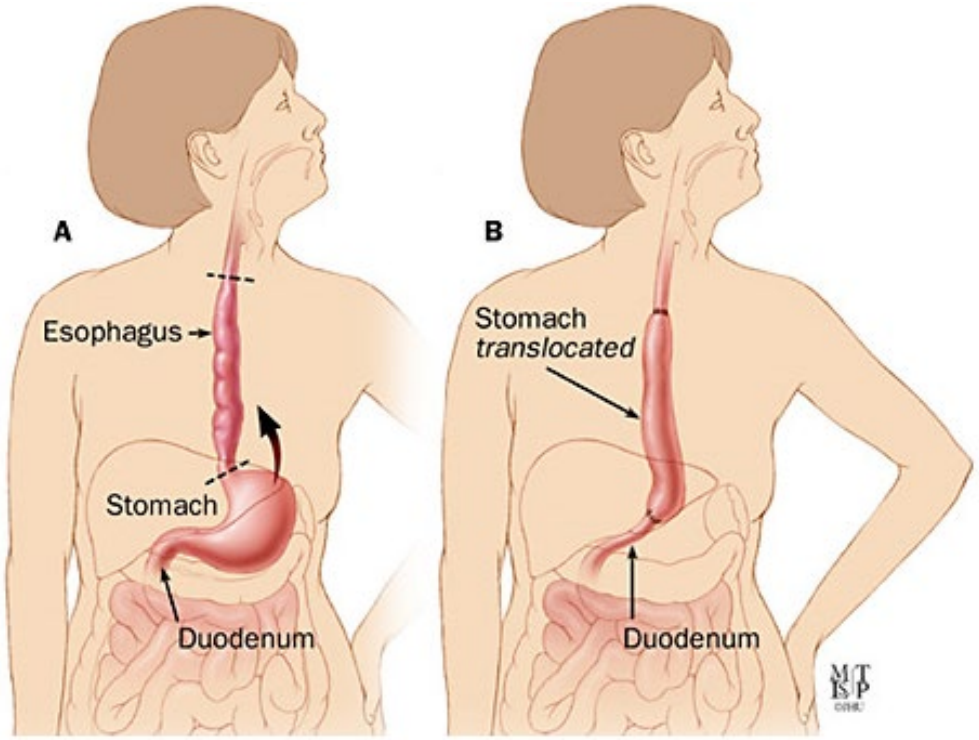
Survival over time (from 1971- 1 year survival) oesophageal cancer.

- There have been improvements in survival over the decades.
- But the outlook remains poor, mainly due to late stage at diagnosis.
- Stark contrast to many other cancers such as breast or prostate where most survive for 10 years or more.



Stage 1, 2, 3 oesophageal cancer treatment.

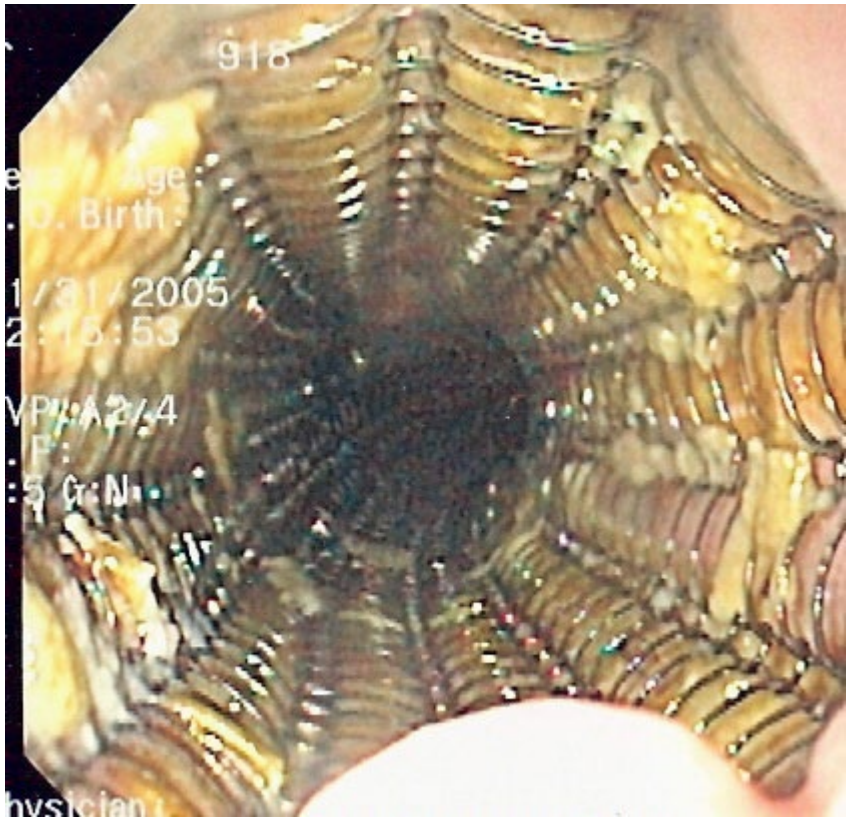
- Surgery the mainstay of treatment for Stage 1.
- Remove some, or all, of the oesophagus.
- If squamous cell carcinoma may have chemoradiotherapy.
- For Stage 2 and 3 the combination of chemotherapy, radiotherapy and surgery depends on whether squamous or adenocarcinoma.



Hull University Teaching Hospitals.

Later stage oesophageal cancer.

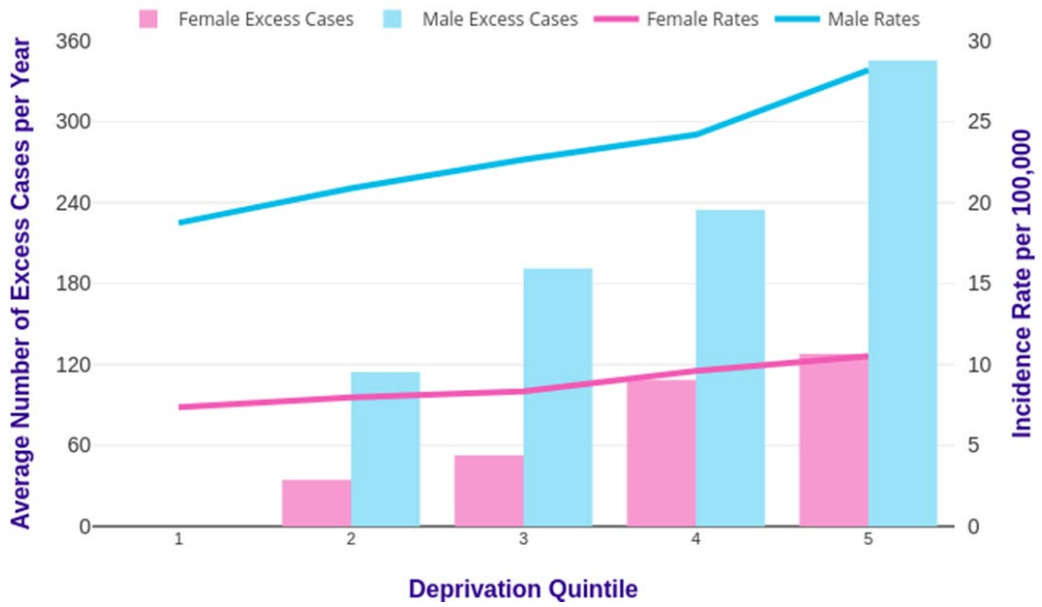
- The later the stage the more likely chemotherapy and radiotherapy will be used.
- Especially for squamous cell carcinoma, and metastases.
- Long term prognosis not good, so much treatment is to improve symptoms.
- May need a stent to keep oesophagus open (R).



Samir/Wiki

There is a strong socioeconomic and gender disparity for oesophageal cancer. (CRUK)

- More common in white than Black of Asian British males and females.
- About 35% of cases linked to smoking.
- Obesity increases risk.
- Alcohol increases risk of squamous cell carcinoma.
- Gastro-oesophageal reflux and Barrett's increases risk of adenocarcinoma.



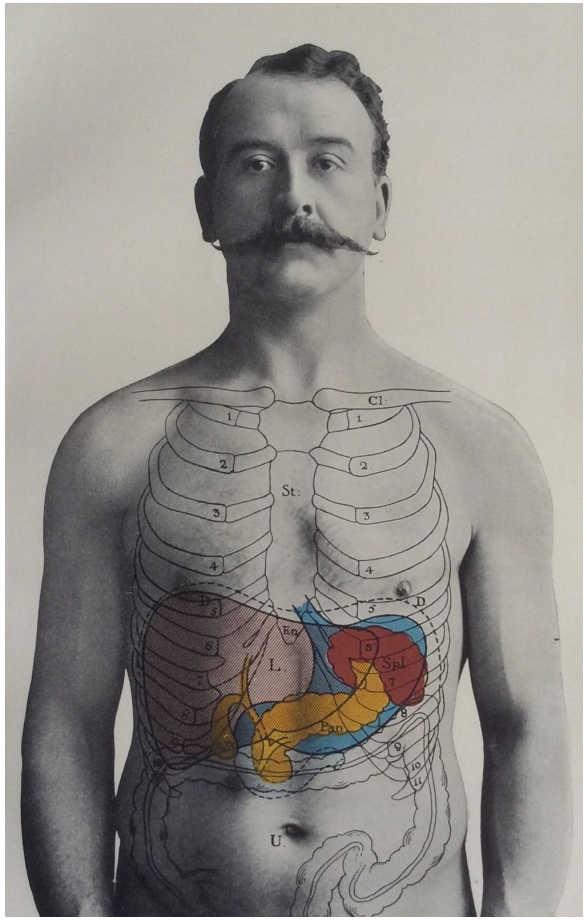
Screening for oesophageal cancer?

- Very early disease (Stage 0, or high grade dysplasia) can be treated by ablation down an endoscope.
- May be removal of the lining, or photodynamic ablation (light) or radiofrequency ablation (heat).
- Can we screen?
- Trials of cytosponge screening for Barrett's.

Source: Kadri et al. 2010.[1]

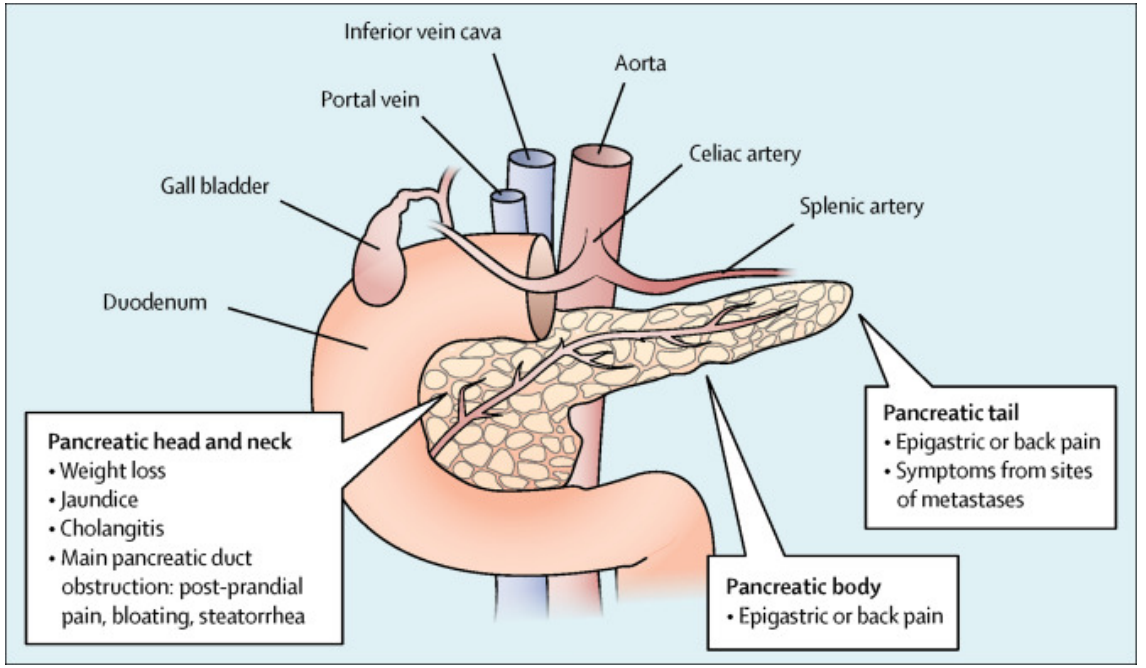
The pancreas has several functions.

- Includes
- Digestive enzymes. Most cancers arise from these cells, majority adenocarcinoma (around 85%).
- Producing insulin, glucagon. Neuroendocrine tumours (PanNETs). Outlook much better.



Symptoms are late and often vague.

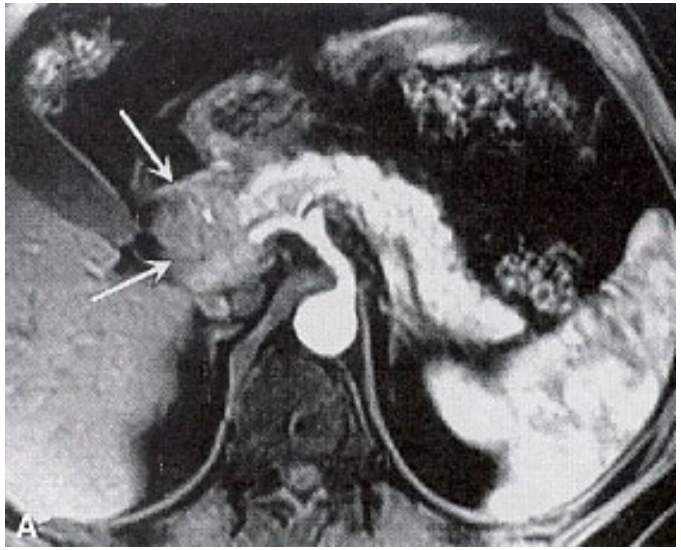
- Depend on site of tumour.
- Head of pancreas (60-70% tumours) more likely to have weight loss, jaundice, bloating, pain after eating and changed stool.
- Because of blockage of the common bile duct.
- Other sites more likely to have epigastric or back pain.
- Abdominal pain 40%, jaundice 30%.

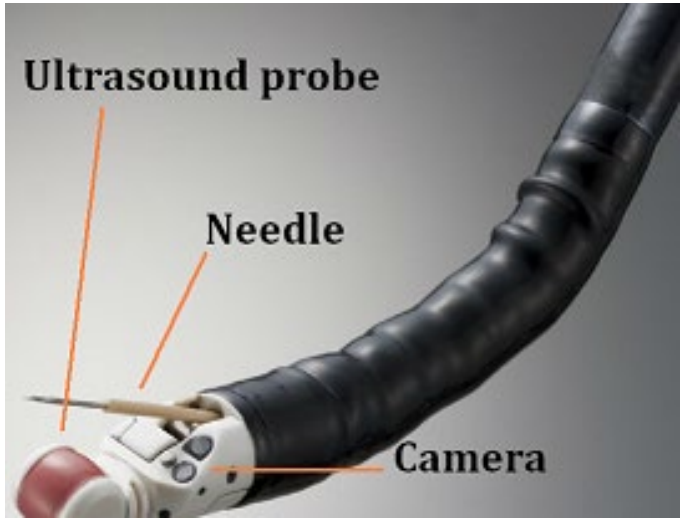


Mizrahi J et al Lancet 2020

Diagnosis.

- Radiographic: CT, CT angiography, MRI.
- Might have endoscopic ultrasound to detect nodes or get biopsy.
- Blood markers such as CA19-9 can help track effect of treatment.
- No ideal screening test yet.

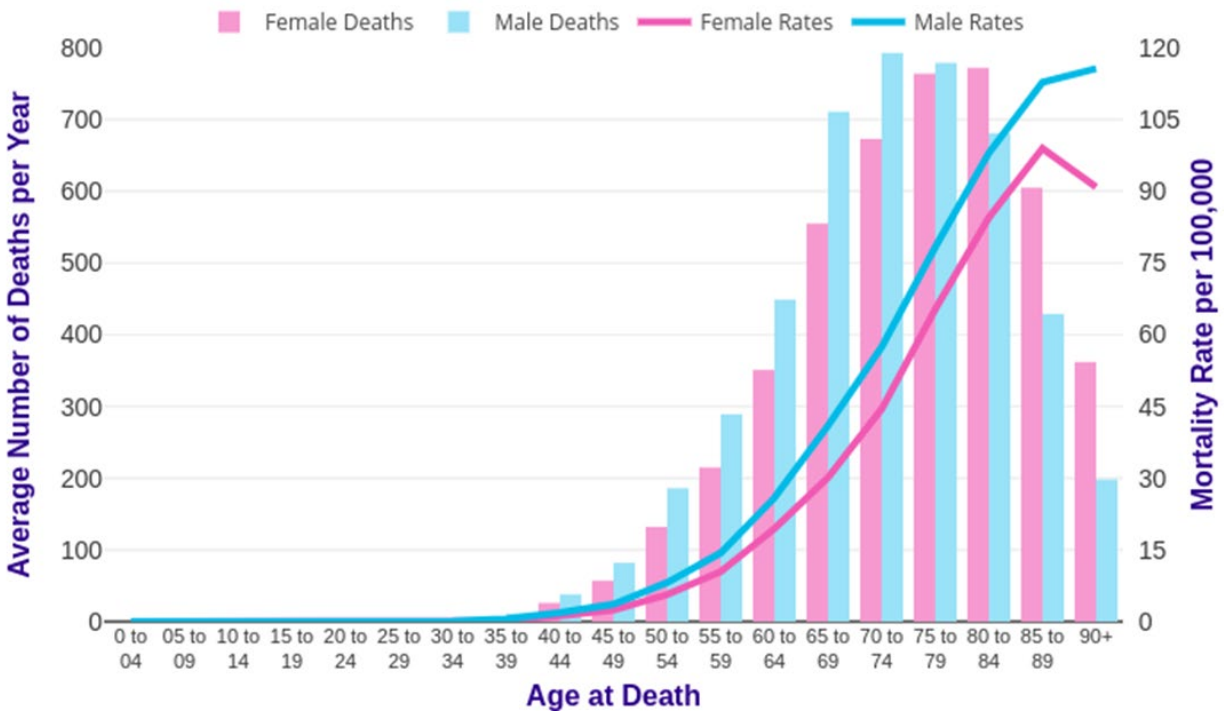


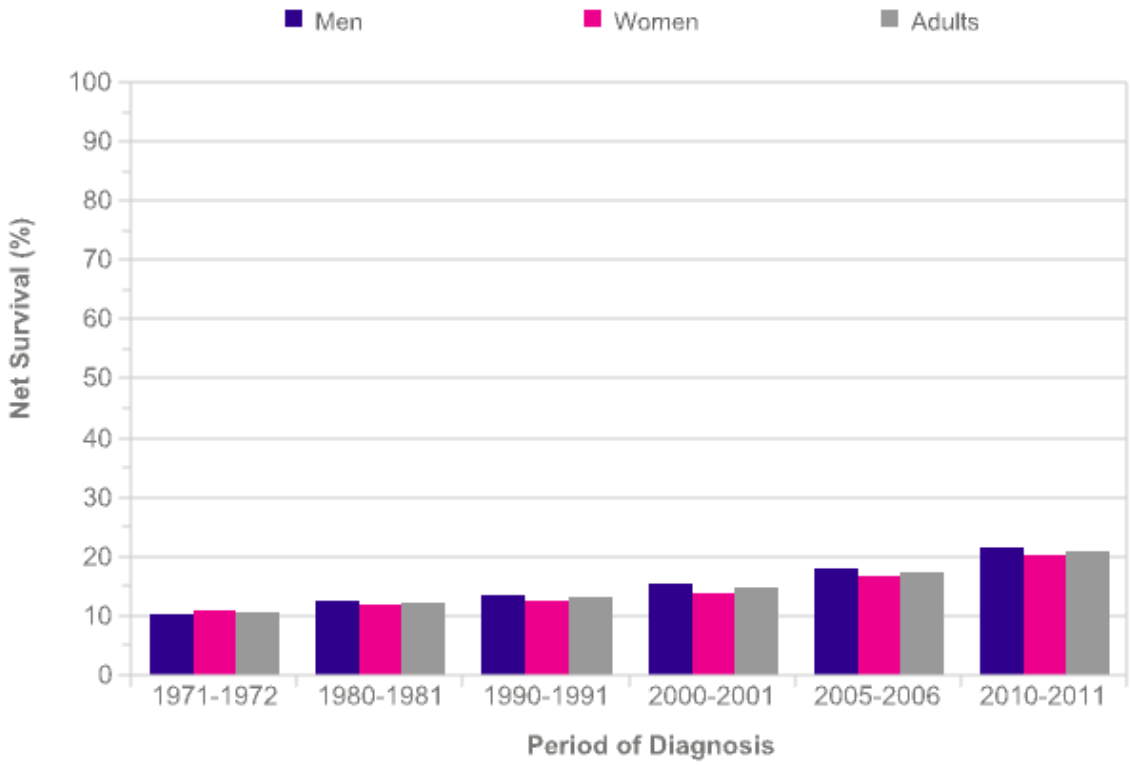


Azvolinsky A 2015 Cancernetwork/ USF Health

Pancreatic cancer; deaths by age and 1 year survival over time.

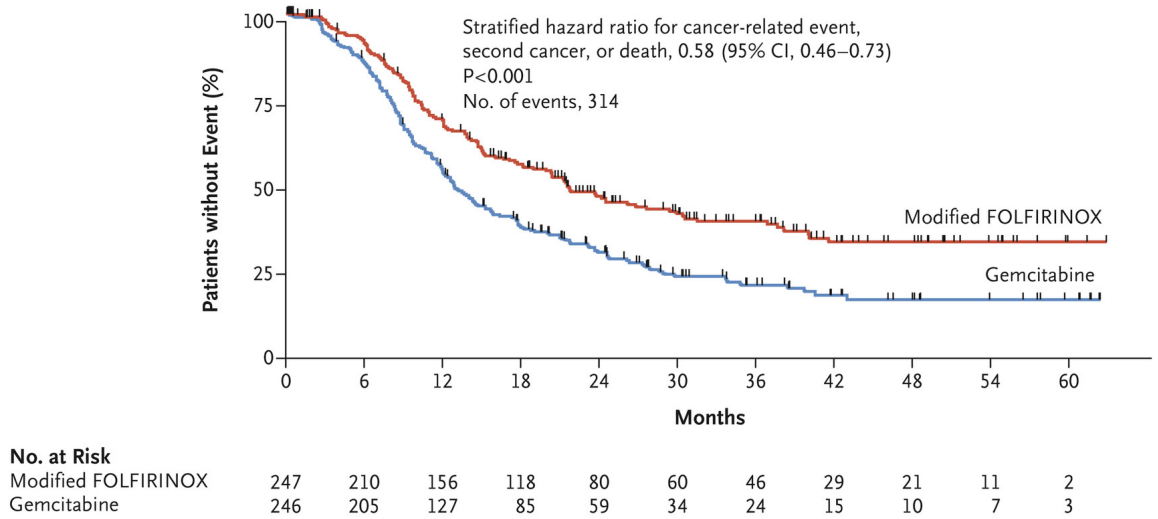
(CRUK).





Surgery for pancreatic cancer.

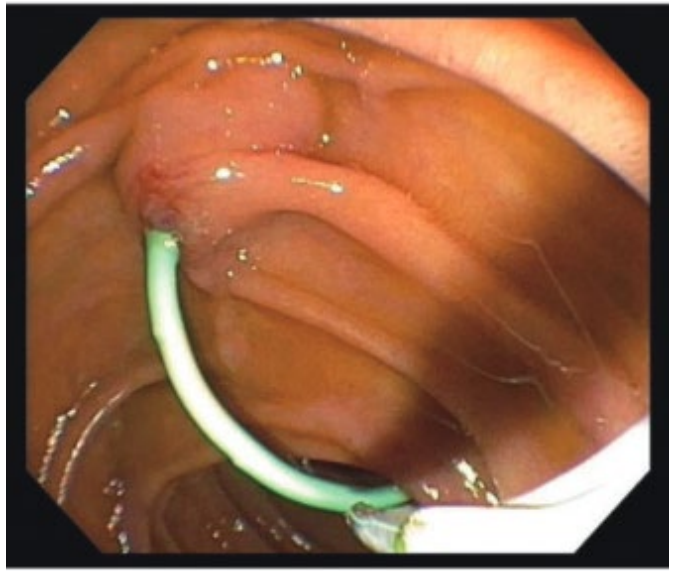
- Resectable, borderline and non-resectable.
- Over 80% present when it is not possible to remove it surgically.
- Major operation.
- Chemotherapy improved survival in those with surgery. 6 months of mFOLFIRINOX currently.
- R trial of mFOLFIRINOX- disease free survival. 21.6 months v 12.8 months.



Conroy T et al NEJM 2018

Pancreatic cancer treatment if surgery not possible.

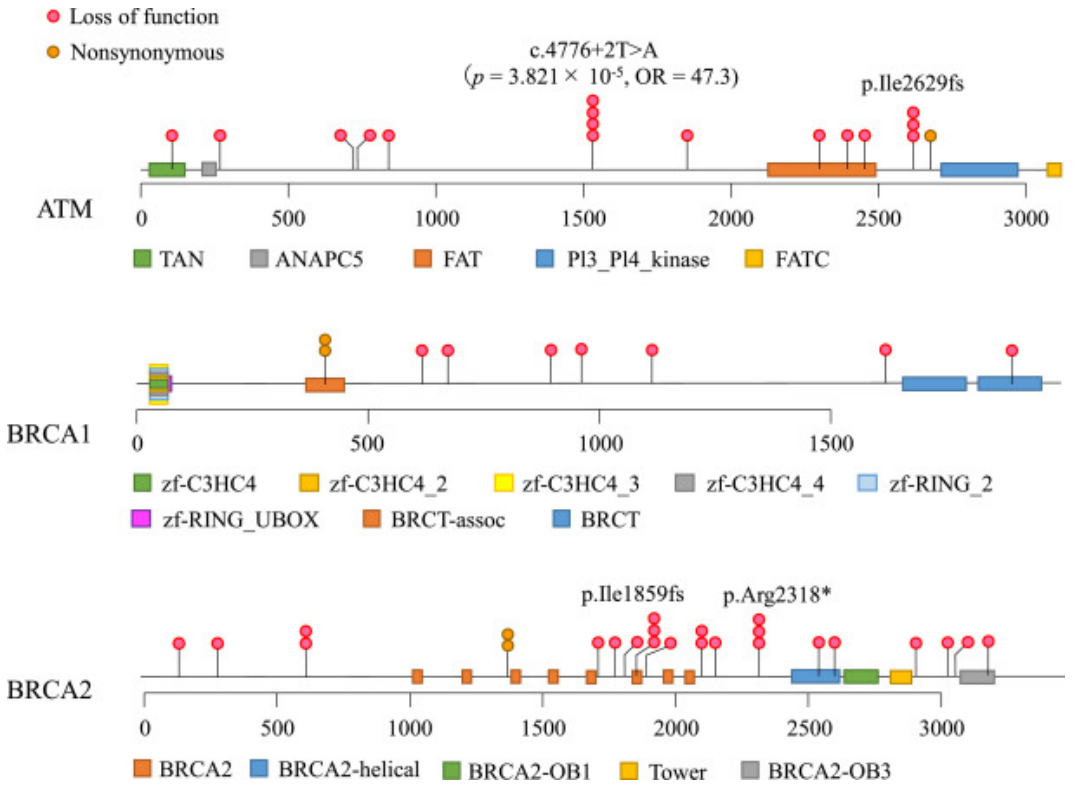
- Chemotherapy remains the mainstay of treatment currently.
- Targeted therapy and immunotherapy being investigated, but only incremental progress.
- May have stent (R) if the pancreatic duct blocked.
- Pain management very important. Pain and depression common.



Thaker A et al. 2014.

Risk factors for pancreatic cancer.

- Obesity.
- Smoking.
- Type 2 diabetes.
- Chronic pancreatitis.
- 5-10% due to inheritable factors including BRCA1 and BRCA2 mutations, and Lynch syndromes. BRCA2 RR 3.5.
- R pathologic variants of 3 genes associated with pancreatic cancer.
- It may become relevant to screen people at high genetic risk.



Mizokumi K et al EBioMed 2020.

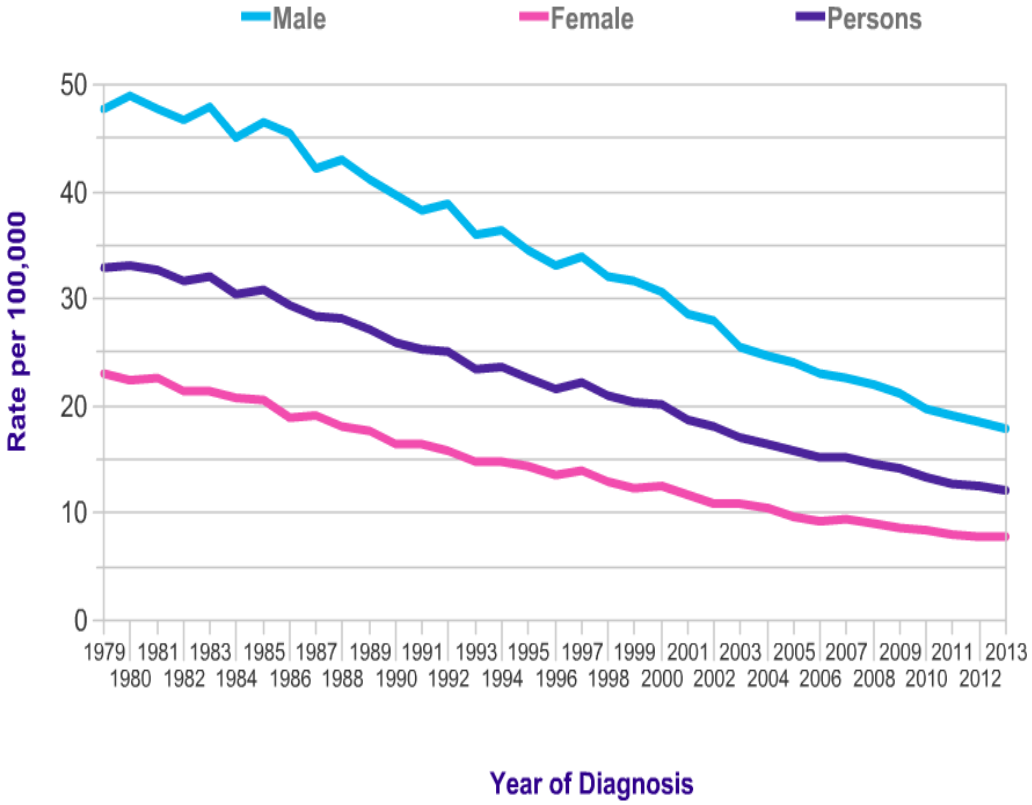
Gastric (stomach) cancer and *H. pylori*.

- Gastric cancer has decreased substantially in the UK.
- H pylori best known as the major cause of peptic ulcer disease.
- Increases risk around 6-8x for non-cardia gastric cancer (the main type).
- May reduce cardia gastric cancer (not yet clear).
- A major risk for a rare gut lymphoma (MALToma).

Electron micrograph *H. pylori.*
Dr. Y. Tsutsumi

Does treating *H. pylori* prevent gastric (stomach) cancer?

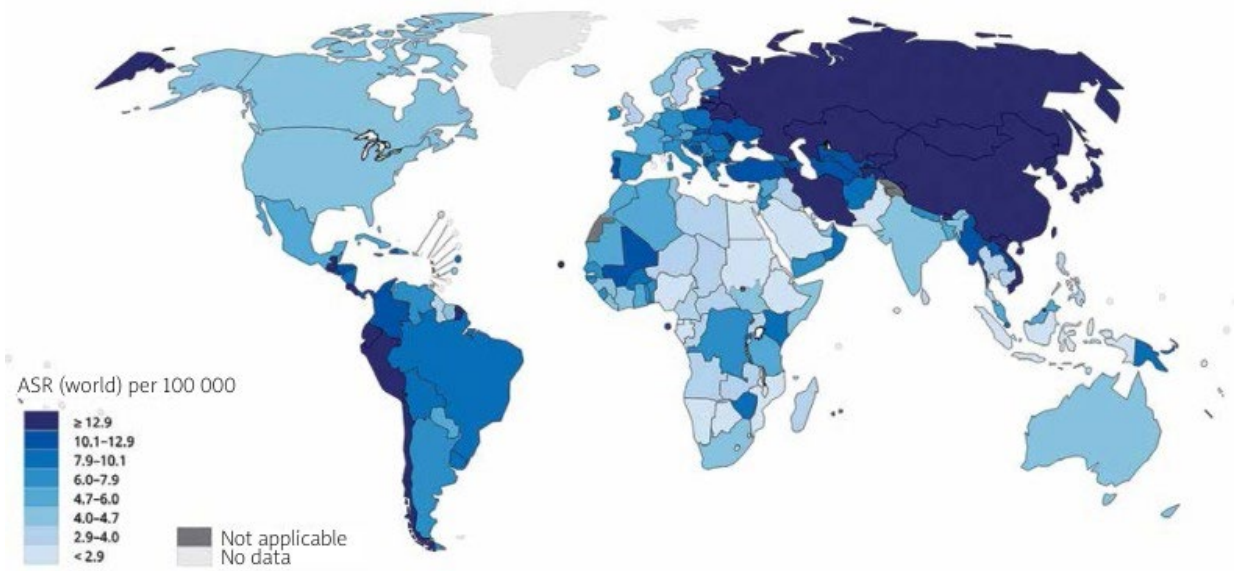
- Almost certainly yes, RR around 0.65 in meta-analyses in trials of around 8000 patients. Most from China.
- May not once pre-cancerous cells identified.
- Around 6700 cases of stomach cancer in UK annually. High mortality, although improving.
- Around a third of UK stomach cancer *H. pylori* related. Often treated for ulcers.
- Smoking, diet also important.



Stomach cancer incidence decreased 62% in UK since 1970s. Projected to fall 17% more by 2035 *(CRUK)*

Stomach cancer is particularly common in Asia

- Globally stomach cancer is common. Around 2/3rds due to *H. pylori*.
- Most people with *H. pylori* do not get cancer.
- Epstein-Barr virus may also contribute.
- Around 950,000 cases globally.
- Historically (pre 1930s) probably the most common fatal cancer.



IARC data

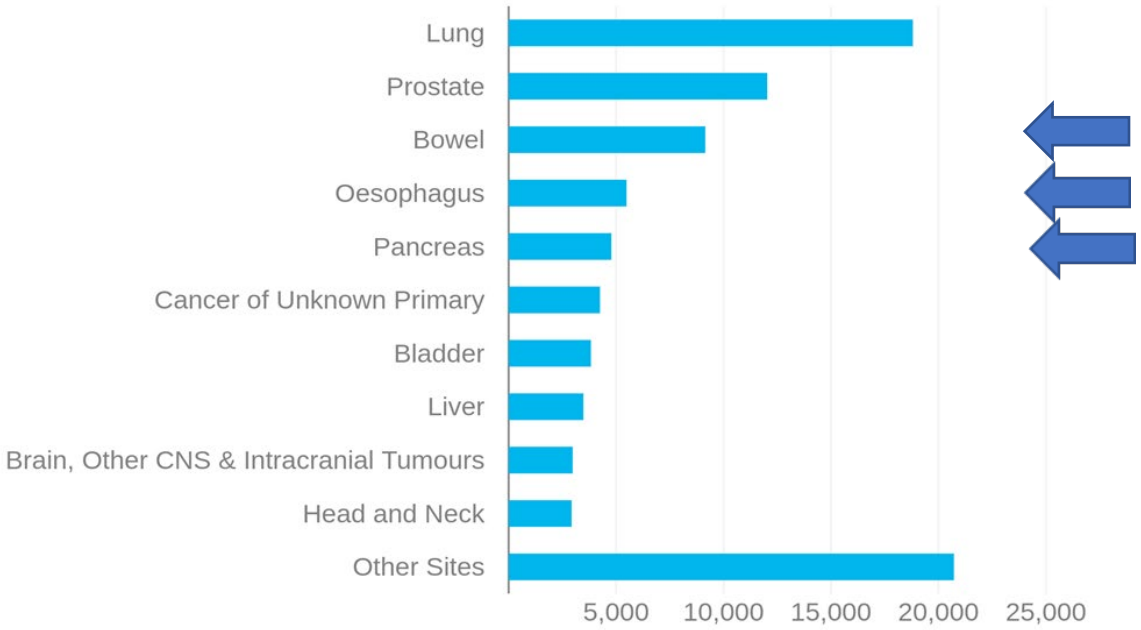
This lecture has considered major cancers of the digestive tract.

Good prognosis for bowel cancer if detected early.

Pancreatic and oesophageal cancer often detected late.

Several modifiable risk factors, especially smoking and obesity.

Males UK mortality.



Females UK mortality.