How to prevent Gastrointestinal and Liver Cancer

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Objectives

- Screening – Organised vs Opportunistic
- Oesophageal Cancer
  - What increases the risk?
  - What decreases the risk?
  - Does screening work?
- Gastric Cancer
- Liver Cancer
- Bowel Cancer

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NZ Cancer Registry

Select a cancer group: Digestive organs - C15-C26

Registrations

	Number of registrations, 2015			Rate (registrations per 100,000)		
Cancer (ICD Code)	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**
Digestive organs - C15-C26	2802	2360	5162	81.0	57.9	68.9
Oesophagus - C15	214	95	309	6.0	2.1	4.0
Stomach - C16	235	148	383	6.8	4.0	5.3
Small intestine - C17	63	50	113	1.9	1.3	1.6
Colon, rectum and rectosigmoid junction - C18-C20	1607	1474	3081	46.3	36.5	41.1
Anus - C21	23	38	61	0.7	0.9	0.8
Liver - C22	246	110	356	7.6	2.6	5.0
Gallbladder - C23	21	46	67	0.6	1.2	0.9
Other biliary tract - C24	47	35	82	1.3	0.7	1.0
Pancreas - C25	294	287	581	8.4	6.9	7.6
Other digestive organs - C26	52	77	129	1.4	1.6	1.5

Source: New Zealand Cancer Registry
Note: rates are expressed per 100,000 population and age standardised to the WHO World Standard Population.

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Organised vs Opportunistic Screening

Organised

- High standard
- Checked and monitored
- All are offered the same services, information and support
- Large numbers invited
- Example: breast, cervical cancer and now bowel cancer

Opportunistic

- Patients ask their doctor or health professional for a check or a test
- Not checked or monitored
- Example: FOBT prior to bowel cancer screening

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NZ: 309 per year M: 214, F 95 4.0/100000 (M: 6.0 F:2.1)

OESOPHAGUS

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Oesophageal Cancer - SCC

Increased Risk

- Smoking and Drinking increases risk (Population based and case control and cohort studies)
- Avoidance of smoking and drinking − decreases risk (Cohort or case controlled studies)

Decreased Risk

- Chemoprevention − Aspirin and NSAIDs OR 0.57 (Small positive, cohort or case control studies) − *but harms with UGIB, Cardiovascular effects, haemorrhagic stroke and renal impairment*

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Oesophageal Cancer – Adenocarcinoma

Increased Risk

- Gastro-oesophageal reflux and Barrett's Oesophagus
- Use of Anti-cholinergics
- GERD is associated with Oesophageal AdenoCa OR 7.7, long standing and severe symptoms 43.5
- Meta-analysis of 1128 individuals from 5 case control studies – higher risk with recurrent heartburn (OR 4.6), regurgitation (OR 4.6) or both (OR 4.8). Daily heartburn and regurgitation (OR 8)
- It is not known whether medical or surgical therapy of GORD will reduce the risk of adenocarcinoma

Decreased Risk

- Aspirin and NSAID use chemoprevention – Adenocarcinoma – unknown. Harms increased risk, small magnitude
- Ablation of Barrett's with Dysplasia
  - RFA with severe dysplasia may lead to eradication of Dysplasia and IM and a reduced risk of disease progression
  - Impact of mortality unknown
  - *Harms: Oesophageal stricture, dilatation and bleeding, low rates in expert centres. Possible overdiagnosis and overtreatment*

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Oesophageal Cancer Screening

- Screening would result in no or minimal decrease in mortality from Oesophageal Cancer in the US population – *Cohort and Case control studies*
- Harms – Uncommon but serious side effects associated with endoscopy (perforation, Cardiovascular events and aspiration, bleeding requiring hospitalisation). Psychological harms identifying Barrett's (annual risk of Adenocarcinoma <0.4%/annum)

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NZ: 383 per year M: 235, F 148 5.3/100000 (M: 6.8 F:4.0)

GASTRIC CANCER

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Gastric Cancer

- Elderly patient with Atrophic Gastritis or Pernicious Anaemia
- FAP
- Sporadic gastric adenomas
- Immigrants with high rates of gastric cancer
- Workers in the rubber and coal industries

Gastric Cancer

- USA : age adjusted incidence rate 7.7/100000. Men: Women 2:1, Mortality rates 40 deaths per 100000 (1930) − 4.6 deaths per 100000 (2003-7). Annually 28000 in USA, 10960 die.
- 4th most common cancer in the world
- 988,000 worldwide in 2008, estimated deaths 736000
- NZ: 2015 - 383 cases (235M, 148 F) Incidence Rate = 5.3/100000
- 70% from developing countries, 50% from Eastern Asia
- 5 year survival 29.9% - Japan 5 year survival 95%, USA 65%
- Japan − secondary prevention and screening programmes
- Major type is Adenocarcinoma (lymphoma, sarcoma, carcinoids are rare) − diffuse type (worse prognosis) vs intestinal type (ulcerative and distal)

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Gastric Cancer Risk

Increased Risk

- Chronic Atophic Gastritis
- Intestinal Metaplasia
- Gastric Adenoma
- FHx of Gastric Cancer
- Li Fraumeni syndrome
- Blood type A
- Low fruit and vegetable consumption
- Salted, smoked or poorly preserved foods
- Cigarette smoking (60% higher risk in male smokers, 20% female smokers)
- Radiation exposure
- Helicobacter pylori – antrum and body adenocarcinoma and lymphoma

Decreased Risk (Interventions)

- Smoking cessation RR 1.2 vs 1.6
- Hp eradication RR 0.65 (1.7%->1.1%), incidence reduced by 39% (not mortality)

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Gastric Cancer Risk

Inadequate evidence

- Diet – excessive salt, low vegetable and fruit (increases) . Vitamin C in vegetables, fruits and other plant foods associated with reduced risk of gastric cancer. High in whole grain cereals, catotenoids, allium compounds and green tea associated with reduced gastric cancer.
- *Uncertain if changing one's diet to include more vegetables, fruits and wholegrains would reduce the risk*

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Gastric Cancer Screening

- Barium meal photofluorography (participation rates 10-20%), gastric endoscopy and serum pepsinogen does not result in a decrease in mortality from gastric cancer in areas of low incidence of disease eg USA
- PPV in Japan still very low 0.85%
- Pepsinogen PPV 19.5%
- 22.5% for radiography
- Cancer detection rates 0.28%!!
- Trials in Costa Rica and Venezula in the 1980s − not cost effective, PPV 3%, specificity 67%-80%

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Gastric Cancer Screening

- Endoscopy
  - More sensitive
  - Intially studies suggest 2-fold decrease
  - Chinese study − n=4394 35-64 years=, OGD every 4 years
  - High risk group 2 yearly − 58/85 cancers detected by screening
  - Standardised mortality ratio − no different
  - Limitations − screening interval too long, those with hypertension, liver disease, COPD excluded (high risk group)

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Gastric Cancer Screening

- Serum Pepsinogen
  - Low Pepsinogen − Atrophic Gastritis − can detect intestinal type Adenocarcinoma vs diffuse type. PPI use and Hp eradication can caused low levels too
  - Japan: Pepsinogen I and II levels plus Endoscopy = levels < 70ng/ml for PGI and < 3ng/ml for PGI:PGII ratio − sensitvity 84.6% and Spec 73.5% PPV 0.81% NPV 99.6%

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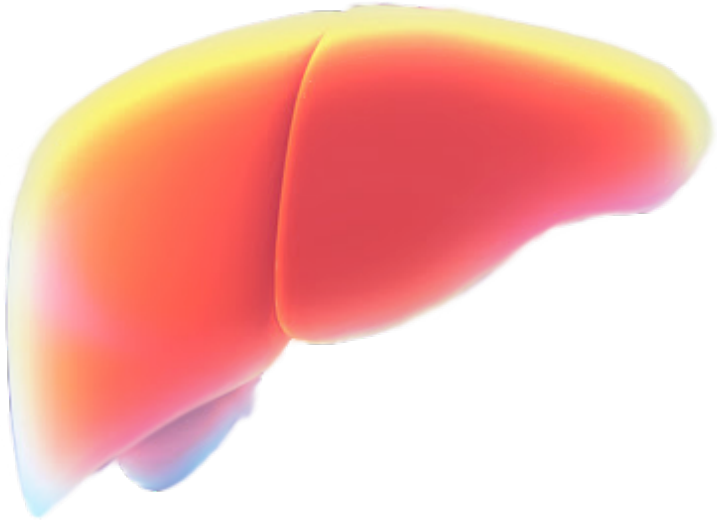

NZ: 356 per year M: 246, F 110 5.0/100000 (M: 7.6 F:2.6)

LIVER

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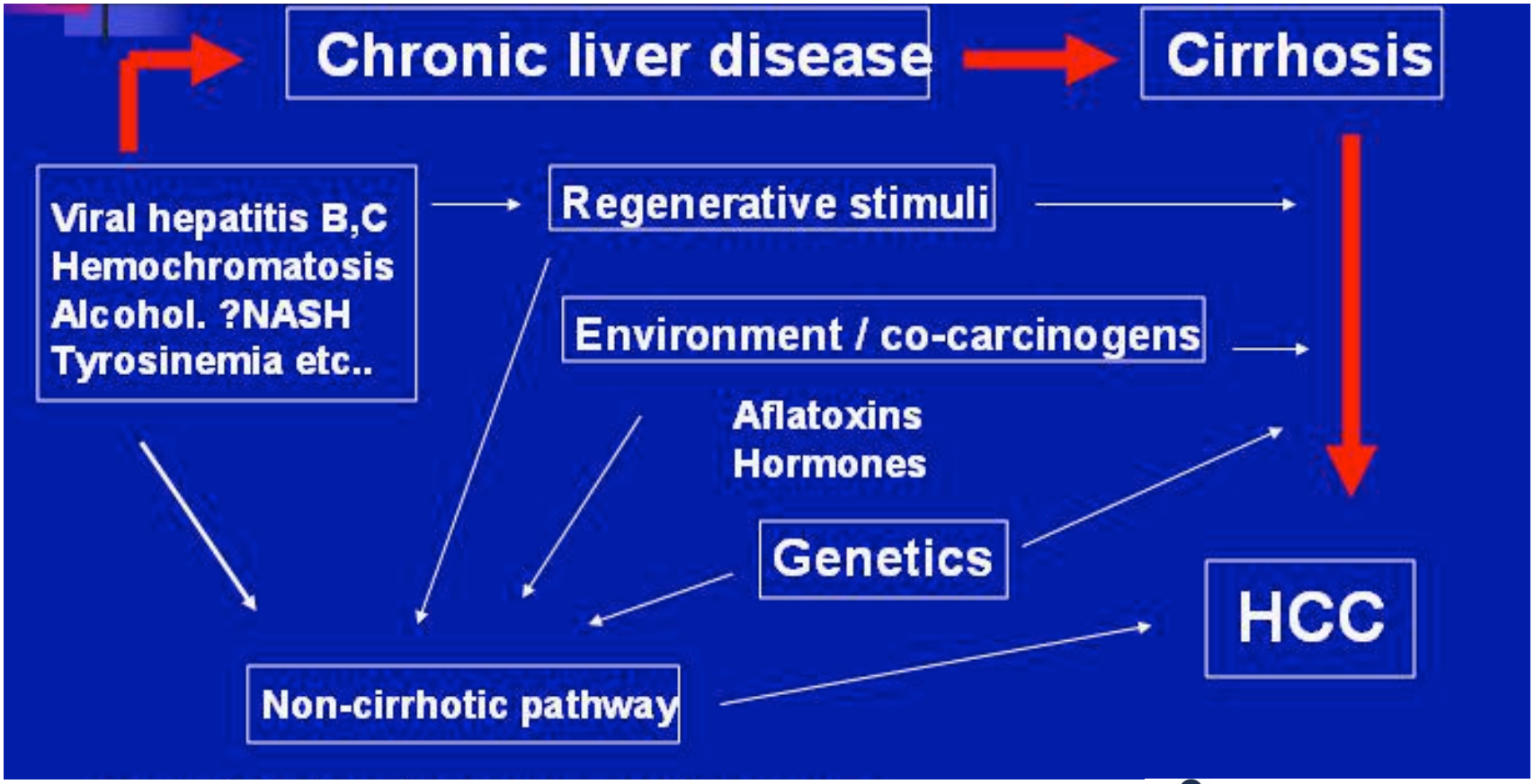
HCC: Pathobiology



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Liver Cancer: Prevention

- Liver Cancer Burden
- Screening of persons at elevated risk does not result in a decrease in mortality from Hepato-cellular cancer
- Hepatitis B vaccine to prevent HCC – solid evidence shows that immunizing individuals would lead to a decrease in HCC

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The Magnitude of the problem

- USA - 2017
  - New cases 40710
  - Deaths 28920
- NZ 2015 (NZ Cancer Registry published Dec 2017)
  - New cases 246 Male 110 Female, Total 356 Males: 7.6/100000, Females: 2.6/100000 Overall 5.0/10000
  - Deaths
- China 27-36/100000
- Incidence is rising in the USA due to Hepatitis C
- Worldwide HCC is the 6th most prevalent cancer and the third leading cause of cancer deaths

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Risk Factors

- Hepatitis B and C are the most significant causes of HCC worldwide
  - Hepatitis B – Asia and Africa
  - Hepatitis C – North America, Europe and Japan
- Hepatitis B – Annual incidence 0.5-1.0% per year in non cirrhotics, 2.5% per year in cirrhotics. RR 100
- Hepatitis C – Population based study n=12000, presence of Anti HCV Ab – 20 fold increased risk of HCC. HCC may occur in HCV with bridging fibrosis. Cirrhosis 2%-8% per annum

Risk Factors

- Alcoholic Cirrhosis − True incidence unknown
- Metabolic Syndrome − insulin resistance, Hypertension, Dyslipidaemia, obesity -> NASH. Incidence unknown. Probably around 5-10% have cirrhosis, 1-5% HCC
- Biliary Cirrhosis − Similar to Hepatitis C
- Chronic Liver Injury − Cirrhosis, 5 year risk of HCC ranges between 5-10% depending on aetiology (highest for HCV) and stage of cirrhosis
- Haemochromatosis − RR 20
- Aflatoxin B1 − produced by fungi of the Aspergillus species common contaminant of grain, nuts, vegetables in Asia and Africa. Implicated as a co-factor for HBV carriers increases neoplastic risk 3 fold

Diagnosis

- Lesions smaller than 1cm detected during screening at high risk for HCC more likely due to cirrhosis with regeneration − close follow up at 3 monthly intervals
- Lesions >1cm − further imaging or biopsy

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Diagnostic Imaging

- Triple phase contrast enhanced CT or MRI – Radiological characterisitics of enhancement in arterial phase and washout in venous phase
- Arterial uptake 95-100% specificity for HCC (Hepatic artery supply) virtually diagnostic for HCC
- If the first imaging modality (either CT or MRI) is inconclusive sensitivity can be increased from 33-41% for CT and 76% for MRI
- If there is any doubt, biopsy

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Alpha-fetoprotein

- Not sufficiently sensitive or specific alone
- Can be raised in Cholangiocarcinoma or Metastatic Colon Cancer
- Positive for 70% HCC only
- If raised can be used to monitor for recurrence

Prognosis – early tumours

- Natural course of early tumours is unknown because most receive treatment − older data 13-21% 3 year survival
- Currently 10-23% are candidates for treatment with curative intent
- Overall 5 −year survival for early HCC undergoing liver transplant is 44-78%.
- Overall 5 − year survival for early HCC undergoing resection, 27-70%

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Prognosis – advanced HCC

- Untreated usually survive less than 6 months
- 1 year survival 10-72%
- 2 year survival 8-50%
- NZ data

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Survival

- Affected by tumour stage at presentation and liver function
- Anatomical extension (tumour size, number of lesions, presence of vascular invasion and extra-hepatic spread), Performance status and Function hepatic reserve (Child Pugh Score, MELD) guides treatment choice

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Prevention: Vaccination

- Reduction in risk with childhood vaccination
  - Reduction in annual HCC incidence from 0.70 per 100000 children (1981-1986) to 0.57 and 0.36 for the time periods of 1986-1990 and 1990-1994 respectively ($p<0.01$)
  - *NEJM 336(26):1855-9, 1997*
  - *Clin Cancer Res 11 (21):7953-7, 2005*

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Fibroscan

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PDF – printable version

FibroScan®

FibroScan® is a diagnostic test used to measure liver scarring or fibrosis caused by a number of liver diseases. Similar to ultrasound, FibroScan® is a non-invasive (no needles) alternative to liver biopsy.

Greenlane Medical Specialists offers FibroScan® as a quick, painless and easy test to assess liver damage. Your Hepatologist may recommend a FibroScan® if you have a chronic liver condition such as hepatitis B or C, alcoholic liver disease or fatty liver disease.

FibroScan® works by emitting a small pulse of energy, which may feel as a slight vibration on your skin. FibroScan® calculates the speed of this energy to give your healthcare provider an immediate measure of the stiffness of your liver. This stiffness measure can be an important part of understanding your overall liver health.

How to prepare for a FibroScan®

- No food or liquids (including water) for 2 hours prior to your appointment.
- Wear comfortable clothes that will allow your healthcare provider to expose the right side of your rib cage.
- Plan to arrive 15 minutes before your scheduled appointment time.

What to expect during your FibroScan®

- The procedure will take approximately 15 minutes.
- You will lie on your back with your right arm raised behind your head and your right abdominal area exposed.
- Your Hepatologist or Nurse Specialist will apply a water based gel to your skin and then place a non-invasive probe over your liver.
- During the procedure you may feel a slight vibration on the skin at the tip of the probe.
- **FibroScan® is a quick and painless procedure – no sedation is required!**

What to expect after FibroScan®

- FibroScan® results are provided instantly after the test. Your Hepatologist or Nurse Specialist will be provide you with a copy of your results.

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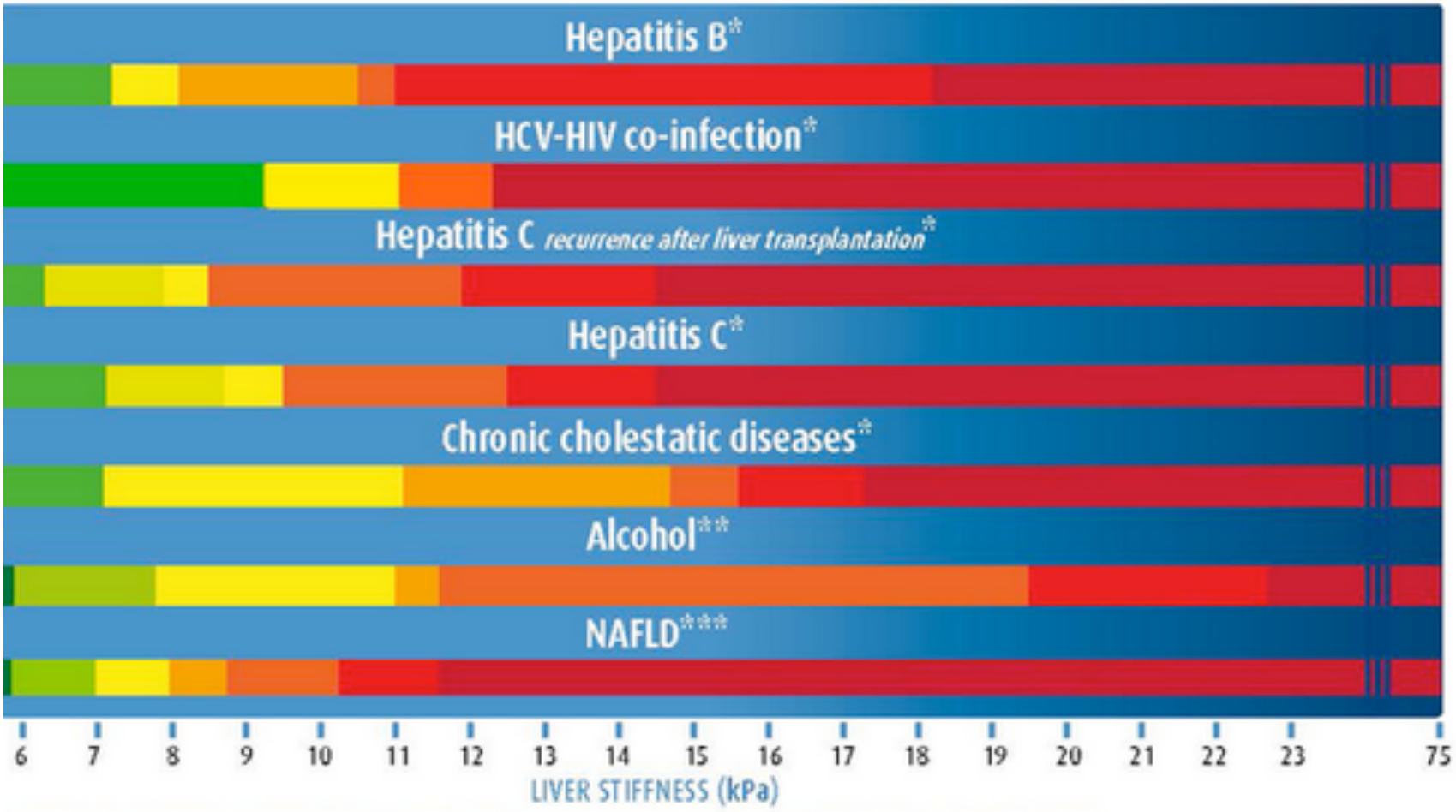
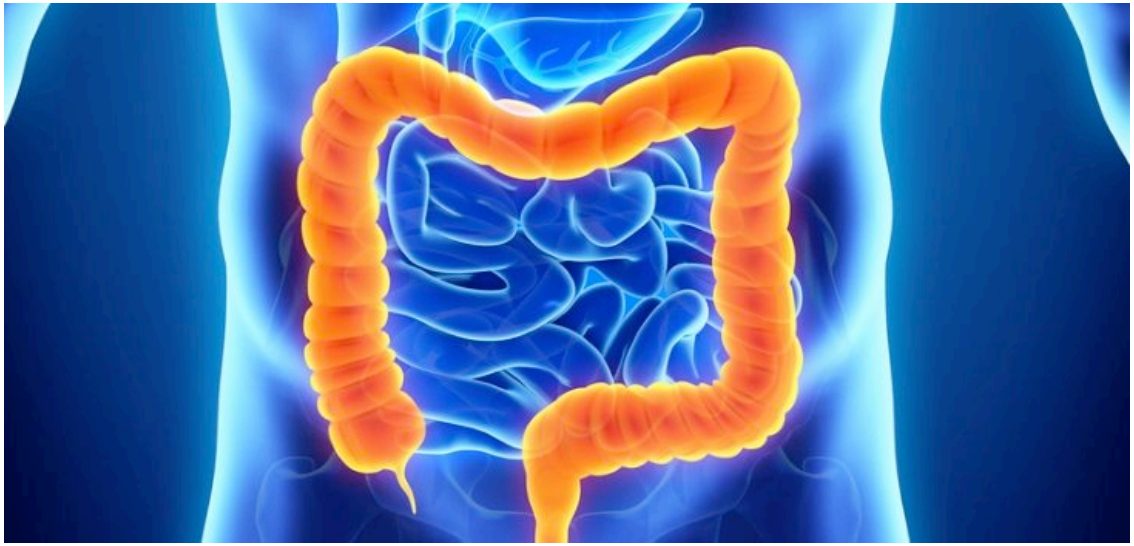
Fibroscan Cut-off Values





NZ: 3081 per year M: 1607, F 1474 41.1/100000 (M:46.3 F:36.5)

BOWEL CANCER

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Colorectal Cancer Prevention

Risk Factors

- Biggest risk is increasing age
- 90% >50 years
- FDR < 55y – Doubles risk
- Personal Hx CRC, High risk adenomas, Ovarian Cancer increases the risk
- Other: IBD > 8 years
- Genetic <5% - eg FAP (lifetime risk 100%), HNPCC (80%)
- Increased Risk with
  - Excessive Alcohol (>45g per day)RR 1.41
  - Cigarette smoking RR 1.18
  - Obesity BMI >29 RR 1.45
  - Personal and FHx CRC

Risk Reduction

- Physical Activity – 24% reduction (52 observational studies – meta-analysis)
- Aspirin – 10-20y 40% reduction. 75-1200mg for 20 years (HR 0.67), but 14 additional GI bleeds 14 and 3.2 more haemorrhagic strokes per 1000 persons over 10 years
- Hormone Therapy (Oesotrogen plus Progesin) HR 1.29, but more breast cancer, heart disease and stroke!
- Polyp removal – effective, probably more effective for larger polyps >1cm. Harms –

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Colorectal Cancer Prevention

Inadequate Evidence

- NSAIDs – Cox 2 with prior polyp decreased recurrence. NSAIDs also seems to reduce the risk of adenomas but extent on reduction of CRC? *Harms: Common and serious – UGIB, Chronic kidney disease, MI, heart failure, haemorrhagic stroke. Serious cardiovascular events up by 50-60%. NSAID risk 4-5/1000 people UGIB – bleeding risk from COX2 and NSAIDs similar from recent Arthritis studies.*
- Calcium supplementation – inadequate evidence
- Dietary factors – no evidence

Not associated

- Oestrogen only therapy
- Statins

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