

The Burden of Cancer

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The Burden of Cancer

1. Something that is carried.
2. a. Something that is emotionally difficult to bear; b. A source of great worry or stress.
3. A responsibility or duty.
4. The amount of a disease-causing entity present in an organism.

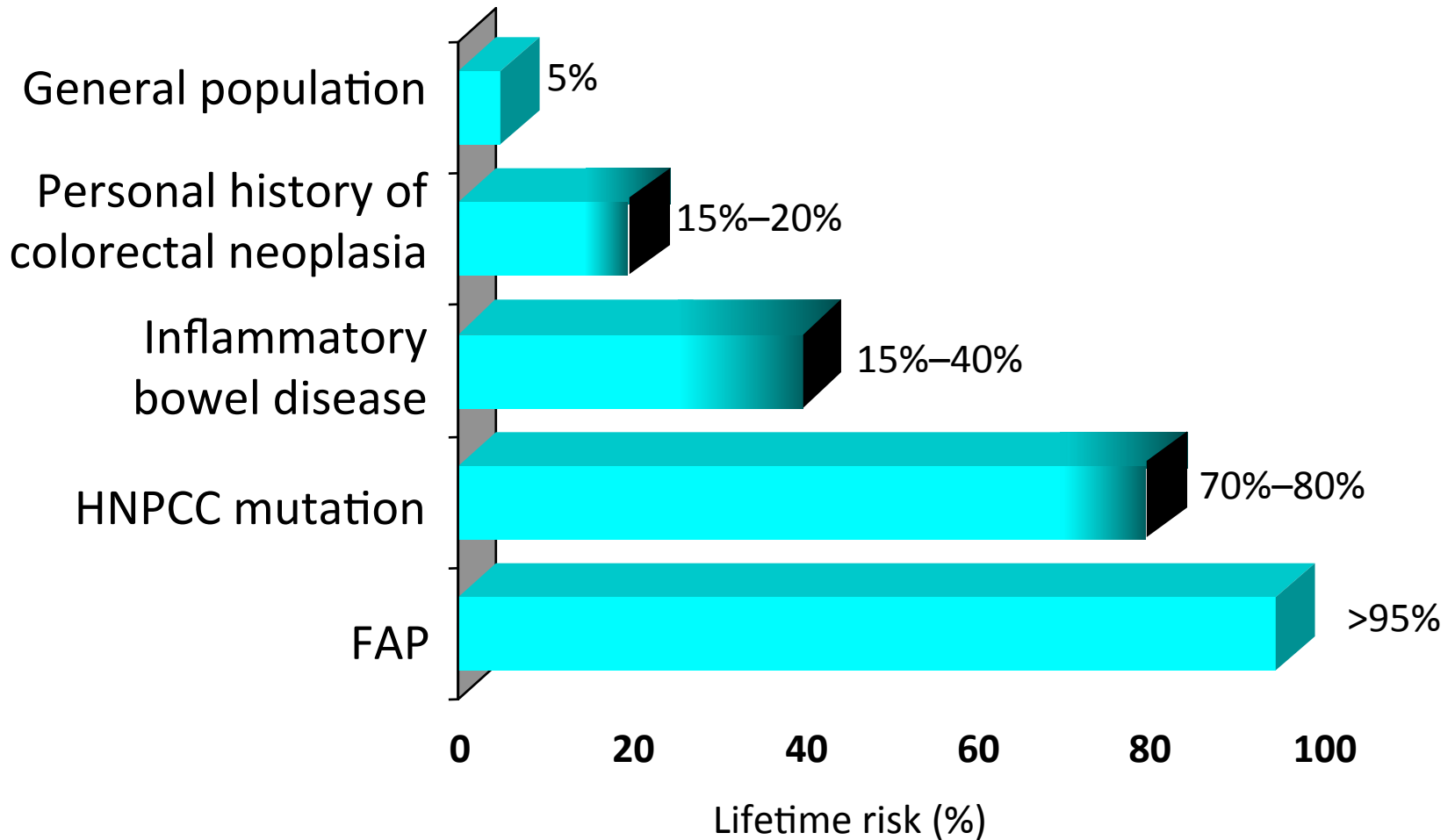
The Burden of Cancer

- Cancer Introduction
- Epidemiology and economics
- Extent of disease and interventions
- Emerging science and medical practice

Cancer

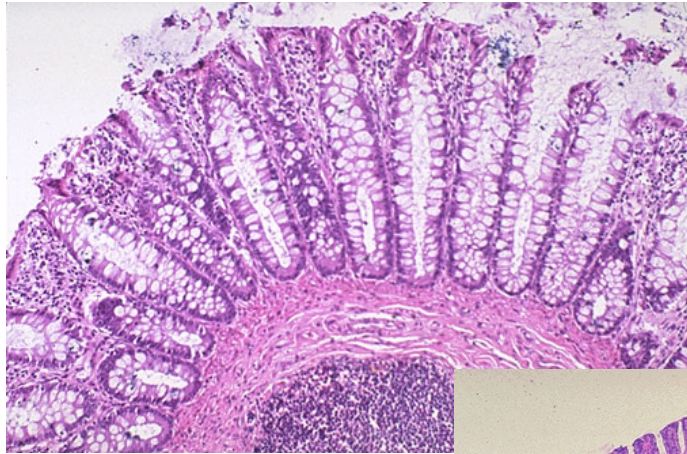
- A class of > 100 diseases in which cells display uncontrolled growth, invasion and potential spread to other organs.
- Hereditary or acquired abnormalities in regulatory genes lead to the development of cancer.
 - *Environment*: tobacco, diet and obesity, infections, radiation, lack of physical activity, pollutants
 - *Hereditary*: 0.3% of the population are carriers of a genetic mutation which has a large effect on cancer risk. They cause < 3–10% of all cancer
- Long latency to accumulate genetic alterations
- Heterogeneity between patients and within patients over time.

Risk of Colorectal Cancer (CRC)

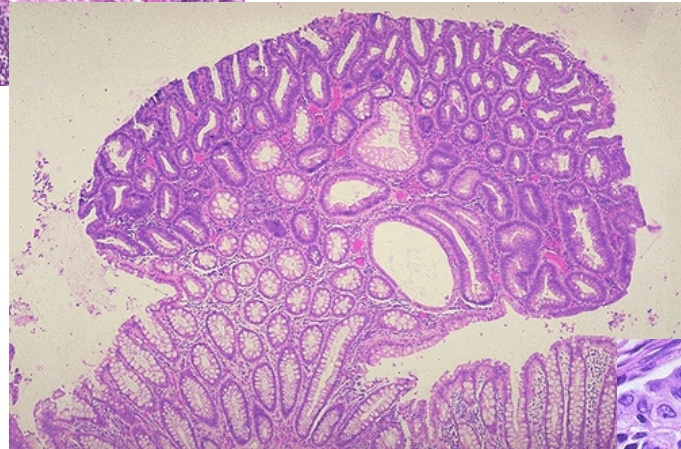


Increasing Disorder

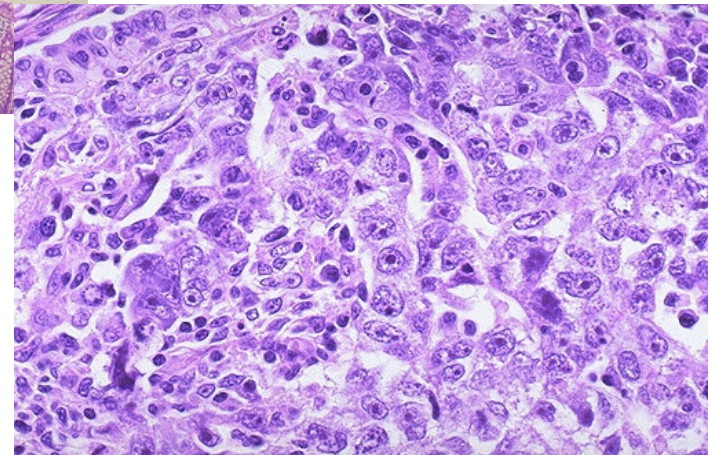
Cancer arise from a series of molecular and histopathological changes that transform normal epithelial cells.



Normal



Adenoma

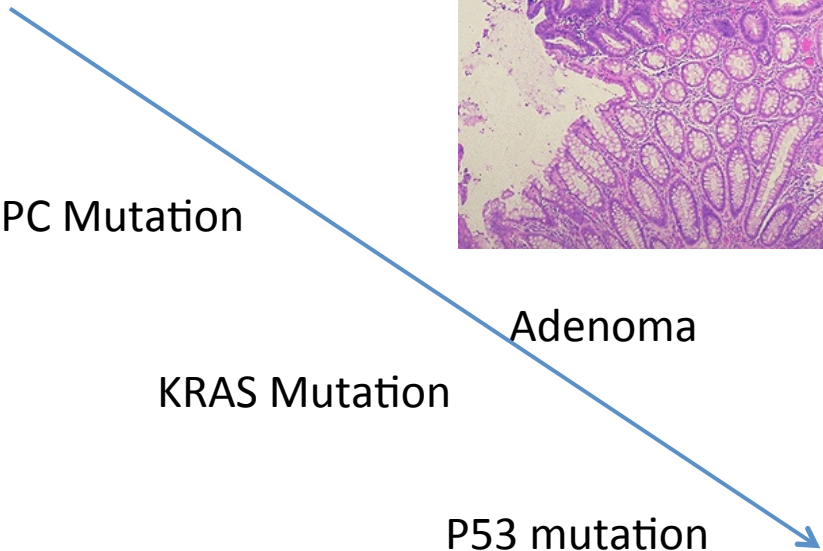


Cancer

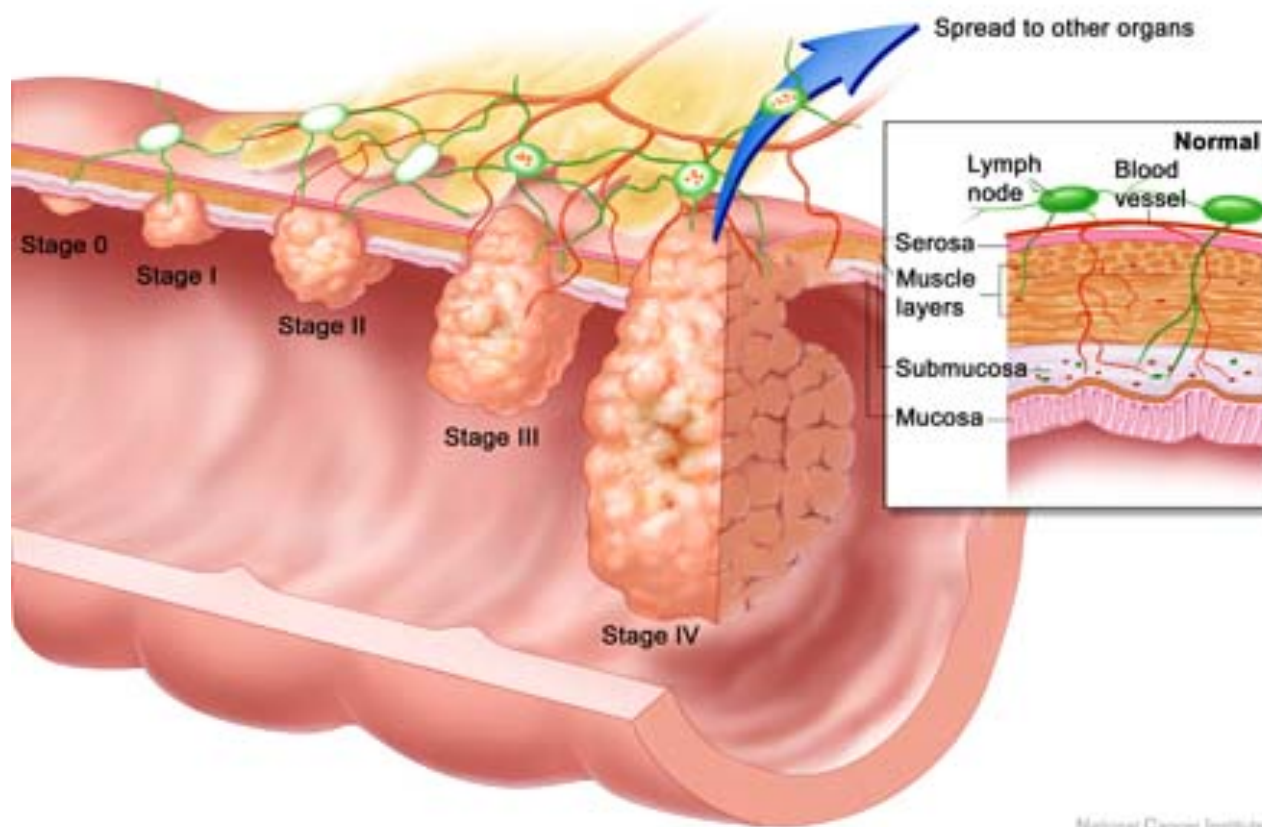
APC Mutation

KRAS Mutation

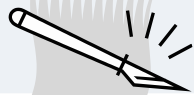
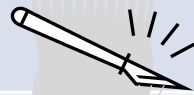
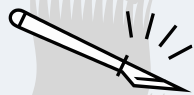

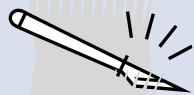



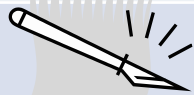


P53 mutation



Colon Cancer Stage and Prognosis



Treatment and Prognosis by Stage

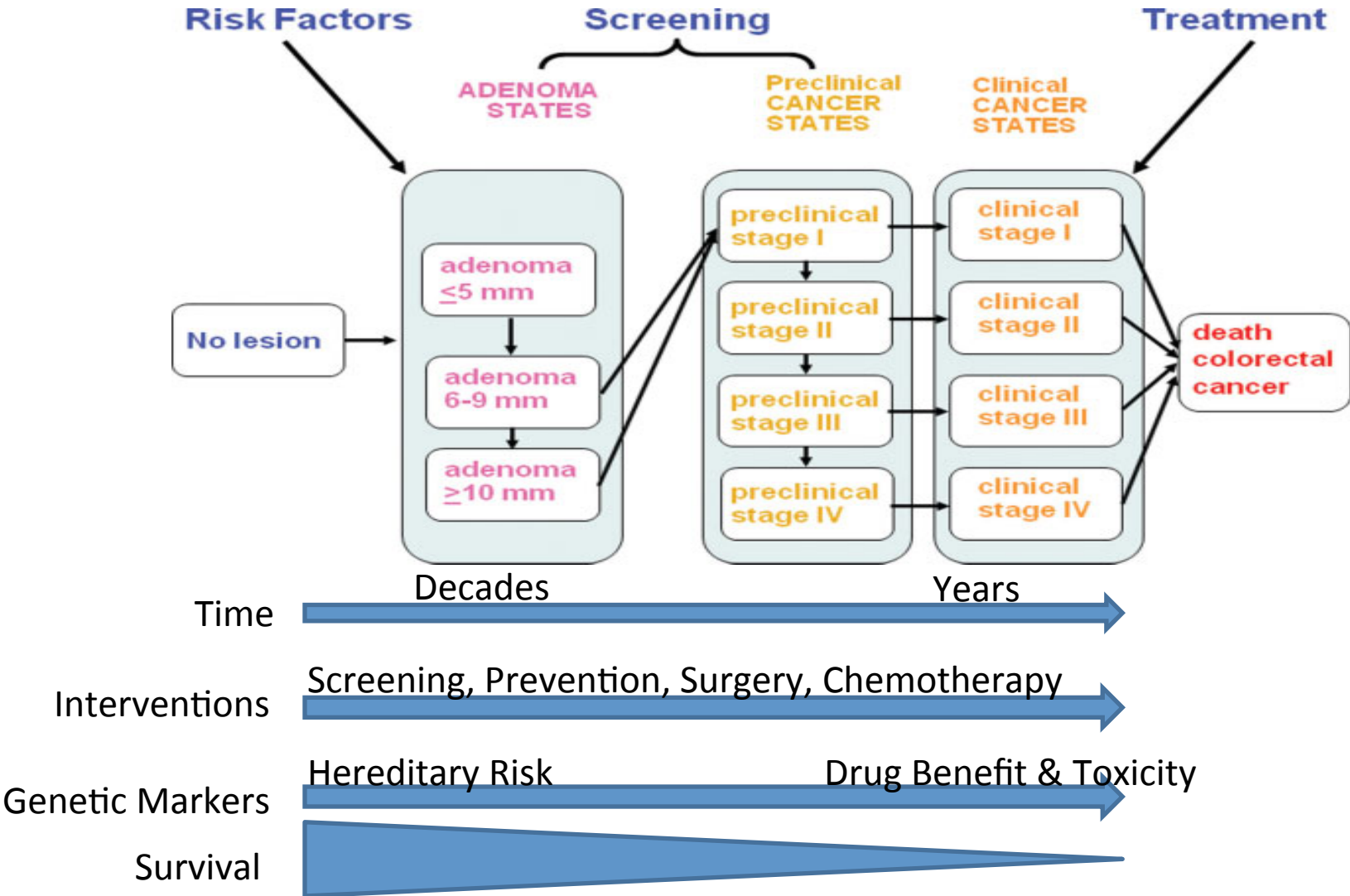
Stage	Surgery	Chemotherapy	5 year Survival
0			100
1			93.2
2a T3			84.7
2b T4		 ?	72.2
3a T1 or T2 N1			83.4
3b T3 or T4 N1			64.1
3c Any T N2			44.3
4 Any T, N, M1			8.1

Determinants of Survival

The prognosis of a person with cancer may be influenced by several factors:

- Host factors
 - age, sex, co-morbid conditions, socio-economic status and lifestyle factors
- Tumour-related factors
 - stage of disease, histological subtype, responsiveness to treatment
- System factors related to cancer control
 - availability and quality of early detection, diagnostic and treatment services

Natural History of Cancer



Cancer Incidence and Mortality

- One in two Canadians will develop cancer
- One in four will die of the disease.
- Cancer is the leading cause of death of Canadians
 - 177,800 new cases of cancer (est. 2011)
 - 75,000 deaths from cancer
 - ~ 50% of the newly diagnosed cases will be lung, colorectal, prostate and breast cancers.
 - 27% of all cancer deaths are attributed to lung cancer.
 - 5 year relative survival for all cancers is 62 per cent.
 - Relative survival is > 90 % for thyroid, prostate and testicular cancers,
 - Relative survival is < 16% for lung, esophagus and pancreatic cancer

Note: 5-year relative survival ratio is the proportion of people alive five years after cancer diagnosis compared to the proportion of people in the same general population after 5 year.

Source: Canadian Cancer Society, 2011

Prevalence, incidence and mortality

- There is an annual increase in the number of new cases of cancer.
 - Population growth
 - Population aging
- Cancer prevalence is rising
 - Canadians diagnosed with cancer
 - Cancer survival is increased.
- The overall cancer incidence rate in males has been dropping,
 - declining rate of lung cancer
- The overall incidence rate in females has begun to level off.
- Since 1989, the mortality rate for all cancers combined has been dropping for males up to age 79 and females up to age 69.

The Economic Burden of Illness in Canada

- The diagnostic categories with the highest total attributable costs (direct and indirect)
 - Musculoskeletal diseases (\$22.3 billion, 12%),
 - Cardiovascular diseases (\$22.2 billion, 12%),
 - Neuropsychiatric conditions (\$20.3 billion, 11%),
 - Malignant neoplasm (cancer) (\$17.5 billion, 9%)
 - Injuries (\$14.8 billion, 8%).

Direct Costs – Hospital, doctor, drugs; Indirect Costs – lost production due to premature mortality, disability

K Eng et al. EBIC 2000 data. <http://ihea2011.abstractsubmit.org/sessions/202>

The Burden of Cancer

- The Burden of Disease
 - Symptoms, signs, emotional distress, economic impact of an often life-threatening disease
- The Burden of Treatment
 - Acute and long term morbidity of surgery, radiation, chemotherapy

Burden of Cancer

- To reduce the burden of cancer will require
 - Reduction in cancer incidence
 - Prevention of cancer
 - Life style
 - Environment
 - Reduction in cancer mortality
 - Early diagnosis
 - Better treatment
- To reduce the burden of treatment will require
 - Determination of who benefits, who is at risk and alternative treatments

“If new refrigerators hurt 7% of customers and failed to work for another one-third of them, customers would expect refunds.”

BJ Evans, DA Flockhart, EM Meslin Nature Med 10:1289, 2004

Biomarkers to Reduce Cancer Burden

- Risk stratification
- Surrogate/intermediate endpoint
- Diagnosis
- Prognosis
- Prediction of treatment benefit or risk

Biomarkers to Reduce Cancer Burden

	Prevention	Screening	Treatment
Risk	√	√	√
Diagnosis		√	√
Prognosis			√
Prediction			√
Intermediate Endpoint	√		√

Prevention - Challenges

- **When, how, who to intervene**
- **How to assess the intervention**
 - **Surrogate End-Points in Cancer Chemoprevention Studies**
 - Adenomas as surrogate intermediate markers for colorectal cancer.
 - yearly conversion rate from adenoma to carcinoma has been calculated to be 0.25%
 - polyps greater than 1 cm this rises to 3%,
 - for villous adenomas to 17% and
 - for adenomas exhibiting high-grade dysplasia to 37%
 - Agents acting at later stages of tumour development
- **Uptake in the population**
 - **Tamoxifen in breast cancer**

Chemopreventive Agents for CRC

Fiber	Not effective
Aspirin	Probably effective
NSAIDs (ibuprofen, etc)	Probably effective
Vitamin E, vitamin C, beta carotene	Not effective
Folate	May be effective if obtained in diet
Calcium	May be effective
Estrogen	May be effective, but has other problems

Screening

- Pros - Reduction in mortality
 - Cervical cancer – PAP Test
 - Colorectal cancer – FOBT, +/- sigmoidoscopy, colonoscopy
 - Breast cancer - Mammography
 - Lung cancer – CT Scan
 - ?Prostate cancer - PSA
- Risk based screening
 - Early, more frequent, more intensive
 - Familial Breast Cancer (BRCA1/2) - MRI
 - Hereditary CRC, Inflammatory bowel disease - Colonoscopy
- Cons – Screening adherence; Sensitivity – missed cases; Specificity – false positives
 - Adherence 30-45%
 - 15% and 25% small adenomas (< 1.0 cm) missed at initial colonoscopy
 - Imaging based screening identifies abnormalities that require definitive histological diagnosis

Results of Screening

- Some individuals will be diagnosed earlier than they would have otherwise.
- Early diagnosis may provide
 - benefit because early treatments were effective
 - no clinical benefit because the treatments were ineffective.
 - no clinical benefit because these individuals were not destined to die from the cancer.
- Ideally, screening would detect whether a lesion is cancer and whether that cancer has lethal potential
 - Lung cancer versus prostate cancer
 - Also, inexpensive, easy to implement and with acceptable uptake in the population

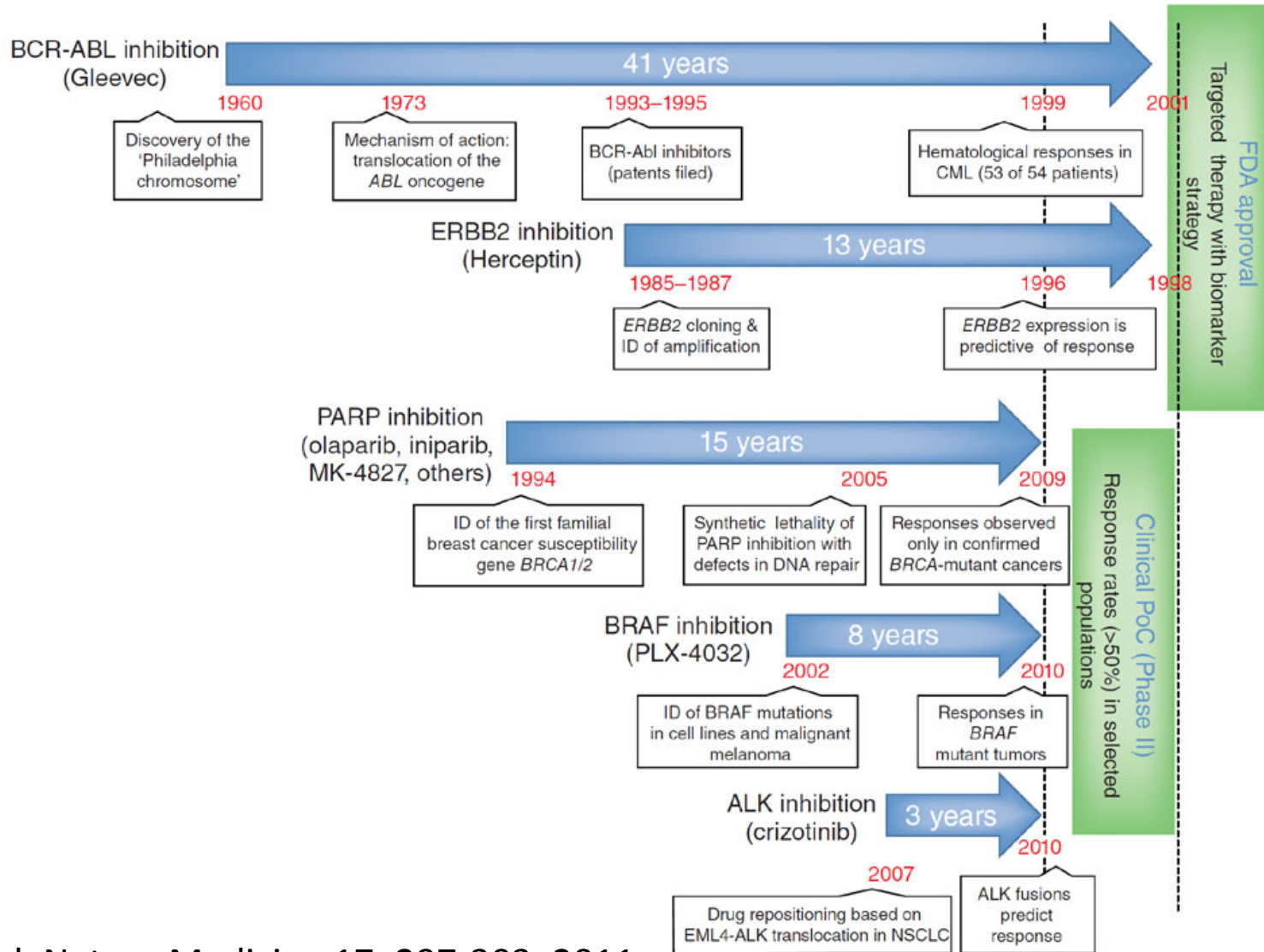
Colorectal Carcinoma Screening

- Colorectal cancer is the second leading cause of cancer death
- Based on randomized controlled trials, fecal occult blood screening could reduce CRC mortality by 15% to 33% in a targeted population of 50 to 74 year olds.
- Only 32% of Canadians in this age group report having a screening test.
- If 80% of Canadians aged 50+ were screened over the next 10 years, it is estimated that 10,000 to 15,000 deaths could be prevented.
- “Get your Butt over here” takes on a whole new meaning

Colorectal Cancer Treatment

- Early stage disease
 - Who will be cured with surgery?
 - Who will benefit from additional chemotherapy?
 - Who may benefit from experimental therapies?
- Late stage disease
 - Who will benefit from chemotherapy
 - Who may benefit from experimental therapy
- Who will experience unacceptable toxicity?

Cancer Genetics and Therapeutics



Drugs For Colorectal Carcinoma

Drug	Class	Indication	Biomarker for Toxicity	Biomarker for Efficacy
5-Fluorouacil	Anti-metabolite	Adjuvant & Advanced	DPD Deficiency	
Capecitabine	Anti-metabolite	Adjuvant & Advanced	DPD Deficiency	
Oxaliplatin	Platinum	Adjuvant & Advanced		
Irinotecan	Topo-1 Inhibitor	Adjuvant & Advanced	UGT1A1 7/7 polymorphism	
Cetuximab	EGFR moAb	Advanced		KRAS, ?BRAF
Panitumumab	EGFR moAb	Advanced		KRAS, ?BRAF
Bevacizumab	VEGF moAb	Advanced		

Cetuximab for the Treatment of Colorectal Cancer

Derek J
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Rafal W

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K-ras Mutations and Benefit from Cetuximab

Christos S. Kar
Dongsheng Tu, P
Sonia Ro
Chi

Prospective Cost-Effectiveness Analysis of Cetuximab in Metastatic Colorectal Cancer: Evaluation of National Cancer Institute of Canada Clinical Trials Group CO.17 Trial

Nicole Mittmann, Heather Jane Au, Dongsheng Tu, Christopher J. O'Callaghan, Pierre K. Isgai

Christos S.
Bruce Colw
on Econom
Gastrointes

Association of *KRAS* p.G13D Mutation With Outcome in Patients With Chemotherapy-Refractory Metastatic Colorectal Cancer Treated With Cetuximab

De Rook W et al. JAMA. 2010;304(16):1812-1820

Summary and Conclusions

- With a growing and aging population, more Canadians will require ongoing medical treatment, surveillance and supportive care for cancer.
- To impact cancer incidence and mortality
 - Development of new ways to exploit knowledge of genetic and cancer biology knowledge for the benefit of patients.
 - Research and evaluation of new tests and treatments
 - Improve uptake and utilization of best practices
 - Education of patients and physicians
 - High priority on quality assurance and monitoring
 - Ongoing evaluation procedures

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