CANCER EDUCATION DAY

Colon Cancer Management

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WINDSOR REGIONAL HOSPITAL

OUTSTANDING CARE – NO EXCEPTIONS!

PRESENTER DISCLOSURE

- **Relationships with financial sponsors:**
  - **Grants/Research Support:** N/A
  - **Speakers Bureau/Honoraria:** N/A
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  - **Advisory Board:** Novartis

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Colorectal cancer in Canada

Colorectal cancer develops in the cell lining of the colon and rectum. Cells may form benign (non-cancerous) growths called polyps. Over a period of years, a series of DNA mutations can occur, leading polyps to become malignant (cancerous).

The data [1,2]

It is the **3rd MOST COMMON** cancer in Canada

93% of cases occur in **ADULTS AGED 50+**

About **26,900 Canadians** will have been diagnosed with colorectal cancer in **2020**

1 IN 14 MEN & **1 IN 18 WOMEN**

will be diagnosed with colorectal cancer in their lifetime

Risk factors include*

AGING | PHYSICAL INACTIVITY | SMOKING TOBACCO | ALCOHOL INTAKE | OVERWEIGHT OR OBESITY | DIET HIGH IN PROCESSED MEAT, OR RED MEAT | FAMILY HISTORY | COLORECTAL POLYPS OR INFLAMMATORY BOWEL DISEASE

* For more information, please visit: **https://data.prevent.cancer.ca/current**

Screening and detection [2,3]

47% of colorectal cancer cases are diagnosed **EARLY IN THEIR DEVELOPMENT,** at **STAGE I** and **II**

The **PROBABILITY OF SURVIVING** colorectal cancer **AT LEAST 5 YEARS AFTER DIAGNOSIS** is about **65%**

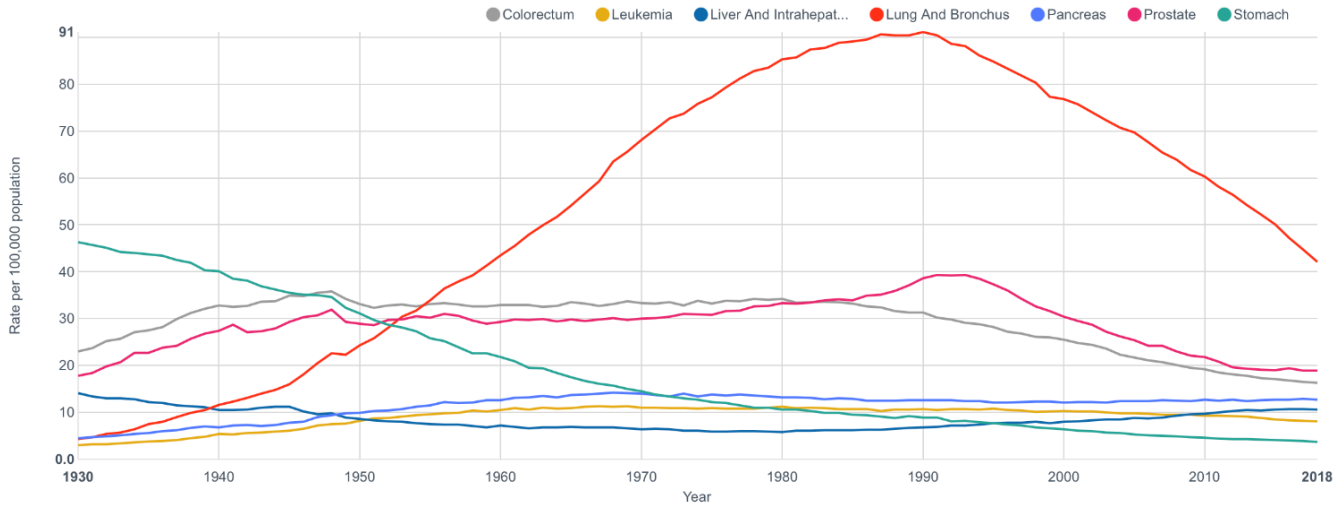
Screening for colorectal cancer is recommended for

AVERAGE-RISK ADULTS AGED 50 TO 74 YEARS

The screening guidelines above are available from the Canadian Task Force on Preventive Health Care.

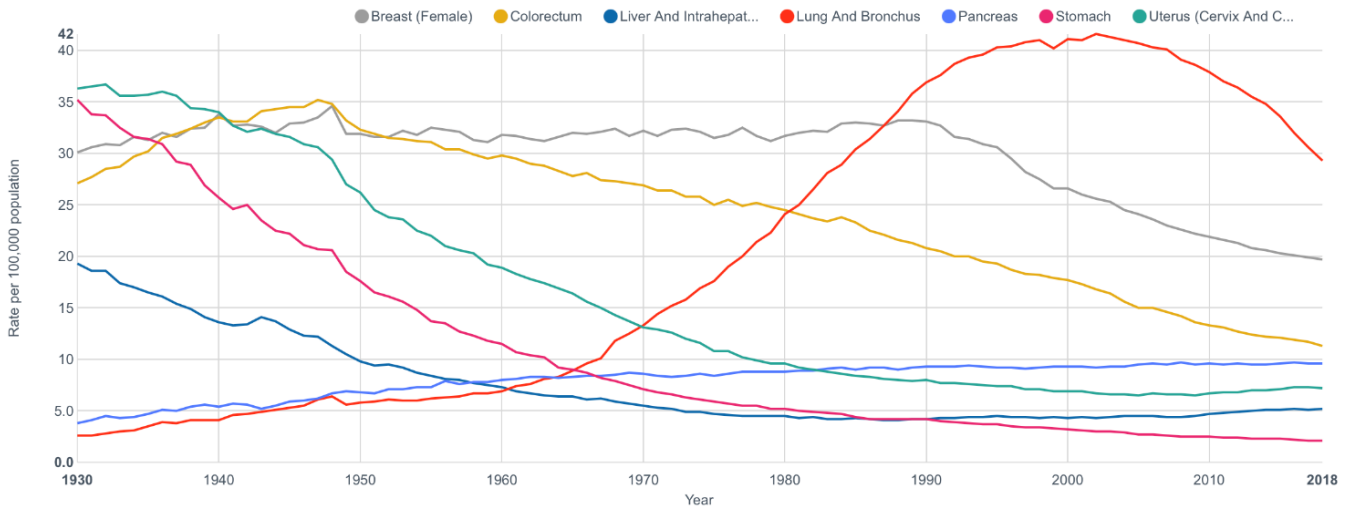
Trends in death rates, 1930-2018

Males



Trends in death rates, 1930-2018

Females



ADJUVANT CHEMOTHERAPY: STAGE 3

- Definite benefit in Stage 3 [Node positive]
  - Improves DFS and OS
- Duration is 3 to 6 months
- Ideal timing is 6 to 8 weeks after definitive surgery
  - Delay beyond 8 weeks does decrease OS
  - Can still have benefit for up to 6 months.
- Who benefits from chemotherapy?
  - 30% of patients actually benefit
  - 50% are cured by surgery alone
  - 20% recur even with treatments

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CHEMOTHERAPY REGIMEN

- In 1990s 5 FU/ Leucovorin – Mayo or Rosewell park regimen
  - Reduction of death by 15% at 5 years
- 2000-Oxalipaltin based chemo FOLFOX – with 5 FU.
- CAPEOX : Capecitabine based. With Oxali.
- Irinotecan based regimen
  - Useful for metastatic but did not benefit in Adjuvant setting.
- VEGEF[bev.] or EGFR [cetuximab or panitimumab based therapy did not benefit as adjuvant treatments

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CHEMOTHERAPY DURATION

- **3 MONTHS vs 6 MONTHS**
  - IDEA Collaboration – pooled analysis of 3 studies over 12,000 patients with Stage 3 Colon cancer
    - Non inferiority not confirmed in whole population
  - T1-3, N1[low risk]: 60% of all Stage 3 patients
  - 3 months of CAPEOX not inferior to 6 months of FOLFOX
    - DFS – 80% at 3 years
    - But 3 months of FOLFOX not as adequate
  - T4 and/or N2 [high risk]: 40% of all Stage 3 patients
  - 3 months of CAPEOX slightly inferior to 6 months of FOLFOX
    - DFS – 60% at 3 years.
    - Advantage: Less neurotox : 45% compared to 14%

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ELDERLY PATIENTS

- > 80 years old not usually included in studies
- Oxaliplatin of minimal benefit in patients > 75 years old
  - < 75 years old can treat as in others
  - 70-75 years old: avoid if multiple co-morbidities
- Always consider
  - Co-morbidities
  - Life expectancy
  - P.S.
  - Expectations
  - Balance risk vs benefits
  - Geriatric evaluation
- Adjuvant chemotherapy studies in elderly patients pending

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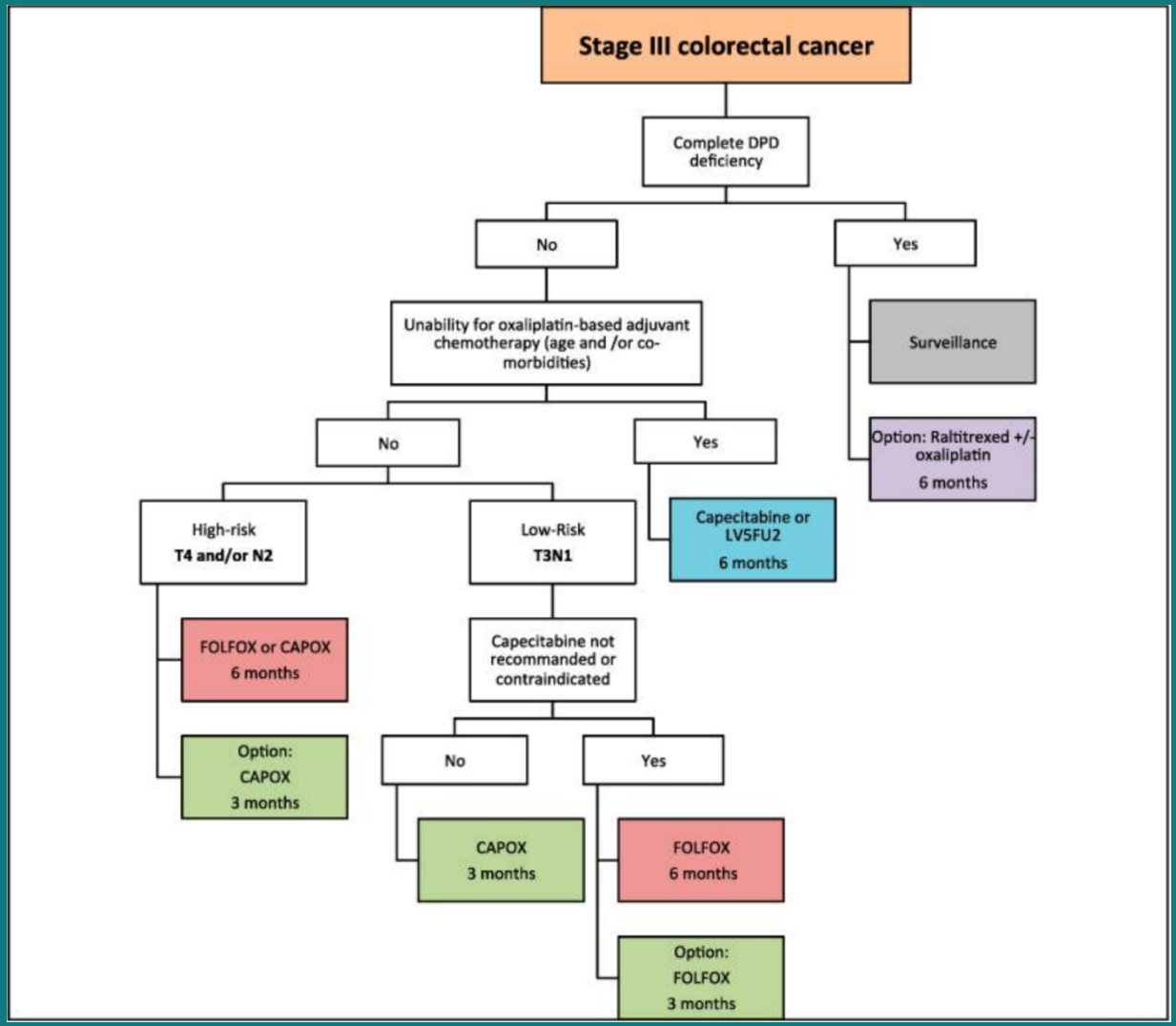

Source: Cancers(Basel). 2020 Sep; 12(9): 2679

IS ADJUVANT CHEMOTHERAPY NECESSARY?

- **STAGE 1:** All agree – no need for adjuvant chemo

- **STAGE 2:** Trial data inconclusive - only small improvements in very large studies
  - FOLFOX vs 5FU/ Leu. non significant improvement
  - Small benefit of chemo - 2-3% of survival benefit
  - CHEMO DISC. IN: High risk: Poorly diff/T4/Obstruction/ Perf./LVI/suboptimal nodal sampling (<14)
  - No benefit in MSI – high
    - Some studies chemo even worse

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MOLECULAR AND GENETIC TESTS

- Various Gene expression tests are available to try and identify high risk patients
  - Oncotype Dx Colon Recurrence Score
  - Coloprint
  - Veridex
  - Gene Fx
- Prognostication not relevant enough to integrate into daily practice
- Mutational analysis/ next generation sequencing (NGS) not recommended as it does not modify current management

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PROGNOSTIC BIOMARKERS

- MSI HIGH 10%
  - Good prognosis in low risk patients
  - Not much benefit with 5 FU chemo
  - Longer DFS but poorer survival if recurrence
  - Responds to immunotherapy in metastatic setting
- BRAF mutation
  - Indicative of poor prognosis
  - 10% of localized colon cancer
- Tumor circular DNA
  - Highly predictive of DFS and OS
  - If undetectable after chemo, did well

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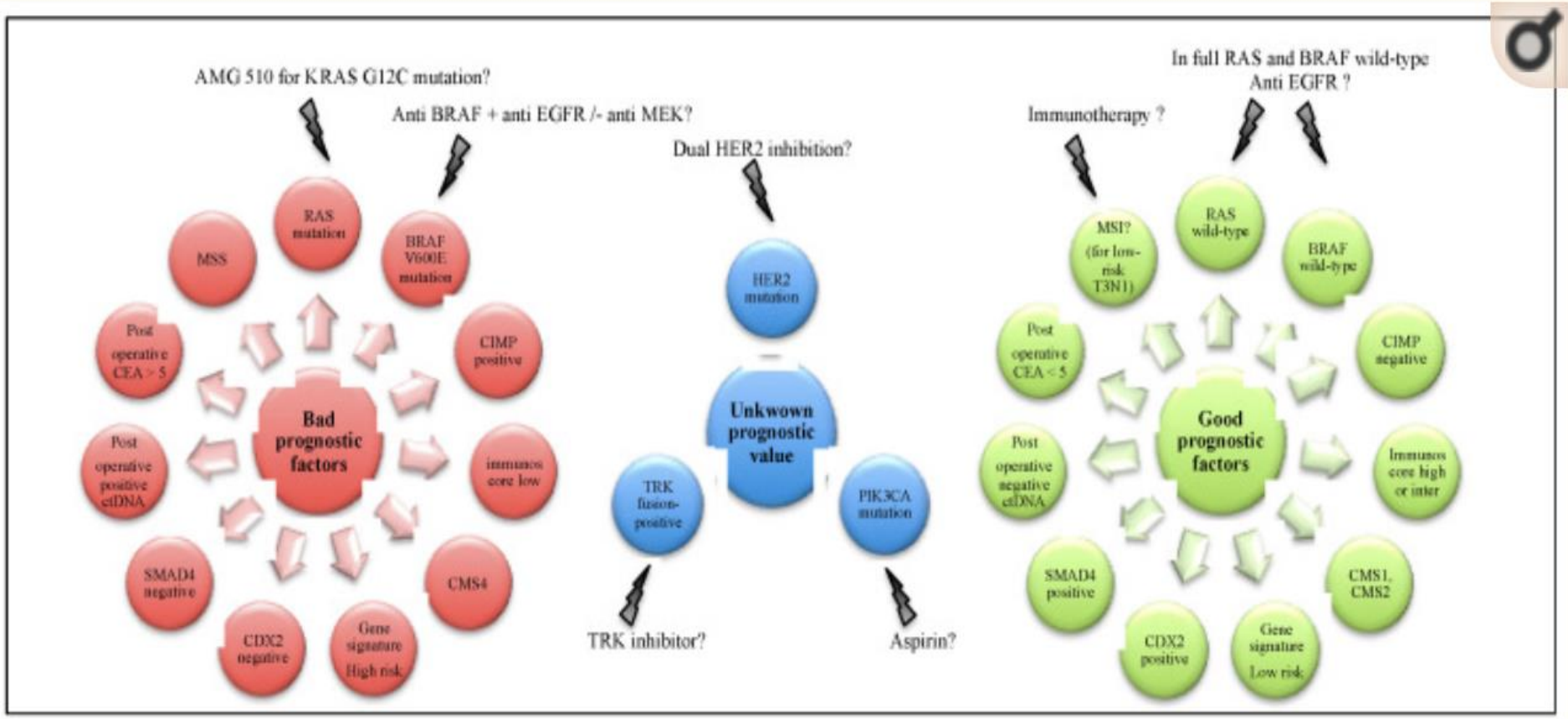

Figure 2

Prognostic markers in stage III colorectal cancer and potential targets for future treatments. Lightnings: potential targeted therapies for molecular subgroups. MSS: microsatellite stable; MSI: microsatellite instability; CEA: carcinoembryonic antigen; ctDNA: circulating tumor DNA; CIMP: CpG island methylator phenotype; HER 2: human epidermal growth factor receptor 2; EGFR: epidermal growth factor receptor; CMS: consensus molecular subtype.

Source: Cancers(Basel). 2020 Sep; 12(9): 2679

CHEMOTHERAPY: SPECIAL CONSIDERATIONS

- Dihydropyrimidine dehydrogenase deficiency (DPD)
  - In 0.3% of population – severe toxicity with 5 FU
- Chest pain on 5-FU –infusion
  - Consider coronary artery spasm
  - Need cardiac work-up
- Oxaliplatin causes significant neurotoxicity
  - 45% grade 2 or higher at 6 months
- Capecitabine may cause significant diarrhea specially if patient has stoma

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METASTATIC COLON CANCER: CHEMO

- First assess liver and lung disease to see if there are any curative surgical options
- Consider liver directed therapy [IR] – RFA, Y-90
- Oligometastatic disease – explore RT options
- Distant metastatic unless amenable to surgery is not curable
  - Chemotherapy can control disease and prolong life
- 5 year survival is 14% for Stage 4 disease

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METASTATIC COLON CANCER: MAIN AGENTS

- 5 FU [+LEUCOVORIN]
- Capecitabine [Xeloda]
- Irinotecan
- Oxaliplatin
- Lonsurf [trifluridine and tipiracil]

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COMMON REGIMEN

- FOLFIRI alone or with bev.
- FOLFOX
- If K-ras wild type
  - Cetuximab alone or with Irinotecan or Panitumumab
- Clinical trials/ targeted agents in pipeline

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NEWER THERAPIES/AGENTS

- Immunotherapy in MSI unstable patients
  - funding still pending
- Her 2 neu positive
  - anti Her 2 neu agents
- AMG 510
  - being studied for K-ras mutation
- Studies in T4 and/or N2
  - Adjuvant FOLFIRINOX

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Thank you
for your attention