The role of health promotion and education in cancer prevention

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- Cancer & Evolution Symposium and Ellison Insights in Medicine Forum Participant
- Reading and writing academic literature advancing biology and cancer curriculum

The literature indicates that cancer can and should be prevented by addressing environment and lifestyle factors[1][2][3][4][5][6][7][8][9][10][11][12][13][14][15][16][17][18][19][20][21][22][23][24][25][26][27][28][29][30][31][32][33][34][35][36][37][38][39][40][41][42][43][44][45][46][47][48][49][50]

Many people are not aware that, beyond the problems of smoking, pollution and pesticides[33]*, lifestyle choices, such as exercise and diet, and environmental exposures including infections determine risk of cancer*[51]*.*

Genetics are only responsible for a small fraction of cancers whereas the majority are due to lifestyle and environmental factors[33][41][44][49]**. Therefore:**

- Avoid or reduce exposure to carcinogens, the "known or probable causes of cancer"[6].
- Curb infection through vaccination, abstinence or safe sex, and safe injections[30][36].
- Beware that traumatic and chronic elevated stress may cause DNA damage[25][32][35].

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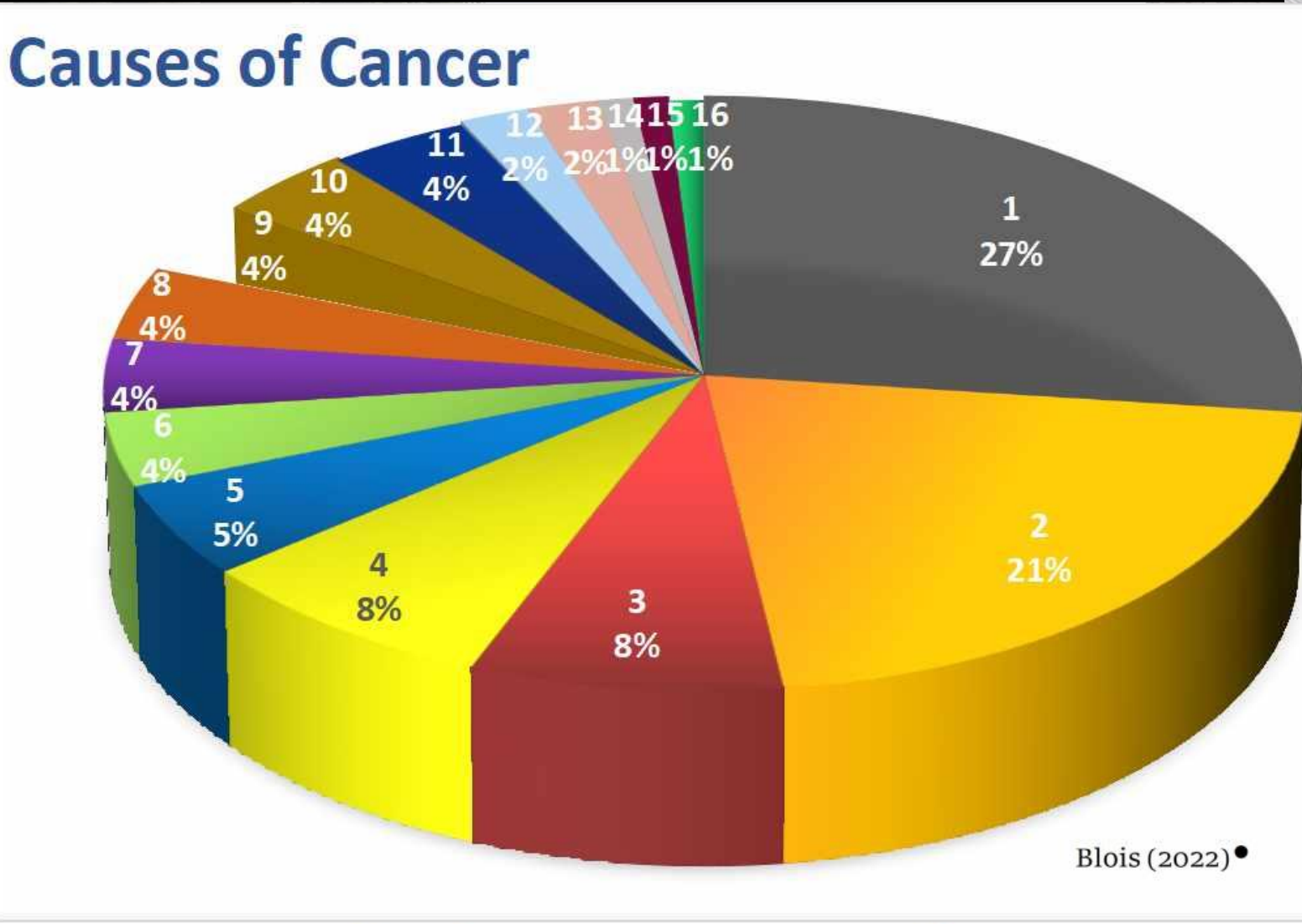
Education can help reduce cancer incidence by increasing awareness of how it can be prevented:

1	Smoking	27
2	Poor Diet, Sedentary life, Obesity	21
3	Adverse Childhood Events	8
4	Infections (vaccination needed)	8
5	Professional exposures (150 types)	5
6	Age	4
7	Alcohol	4
8	Air & Water pollution, Pesticides	4
9	Hereditary factors	4
10	Household fumes from coal etc.	4
11	UV rays, X-rays & gamma radiation	4
12	Low socio-economic status	2
13	Reproductive & Perinatal factors	2
14	Medicinal drugs & procedures	1
15	ELFs, EMFs, Cell-phones, Wifi, etc.*	1
16	Traumatic stress, Bereavement, etc.	1
17	*ELF: Extremely low-frequency, EMF: electromagnetic fields. Cell-phones & wifi emit EMFs & microwaves.	



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- **Integrated Multifactorial Approach:** "Cancer is a multifactorial disease"[1].
  Ex. smoking, alcohol, and air pollution (asbestos, radon, NO_2, $PM_{2.5}$) increase risk of cancer multiplicatively[2][3][4][5][6]. (7)
- **Emphasis on non-intrinsic factors**
  Environment and lifestyle, over which we have some control, are responsible for up to 80% of all cancer[7].
- **Mechanisms of Carcinogenesis:**
  Mutations and DNA Damage: Mutation
  - could be caused by environmental factors[8]
  - could activate an oncogene, ex. RAS[9]
  - could inactivate a tumor suppressor, ex. p53[9]
  - might impair the immune system[9].
  - NHEJ DNA repair may generate mutations[9].

Intrinsic risk factors	Non-intrinsic risk factors	
	Endogenous risk factors	Exogenous risk factors
❖ Random errors in DNA replication	❖ Biologic aging ❖ Genetic susceptibility ❖ DNA repair machinery ❖ Hormones ❖ Growth factors ❖ Inflammation ❖ etc.	❖ Radiation ❖ Chemical carcinogens ❖ Tumour causing viruses ❖ Bad lifestyles such as smoking, lack of exercise, nutrient imbalance ❖ etc.
[Unmodifiable]	[Partially modifiable]	[Modifiable]

Degraded Tissue Quality: Tumorigenesis may be initiated by conditions in the microenvironment[10][11].

- Cell-cell communication as part of the regulatory network may have been disrupted[12][13][14][15].
- Inflammation fosters cancer development[3], and up to "90% of cancers can be partially attributed to inflammation related to lifestyle and environmental exposures"[16]. ***Obesity*** causes hypoxia and increases inflammatory cytokines in fat, demonstrating the close relationship between inflammation and hypoxia[17][18]. ***Therefore address obesity and causal factors of inflammation through diet, behavior, and therapeutics.*** ***Aspirin*** can be life-saving[19], and low-dose (such as 81 mg/d) generally recommended for adults aged 50-59, and somewhat for 60-69, to reduce risk of colorectal cancer[20][21][22].
- Hypoxic, low [O_2], microenvironment may inhibit anti-tumor T-cells, justifying oxygen supplementation[23]. ***Quality of sleep may need to be addressed. Obstructive sleep apnea increases risk of cancer due to hypoxia***[24].
- Most tumors are acidic (pH range 6.4–7)[24][25]. Acidity is related to hypoxia, and acid can damage DNA[25]. Acidosis may result in stem-like, resistant, self-renewing, tumorigenic, invasive phenotypes, and is reversible[26].

4a

It is vital to prevent cancer and nip it in the bud.

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Late-stage cancer is difficult to treat effectively.

Problem 1: Up to 70% of cancer therapeutic drugs harm patients without improving overall survival (OS)[1].
Dozens of studies report drugs that appear successful because they lower cancer burden for a time, but *reduce* OS[2].
26 of 64 European Medicines Agency-approved cancer therapeutic drugs (2009-2013) improved OS, median 2.7 months[3].

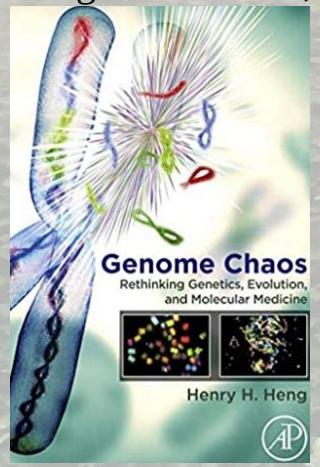
Problem 2: New therapies often only offer a short improvement on previous therapies[4].
The 72 FDA-approved cancer therapeutic drugs (2002-2014) improved average OS by 2.1 months[5].
Immunotherapy improved OS by 3.9 months in treatment of metastatic non-small-cell lung cancer (NSCLC)[6].
Epidermal growth factor receptor (EGFR) **tyrosine kinase inhibitor (TKI)** gefitinib improved OS by 9.3 months over afatinib in handling L858R mutations[7], but the more recently approved EGFR TKI osimertinib did not benefit these patients as much (OS 1.9 mo. less)[8].
Regarding **angiogenesis inhibitor** trials, targeting vascular EGF only prolonged OS by months because of acquired resistance[9].

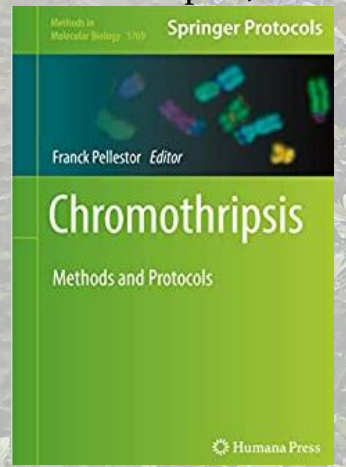
Problem 3: "Surgery and **radiation" are unlikely to cure cancer which has spread beyond what may be excised or irradiated**[10][11].

Problem 4: Therapeutics which target cell growth may cause illness or death before cure is achieved because our life depends on cell growth[10].
When "cytotoxic agents are administered at doses close to maximal tolerable" differences between individuals may "lead to severe toxicities"[12].

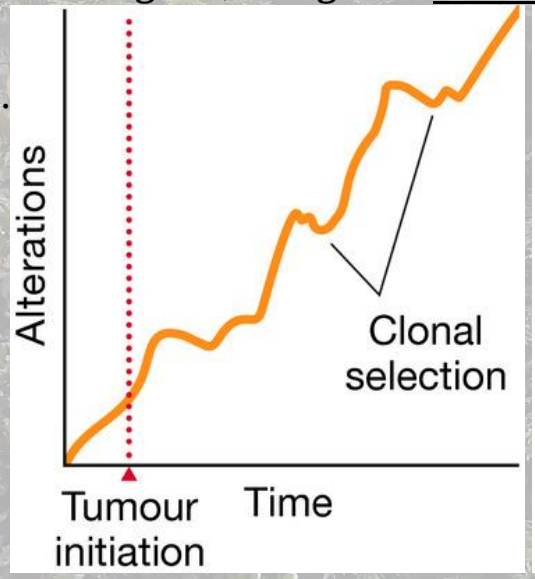
Issue 1: Chemotherapy can weaken our immune system which fights cancer, and is carcinogenic, along with radiotherapy (RT)[13][14][15][16].

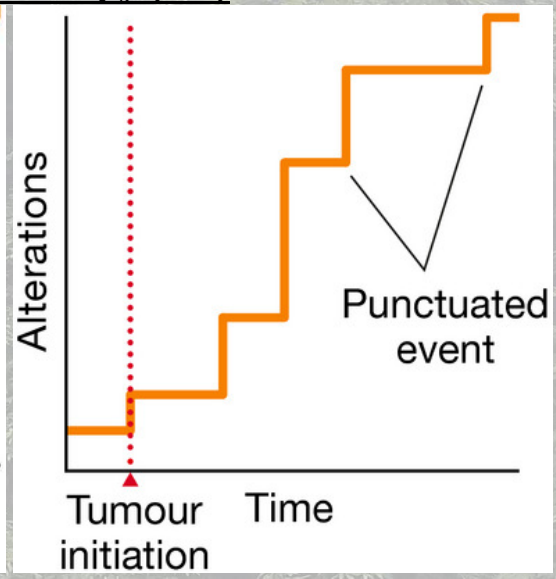
Issue 2: Cancer is often presents as heterogeneous, more so in metastatic late-stage disease[17][18], and genome chaos, chromothripsis, exacerbates diversity[19][20][21][22].





Cancer Evolution Model[23]





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Late-stage cancer is difficult to treat effectively.

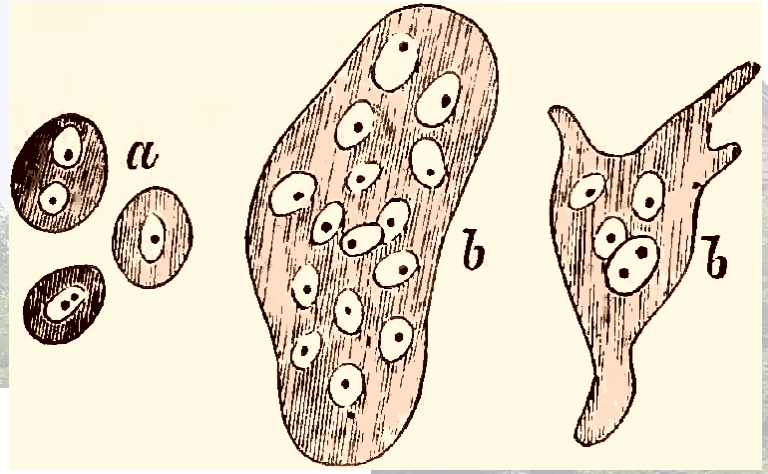
Issue 3: <u>Chemotherapy</u> may not eliminate every cancerous cell, adapted clonal subpopulations survive and regrow, so **<u>targeted therapies</u>** often fail[23][24][25][26].

Issue 4: Cancer therapy may induce genome chaos, increasing genetic change[27][28][29].

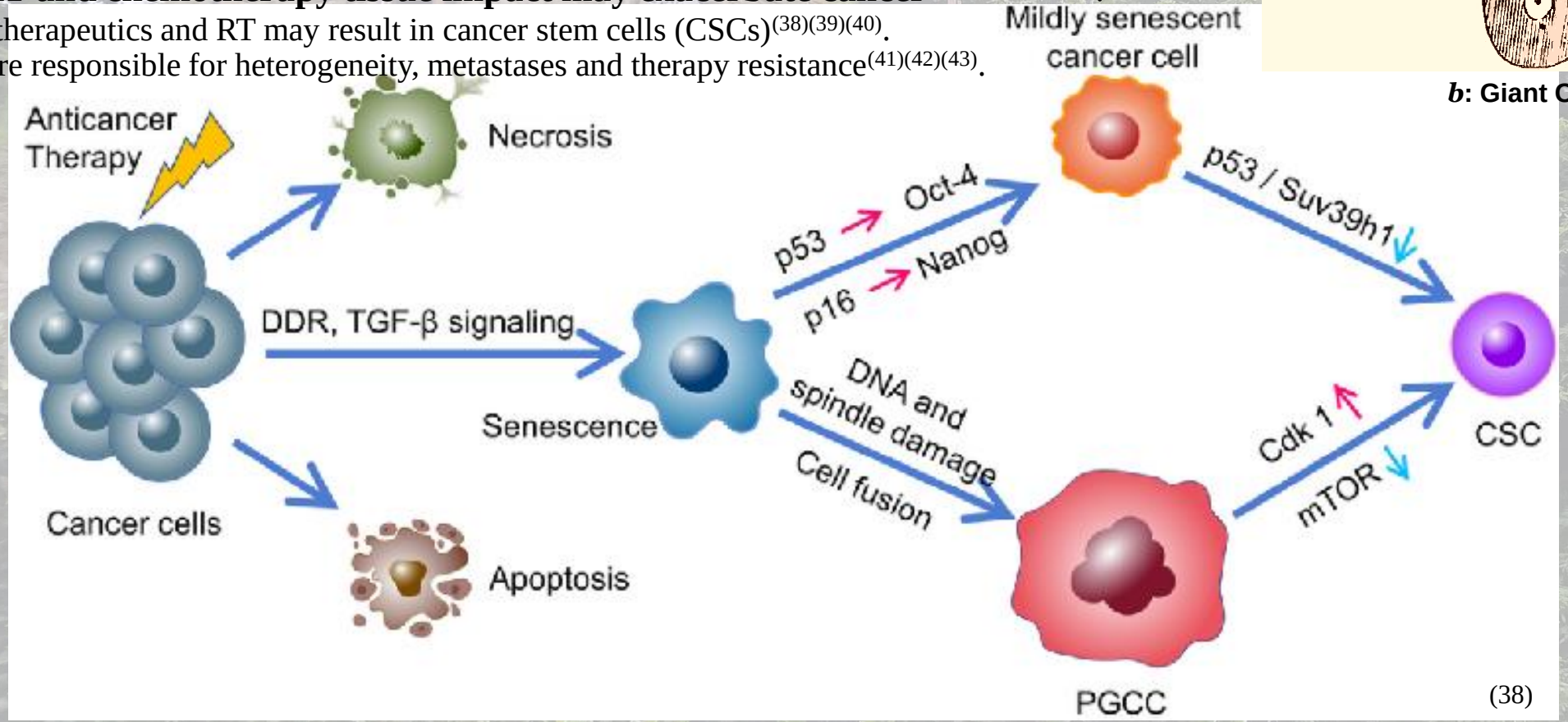
Issue 5: Polyploid giant cancer cells (PGCCs) may cause cancer, are stress induced, and might survive chemotherapy and RT[30][31][32]. See Virchow's figure, right:

Issue 6: RT and chemotherapy tissue impact may exacerbate cancer[34][35][36][37].

Chemotherapeutics and RT may result in cancer stem cells (CSCs)[38][39][40].
CSCs are responsible for heterogeneity, metastases and therapy resistance[41][42][43].



***b*: Giant Cancer Cells**[33]



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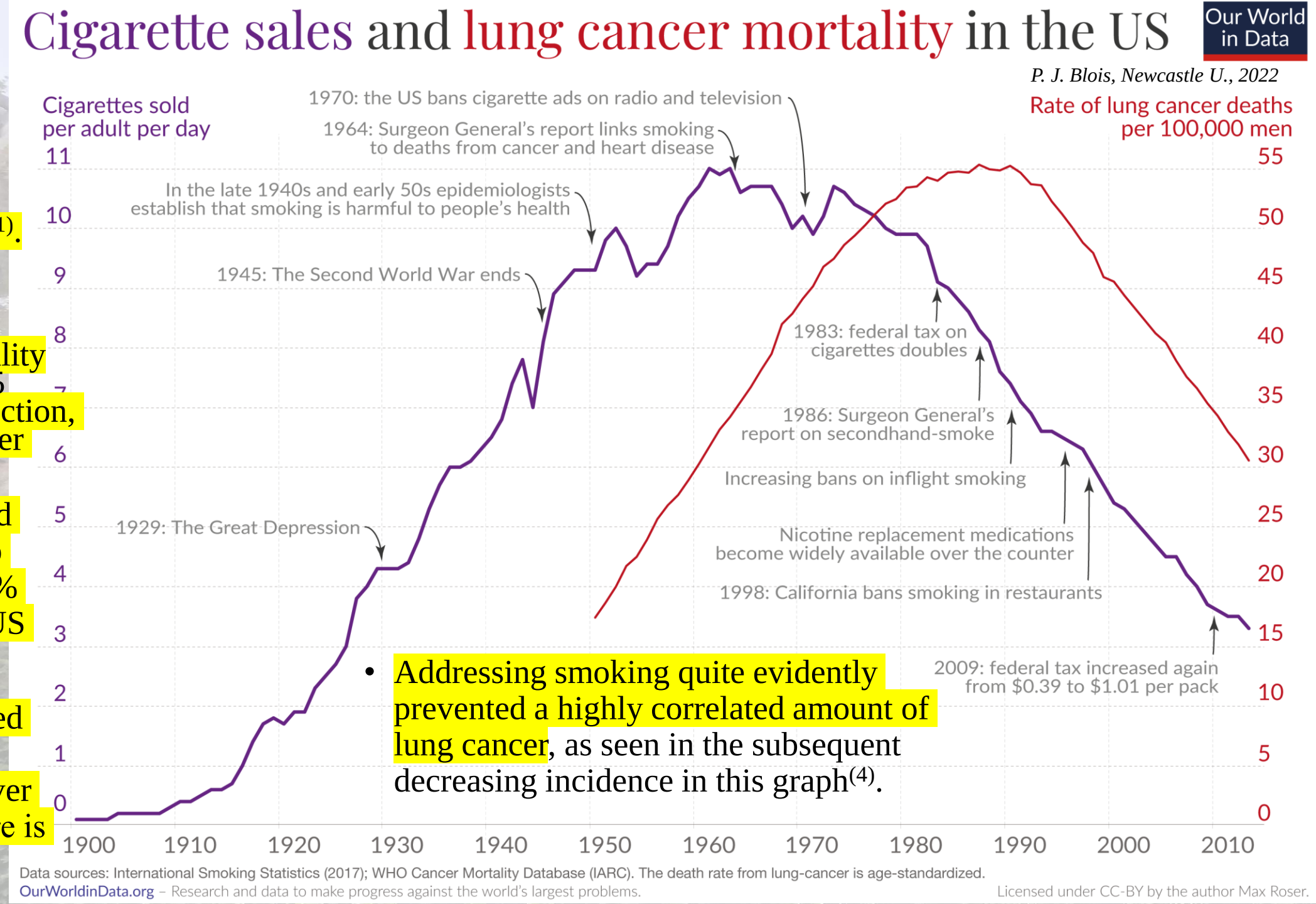
5 Reasons to Embrace Prevention:

- "the most cost-effective" strategy[1].
- **Success stories**:
- A 39% decrease in breast cancer mortality between 1990-2015 thanks to early detection, and colorectal cancer down 46%[2].
- Prostate and thyroid early detection also contributed to >25% overall decline in US cancer mortality[2].
- The Pap test lowered "cervical cancer mortality rate by over 70%" and now there is an HPV vaccine[3].



- Addressing smoking quite evidently prevented a highly correlated amount of lung cancer, as seen in the subsequent decreasing incidence in this graph[4].

Overview of Prevention Mechanisms

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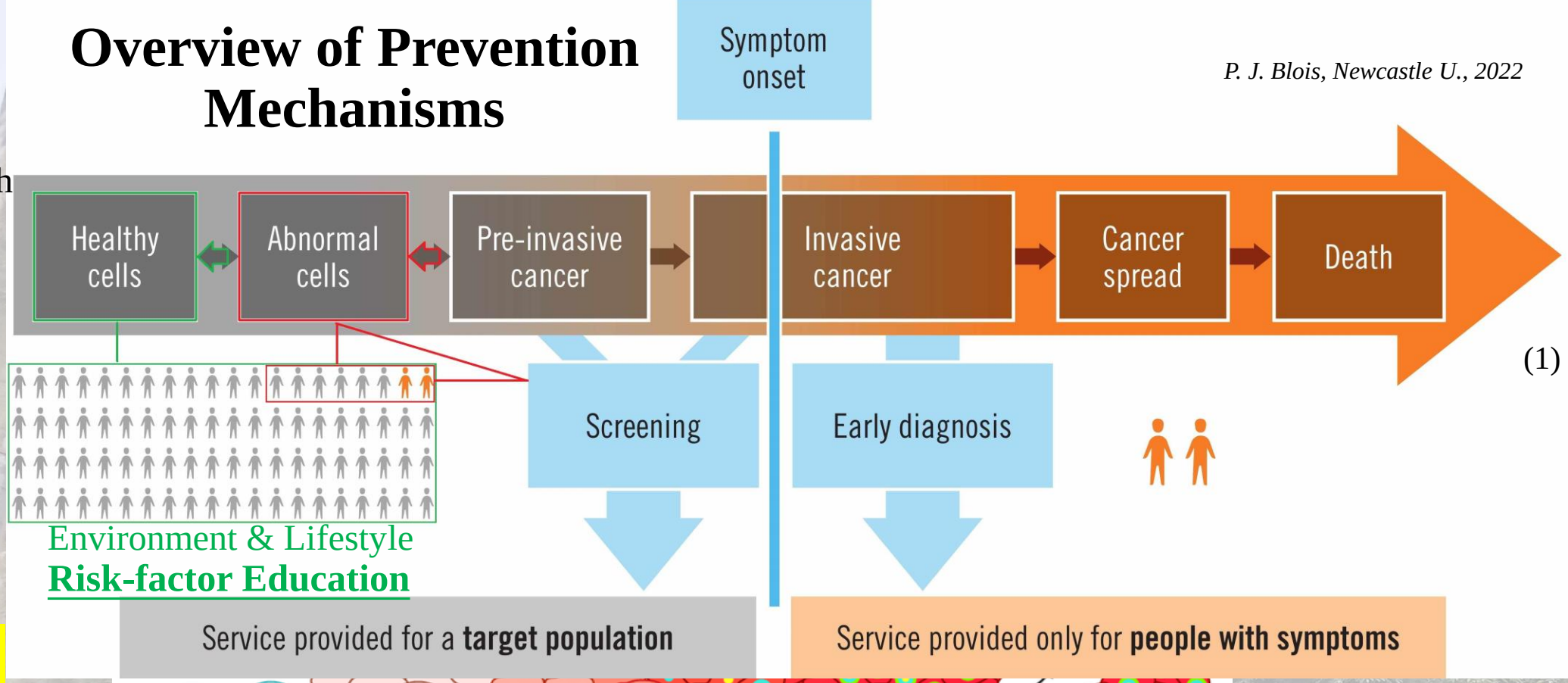
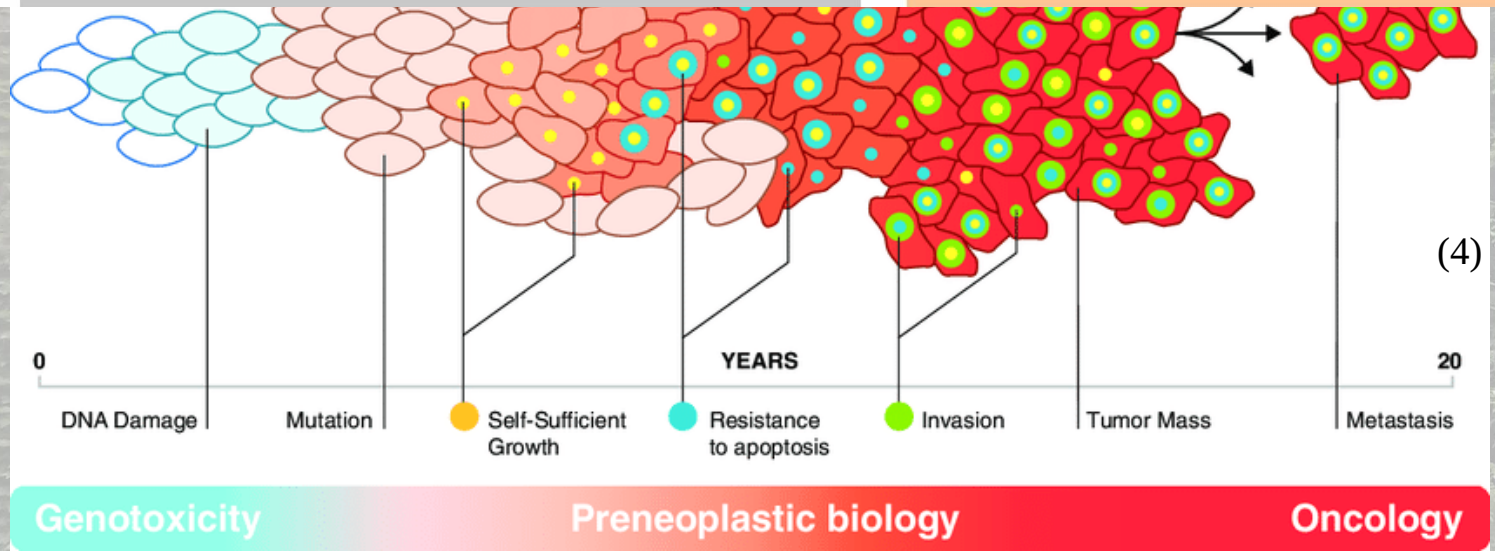
- Carcinogenesis is a long-term process characterized by molecular events which culminate in qualities such as loss of cell homeostatic function that define cancer[2].
- Exposure "begins in childhood and builds up throughout life"[3].
- Diverse interventions can slow or reverse carcinogenesis early along through risk assessment, screening, lifestyle changes (diet, exercise) and more[2].



(1)

Assess & Address Toxcity & the TME hypoxia, inflammation, pH

Blood, Urine, Salivary & Genetic Tests Analyse biomarkers, metabolomics, proteomics, transcriptomics, exosomes and epigenetics[5].



(4)

- Prevention can aim to keep a tumor from becoming invasive cancer (metastatic)[2].
- Prevention can aim to keep cancer from becoming more genetically diverse (resistant).

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Lifestyle-related Environmental Exposures to Avoid: Chemical Carcinogenic Factors[1]

- Avoid nicotine and tobacco, including second-hand and smokeless[1].
- The need to address tobacco-use remains critical, and the problem is particularly pressing in undeveloped and developing countries[2]. E-cigarettes have not consistently helped smokers quit[2]. The FDA has now approved the "Vuse Solo closed ENDS device and accompanying tobacco-flavored e-liquid pods"[3].
- More oncologists (65%) should discuss or offer cessation medication, assistance and referral[2]. ***A****sk* every patient about use, ***A****dvise* every user to cease, ***A****ssess* willingness, ***A****ssist*, ***A****rrange* support in the 1st week[2].
- Stop using asbestos insulation[4] and reduce coal and biomass cooking and heating[5].
- Avoid or reduce exposure to diesel engine exhaust, paint, tar, and welding fumes[1].
- Beware of chlorinated compounds at home, and in the workplace where frequent exposure creates greater risk: chlornaphazine, chloromethyl ether, 1,2-dichloropropane, 4,4'-methylenebis, ortho-toluidine, 2,3,4,7,8-pentachlorodibenzofuran, pentachlorophenol, polychlorinated biphenyls (PCBs), 2,3,7,8-tetrachlorodibenzo-para-dioxin, trichloroethylene, semustine, vinyl chloride[1]
- Beware of mining (ex. hematite), and beware of industrial processes involved in manufacture: aluminum, auramine, coke, iron and steel, isopropyl alcohol, graphite, magenta, rubber
- Beware of many pesticides[6] along with other industrial and medical chemicals: acetaldehyde, acid mists, 4-aminobiphenyl, aristolochic acid, azathioprine, benzene, benzidene, benzopyrene, 1,3-butadine, cyclosporine, diethylstilbestrol, ethylene oxide, fluoro-edenite fibrous amphibole, formaldehyde, lindane, methoxsalen, mineral oils, naphylamine, phenacetin, phosphorus, shale oil, sulfur mustard, welding fumes[1]

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Lifestyle-related Environmental Exposures to Avoid: Biological Carcinogenic Factors

- **Oncogenic Viruses** may cause cancer directly or indirectly by causing inflammation[1].
- Human Papilloma Virus (HPV): Prevent cervical cancer by vaccinating girls 9-13 and through sexual education encouraging delayed sexual initiation, condom promotion and provision and circumcision for those active, and HPV testing of women over 30 to identify those at risk[2].
  Those who remain "infected are at much greater risk of developing cancer": Pap, PCR-screen[1]
- Hepatitis B Virus (HBV), ≈900,000 deaths/year[1]: universal infant HBV immunization recommended[3].
- Hepatitis C Virus[4] (HCV), ≈450,000 deaths/year: sofosbuvir and newer antiviral therapies[1]
- Epstein-Barr Virus[4] (EBV), responsible for ≈200,000 cancer cases: ganciclovir, antiherpesvirus, HIV[1]
- HIV type 1[4]: direct oncogenic effect beyond impairing the anti-cancer, anti-viral immune system[5]
- Human T-cell lymphotropic virus type 1[4]: "allogenic hematopoietic stem cell" transplant possible[1]
- Kaposi sarcoma herpesvirus[4], common cause of African cancer: ganciclovir, antiretroviral, HIV[1]
- **Parasites**: *Schistosoma*[4] (liver and blood flukes) responsible for schistosomiasis, the second-most devastating parasitic disease, associated with chronic inflammation[6].
  Prevention: do not drink, bathe or swim in freshwater unless chlorinated or first boiled 1 min[7].
- **Bacteria**: Ex. *Helicobacter pylori*[4] leads to gastritis which in turn may cause cancer: antibiotics[8]
- **Therapy**: Postmenopause estrogen, menopause estrogen-progestogen and oral contraceptives[4]

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Lifestyle-related Environmental Exposures to Avoid: Physical Carcinogenic Factors[1]

- Avoid unnecessary medical diagnostic x-rays[2], and other forms of ionizing radiation that may result from α, β, γ and neutron emitting material such as plutonium, radium, and thorium[3].
- Educate to prevent *excess* UV exposure, especially the young and people with prolonged exposure or fair skin, in areas with strong light intensity[2]. (Vitamin D: *15 min.* full-body exposure [4].)
- Radon gas levels should be monitored and indoor concentration mitigated[2].
- Radon, the second-leading cause of lung cancer[5], is a colorless, odorless, radioactive gas which releases from "rock, soil, water, and building materials"[6]. Screening and remediation technology is available[5][6]. Mitigation can be achieved though proper ventilation and improved choice of materials and location[7].
- Reduce exposure to particulate matter such as leather, silica and wood dust, soot[3].
- Avoid exposure to toxic heavy metals, particularly "arsenic, cadmium, chromium, lead, and mercury"[8], along with berylium, cobalt, iron, "nickel, titanium, and zinc"[1].
- Beware electromagnetic fields (EMFs) near electronics. Ex. phone on skin[9][10][11].
- Precaution is recommended to limit EMF exposure, "particularly children, mainly deriving from electricity and wireless" communication[2]. High exposure is linked to leukemia and temporal lobe tumors[1].

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Lifestyle-related Environmental Exposures to Avoid: Dietary Carcinogenic Factors[1]

- **Processed red meat should be limited, and alcohol reduced or avoided[1][2][3].**
- **People, esp. children, must be educated, and protected from adverse marketing[4].**
- **People should be educated and encouraged to consume less "salt, sugar and fat" (animal fat in particular[1]) and eliminate "cooking and preservation methods known to increase cancer risk"** resulting in aflatoxins[5] or chinese-style salted fish[3].
  "Aflatoxin producing fungi [which are liver carcinogens] have severely contaminated food supplies", usually cereals, wheat, corn and nuts, "in the field, or during harvest, transport and storage" and aflatoxins in feedstuff can result in contaminated eggs, milk and meat products[6]. Reduce aflatoxin exposure by only buying major nut brands and discard discolored, shriveled and moldy nuts[7].
- **Drink filtered water[8].** Drinking water may contain "arsenic, disinfection byproducts and radioactive contaminants" responsible for an estimated 100,000 US cancer cases (2010-2017)[9].
- **Soak or boil vegetables with 2% salt water** for 10-15 min. **to remove pesticides**[10][11], or better, 4% Acetic Acid = typical vinegar + 0.1% $NaHCO_3$ = 1.0g/L baking soda + 1 lemon/L[12].
- **Betel nut, "also known as areca nut"**, is a stimulant with many side effects[13]. It **is "a highly addictive" carcinogen**[14]. Due to its popularity in Asia, it is most common drug addiction after tobacco, alcohol, caffeine[15][16], "used by almost a tenth of the world's population"[17].
  Betel chewing alters oral pH, **causing inflammation leading to oral cancer and a dozen others**, yet it remains socially popular and lack of education regarding harm is an obstacle to cessation[18][19].
- **Milk and cheese may contribute to breast cancer**[20][21][22][23][24]. Fewer thyroid cancer cases would have occurred after Chernobyl if people had not consumed local milk containing radioactive

"Cancer Risk-Reducing Agents"[1]

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"There is evidence against general use of nutrient supplements for cancer prevention"[1].

- Long-term low-dose supplement results are sometimes beneficial: Ex. 1, "Stomach cancer death" was reduced in China using "15 mg β-carotene/d + 30 mg vitamin E/d + 50 μg selenium/d",
  ex. 2, vitamin D reduced lung cancer risk by 63%[1].
- Long-term low-dose supplement results are sometimes mixed: Ex. β-carotene reduced risk of recurrent colo-rectal adenomas among non-smokers and non-drinkers by 44%, but more than doubled the risk among those "who smoked and also drank more than one alcoholic drink per day"[1].
- Long-term low-dose supplement results are sometimes adverse: Ex 1, supplemental vitamin E "increased prostate cancer risk by 17%", ex 2, selenium increased risk of skin cancer[1].
- Folate facilitates DNA repair and can reduce colon cancer risk in those low in folate[1].
- Beware, folate is also capable of facilitating cancer cell division[3]—some of the first successful chemotherapeutics were *anti*folates[4]. Consult your physician before taking folate supplements.
- Retinoids show promise, but results are mixed, and are there may be associated toxicity:
  50-100mg/m^2/d 13-cis-retinoic acid reduced incidence of head & neck squamous cell carcinoma (SCC),
  oral retinol 25,000 IU/d = 7,500 mcg/d reduced skin SCC incidence—these are options for people at risk[1]
- Vitamin D 1,000 IU D_3/d = 25 mcg/d may benefit adults during times of low sun intensity[4].
- **Extensive data indicates that "diet-derived natural products reduce risk" of cancer** whereas **purified pharmacological forms often do not confer a comparable benefit[1].**

Evidence suggests difluoromethylornithine, statins, metformin, and nonsteroid anti-inflammatories such as aspirin, may help prevent several types of cancer[1]. Ex. statins may prevent prostate cancer[5][6][7][8].
Oral contraceptives decrease risk of uterine and ovarian cancer: chemoprevention for high-risk[9].

Lifestyle Recommendations: Healthy Diet

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- **Citrus fruits** contain anti-inflammatory flavones[2] **and carotenoid-rich consumption from colorful fruits and vegetables** with α- and β-carotene, lutein, lycopene (high in tomato purée: 290 mg/100g, ketchup: 17 mg, tomato sauce: 15.9 mg, tomato juice: 9.5 mg, guava: 5.4 mg, watermelon: 4.8 mg, raw tomato: 3.0 mg[3]) and β-cryptoxanthin **is associated with reduced cancer risk[1].**
- Coffee[4], dark chocolate, cocoa[2] and foods and spices with polyphenols help prevent cancer: berries, curcumin, genistein (a soy isoflavone[3]), ginger, green tea, omega-3 fatty acids and resveratrol[1].
- Curcumin in tumeric is anti-inflammatory, but *when combined with piperine from pepper as found in curry, it can be absorbed more than a thousand-fold*, indicating wisdom in traditional cooking styles[2].
- *Lamiaceae* (basil, mint, oregano, rosemary, thyme) and *Apiaceae* (coriander, cumin, parsley, fennel) herbs have anti-cancer properties such as helping prevent cancer cell growth, and algae helps, too[1].
- Fish omega-3 fatty acids are most effectively absorbed, but there is some effect from walnuts (8.7g/100g), linseeds (7.3g), walnut oil (4.7g), rapeseed oil (4.3g), and soya beans (0.44g)[2]. Many mushrooms are anti-cancerous, too[2].
- Resveratrol is found in grapes (1.5 mg/100g), peanuts (0.15 mg) and peanut butter (0.05 mg)[2].
- Anticancer chlorogenic acid is high in apples (119 mg/100g), pears (59 mg), plums (44 mg), nectarines (28 mg), peaches (24 mg), apricots (17 mg), and cherries (12 mg)[2]. Add anti-cancer cinnamon and clove to that mix[2]!
- Cruciferous vegetable isothiocyanates (leafy greens, cabbage, cauliflower, radishes, turnips, broccoli)[2].
- Allium family (garlic, onions, leeks) bear allicin (converts to sulfur compounds upon crushing & chewing)[2].
- **Phytochemicals reduce and disappear with processing and preparation**: Ex. Isoflavones in soy flour 199 mg/100g, roasted 128 mg, boiled 55 mg, tofu 55 mg, soya milk 9 mg, soy sauce 1.7 mg, soy oil 0 mg[2].

Lifestyle Recommendations: Exercise & Healthy Weight[1]

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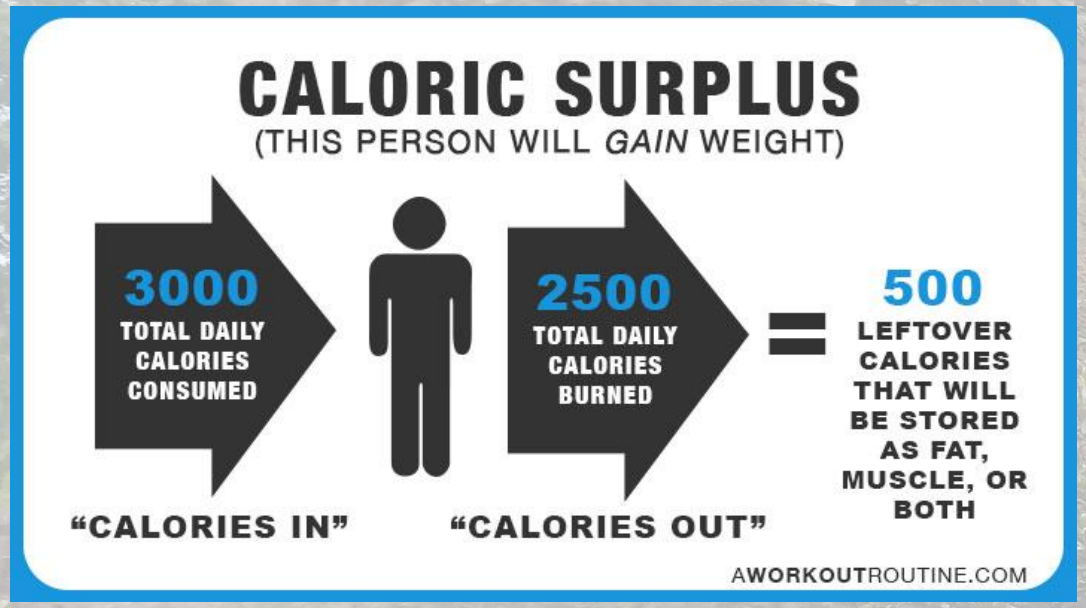
- Oncologists are "uniquely positioned" to encourage their patients and the public in general to live a healthy lifestyle and promote weight management[1].



- **People need specific advice promoting healthy diet and physical activity[3].**
  - Calories must be balanced with activity[4].
  - What specific diet changes need to be made? Ex. reduce high glycermic index carbohydrate intake[4], avoid sugar drinks, fried food, etc.
  - How can ≥ 30 min./d physical activity[4] be achieved?
  - **What kind of support is needed?** Seek help: psychologist, dietician, other specialists[5][6].
  - **What consequences are likely to result if these changes are not made soon? How likely?**

- Obese people (BMI ≥ 30 kg/m^2) are roughly 50% more at risk of cancer than counterparts[1]:
  Increased cancer risk: endometrial: 710%, adeno-esophageal: 480%, gastric, liver, kidney: 180%, meningeal, pancreas, myeloma: 150%, colo-rectal, gallbladder: 130%, ovary, thyroid, post-meno breast: 110%[1].
- Increased physical activity reduces cancer risk[7] by reducing obesity[4], and independent of BMI[1]:
  Reduced cancer risk: adeno-esophageal: 38% lung cancer: 27% squamo-esophageal: 24% gallbladder: 22% liver: 19% kidney: 16% gastric, myeloid, head & neck: 15% myeloma, colon: 13% rectum, bladder: 12% breast: 7% thyroid: 5%[1].
- Sedentary behavior which includes sitting with a device increases cancer risk by 14-20%[1].

"Role of Surgery in Cancer Prevention"[1]

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- Risk-reducing breast surgery[1] may be considered for those with "strong family history of breast cancer", "a >20% lifetime risk" as defined by proper risk assessment, adverse genetic mutations such as BRCA1/2, p53, PTEN, STK11, CDH1, MLH1 & MSH2, PMS2 & MSH6[1].
- **Mastectomy** can reduce risk of breast cancer "by 99% in BRCA1/2 patients with prior oophorectomy and 90% in women with intact ovaries"[1]. Nipple-sparing risk reduction is similar to total mastectomy, making it "a good oncologic and cosmetic option"[1].
- **Salpingo-oophorectomy** (SO) alone reduced risk of breast cancer by ≈50% in BRCA1/2 patients[1].
- Evidence suggests BRCA1/2 carriers undertake surgery soon after completing childbearing[1].
- Given endometrial (uterine) cancer heredity of (Lynch Syndrome), **hysterectomy and bilateral SO** can be a low-cost way to improve quality of life—they "can be performed with minimally invasive surgery and the patient discharged the same day" with few complications if appropriately selected[1].
- "Risk-reducing surgery should be avoided in those who are not good surgical candidates in the absence of a proven mortality benefit"[1].
- RET mutations can help gauge risk of "medullary thyroid carcinoma (MTC)"[1]. Babies identified with level III mutations "should have preventative surgery in the first year of life", level II mutations indicate "total **thyroidectomy** at 5 to 6", level I "before ages 5 to 10"[1].
- For polyposis, adenomas or polyps, surgery may reduce risk of colorectal cancer[1]. "Total **abdominal colectomy**" + **ileorectal anastomosis** for <1,000 polyps <20 adenomas, **proctectomy** for more[1].
- Cervical pre-cancer: **cryotherapy**, **conization** or **electrosurgical excision** if available[3]
- **Bariatric surgery** may reduce risk (by 27 to 59%) of obesity-related cancer[2].

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Conclusion & Highlights

We can strive to prevent cancer, treat pre- and early cancer with greater success:

- Provide health-care professionals with training to educate patients and public with resources[1]. Ex:
- Take cancer risk factors into our locus of control and take action to prevent cancer by taking responsibility for lifestyle[3] and environmental factors that can be changed[4].
- Use of a multi-disciplinary approach to address addictions and lifestyle change[5].
  Ex: tobacco use[6], unhealthy alcohol[7] and drug use[8]
- Advise regular screening for cancer types that can be detected early and prevented[9].
  Ex: cervical 21-65[10], colorectal 45-75[11], breast 50-74[12]
- Those at higher risk for certain forms of cancer should be checked more frequently.
  Ex. screen (ex-)smokers lung 50-80[13]; breast, ovary, tubal, abdominal family history: genetic counsel/test if indicated[14]
- Educate people about cancer symptoms to facilitate early detection[15].Ex. weight loss, pain, nausea, diabetes, itching, fatigue, dysphagia, mass[16]

(2)