Epidemiology of cancer. Preneoplastic disorders.

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Exam questions related to this lecture

B/18. Epidemiology of neoplasms

B/19. Caracteristics and morphology of preneoplastic disorders

B/20. Grading and staging of cancer

B/21. Effects of tumor on host (cancer cachexia, paraneoplastic syndromes)

Lecture outline

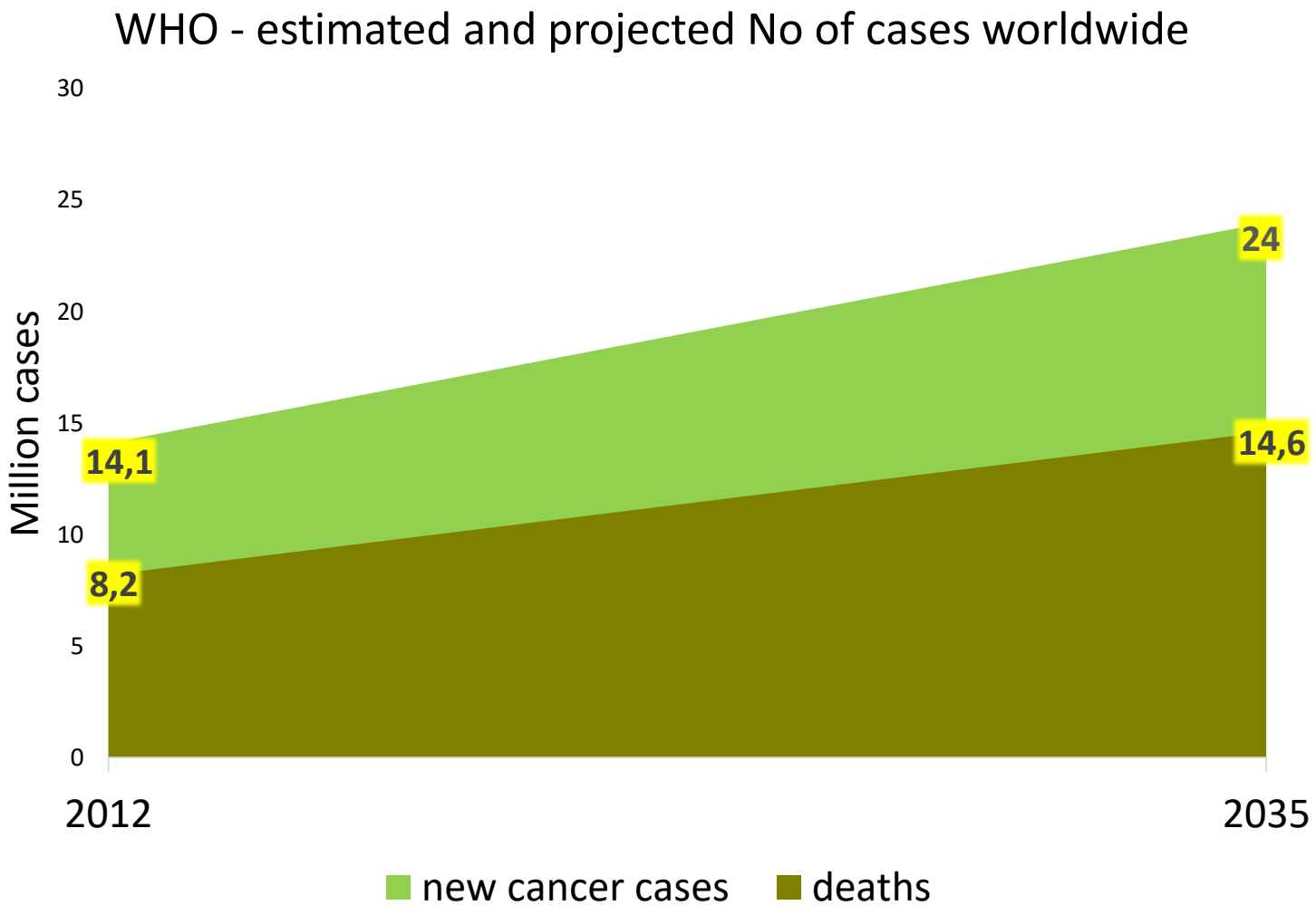
1. Epidemiology of cancer

2. Preneoplastic disorders / precursor lesions

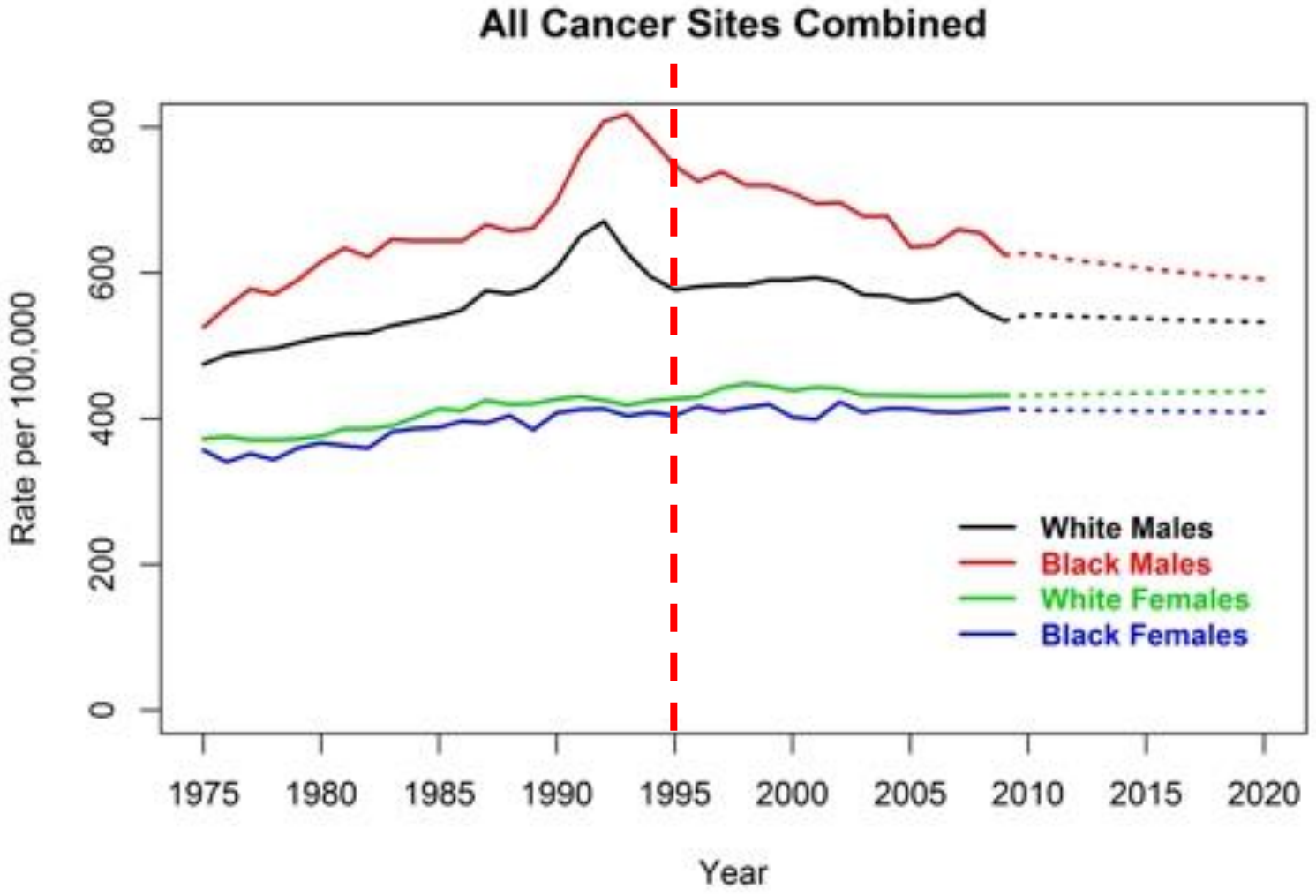
3. Effects of tumor on host

4. Grading and staging of cancer

Cancer incidence (No) is rising (global data)



Cancer incidence rate is roughly stable since 1995 (US data)

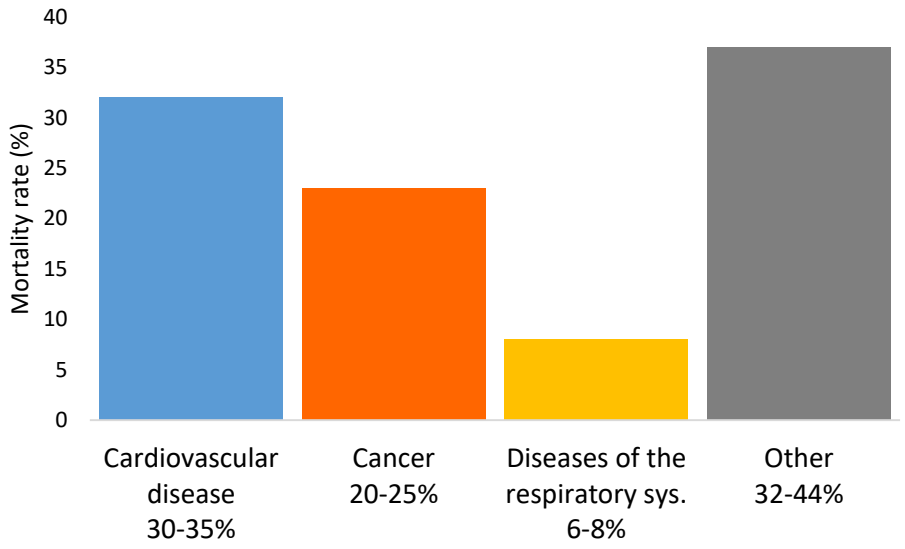


https://www.cdc.gov/cancer/dcpc/research/articles/cancer_2020_incidence.htm

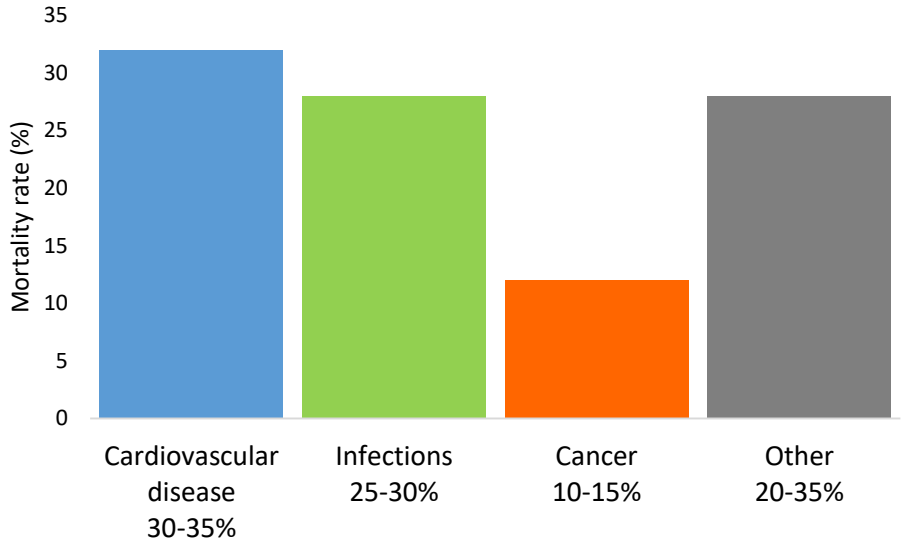
The mortality rate of cancer is ~17% worldwide

- 58.39 million deaths in 2019 → 9.9 million cancer related

Developed countries

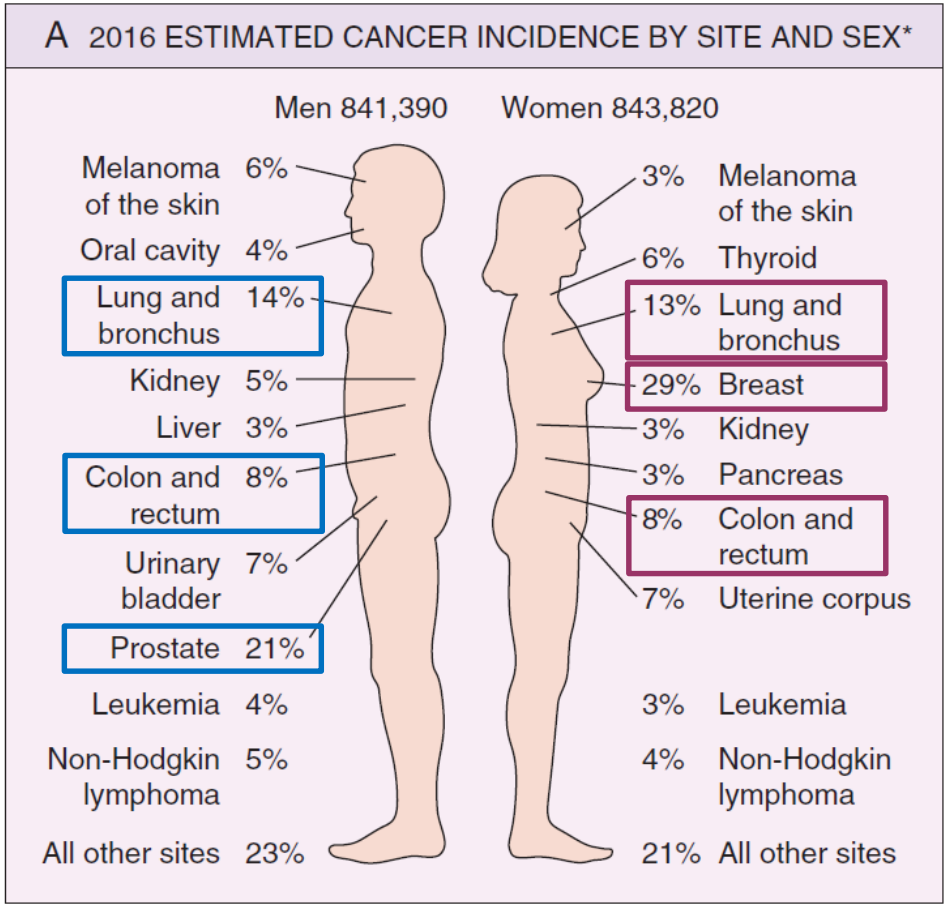


Developing countries

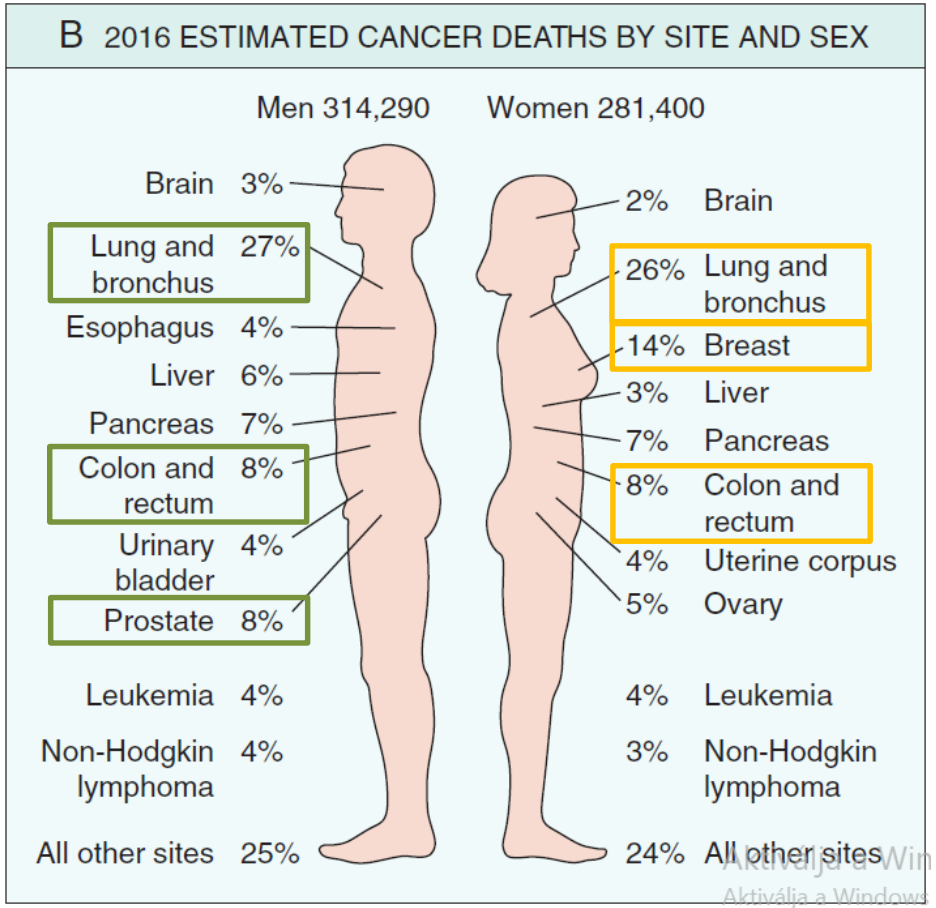


Cancer incidence & mortality in the US by site and sex

Incidence

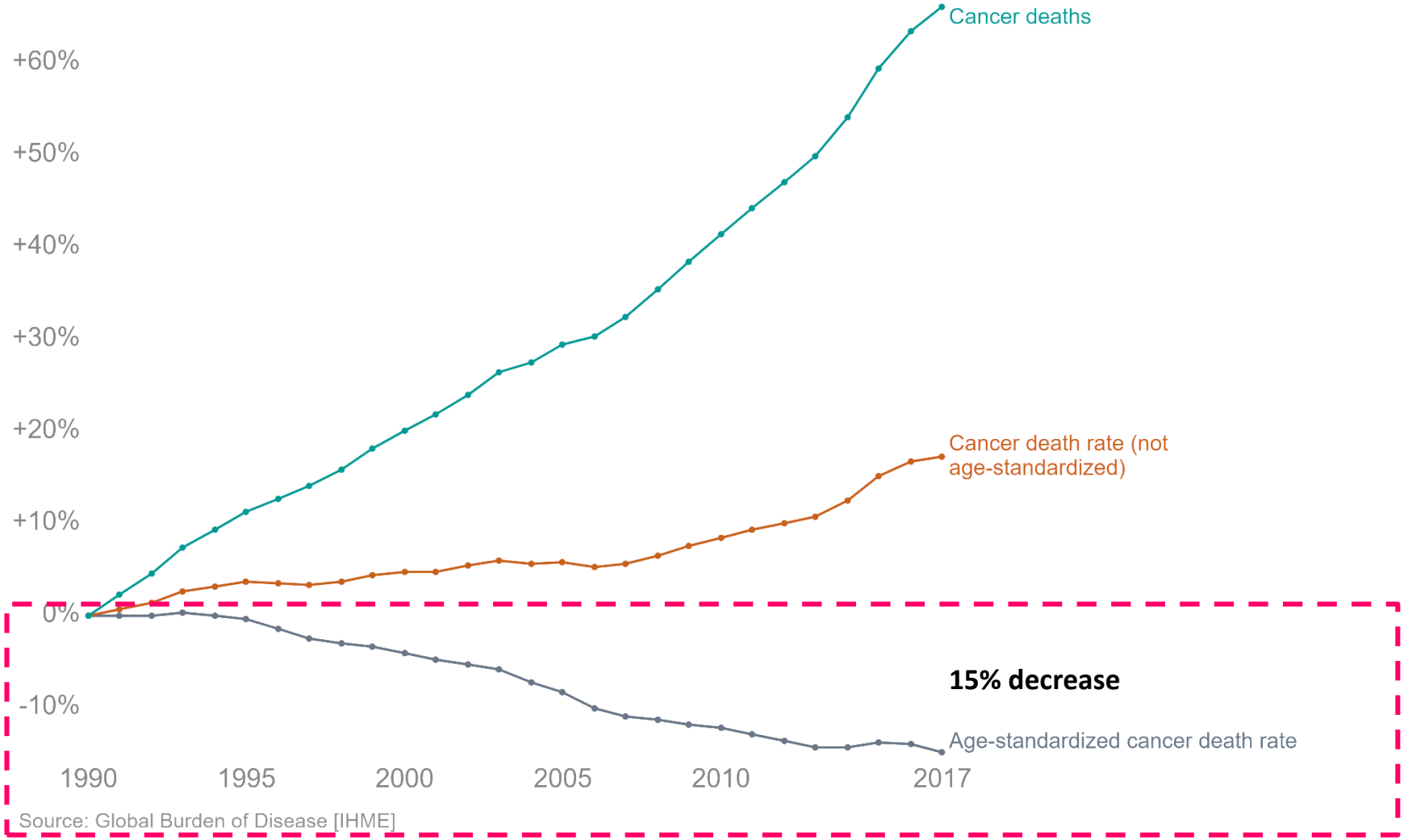


Mortality



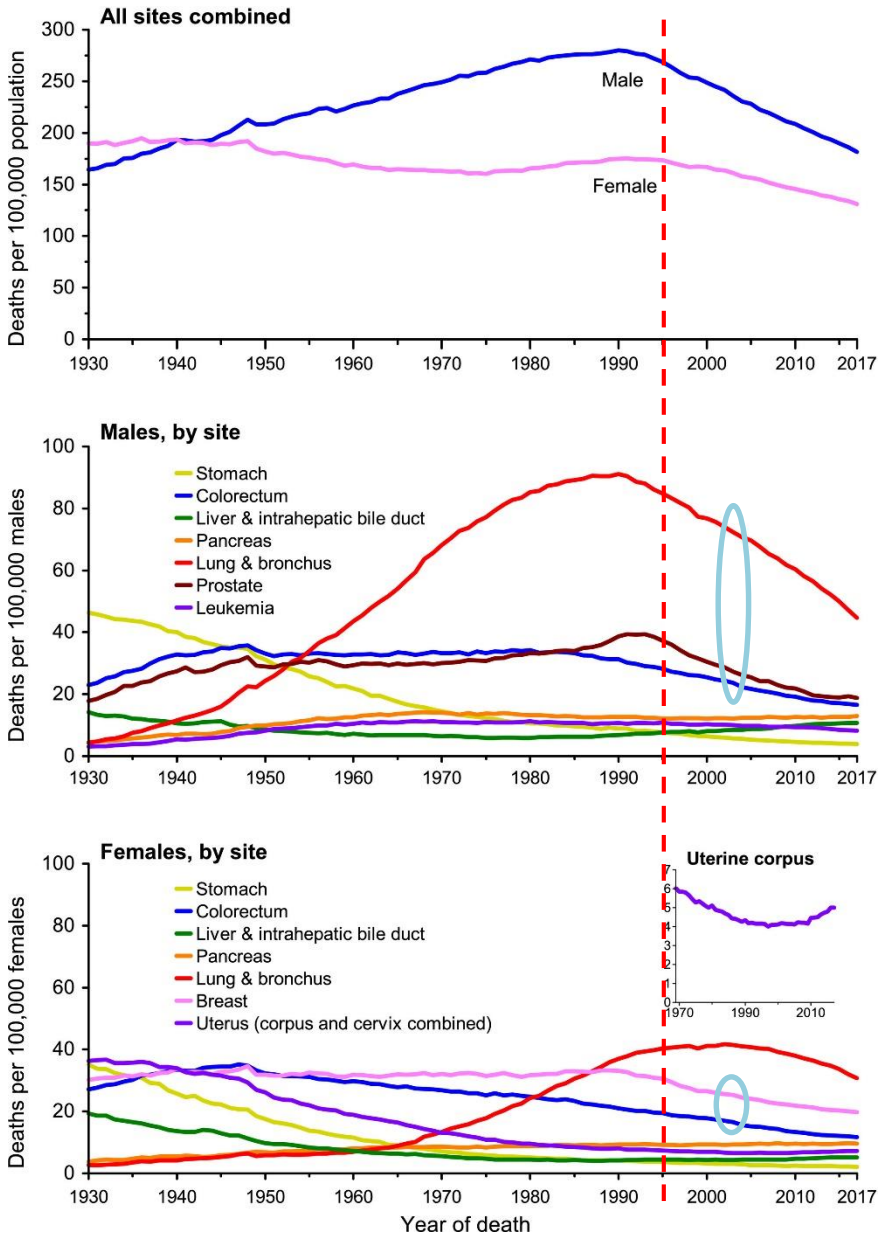
Adapted from Cancer facts & figures 2016. *American Cancer Society. www.cancer.org/research/cancer-facts-statistics/all-cancerfacts-figures/cancer-facts-figures-2016.html.*

Overall 15% decrease in age-standardized death rates



OurWorldInData.org/cancer • CC BY

Overall 15% decrease in death rates



~20% decrease in death rate

~10% decrease in death rate

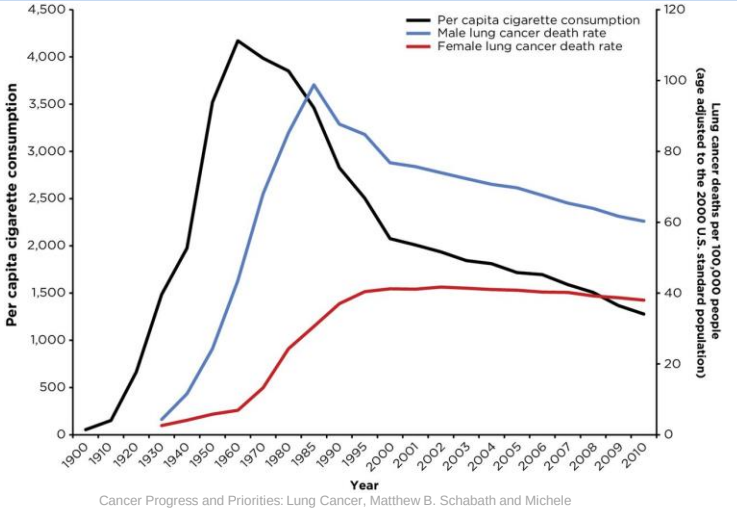
~80% - due to lower death rates for lung, prostate, and colon cancers

~60% - due to lower death rates for breast and colon cancers

CA: A Cancer Journal for Clinicians, Volume: 70, Issue: 1, Pages: 7-30, First published: 08 January 2020, DOI: (10.3322/caac.21590)

Causes of reduction in death rates

1. Decreased use of tobacco products → lung cancer



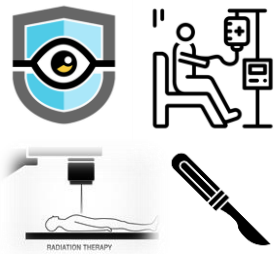
Cancer Progress and Priorities: Lung Cancer, Matthew B. Schabath and Michele L. Cote, Cancer Epidemiol Biomarkers Prev October 1 2019 (28) (10) 1563-1579

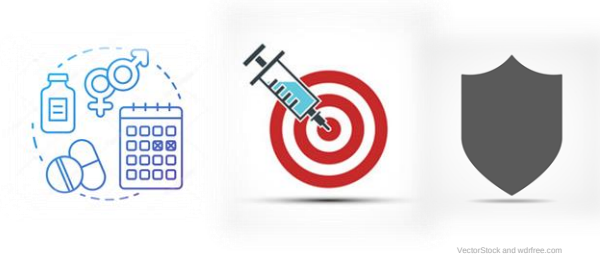
2. Improved detection and treatment → colorectal, breast and prostate cancer

https://columbiasurgery.org/conditions-and-treatments/colonoscopy

https://labblog.uofmhealth.org/health-tech/study-captures-importance-of-screening-mammography-for-women-breast-reconstructions

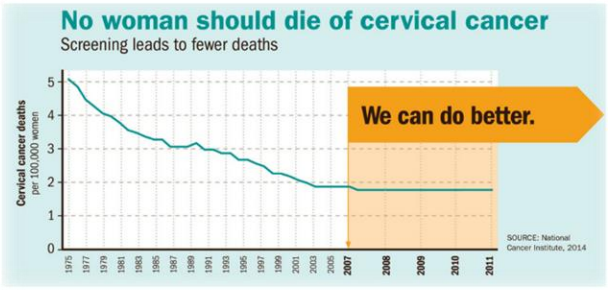
https://www.health.harvard.edu/blog/new-study-once-again-casts-doubt-on-psa-screening-201804063526





VectorStock and wdrfree.com

3. Use of the Papanicolaou smear test for early detection → cervical cancer



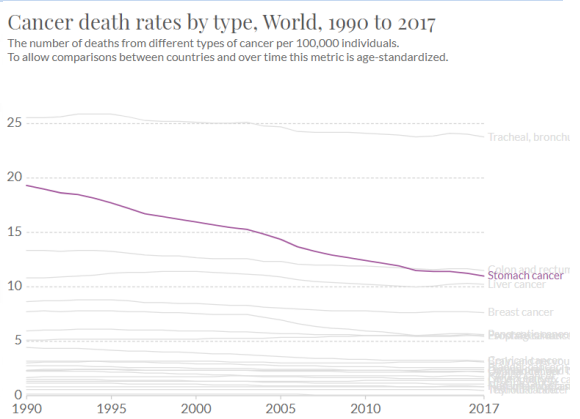
https://www.cdc.gov/vitalsigns/cervical-cancer/infographic.html

By Nephron - Own work, CC BY-SA 3.0,https://commons.wikimedia.org/w/index.php?curid=9084523

May nearly eliminate cervical cancer

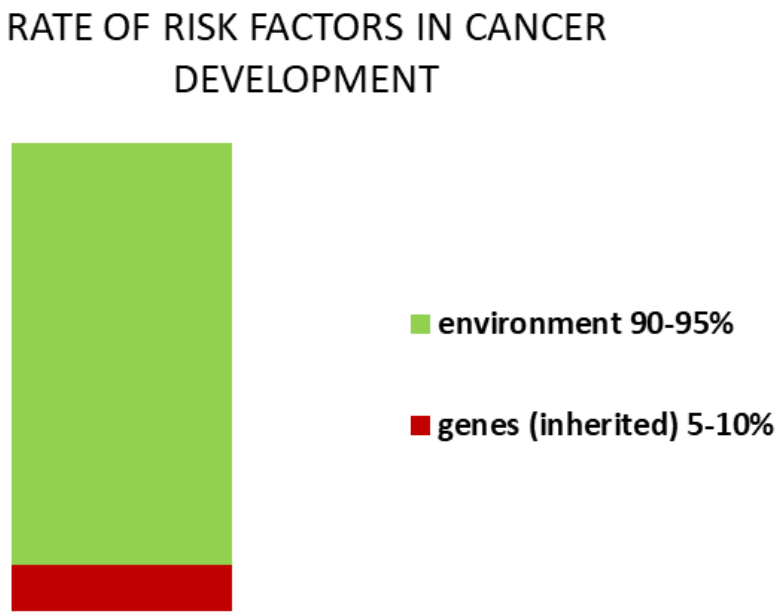
4. ? Decreasing exposure to unknown dietary carcinogens → gastric cancer

http://onedaycart.com/odcb/top-10-cancer-causing-foods.html

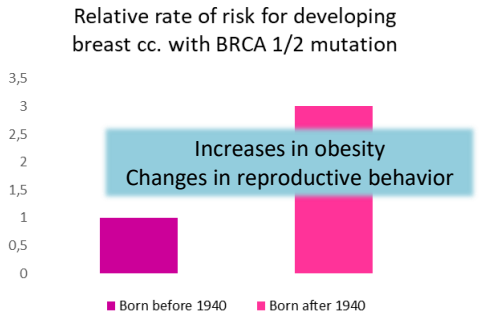


Environmental factors

- Include any cause that is not inherited genetically
- Dominant risk factors for many cancers

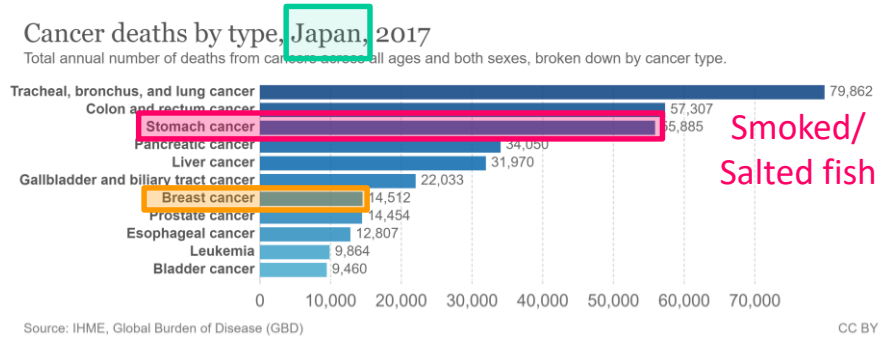


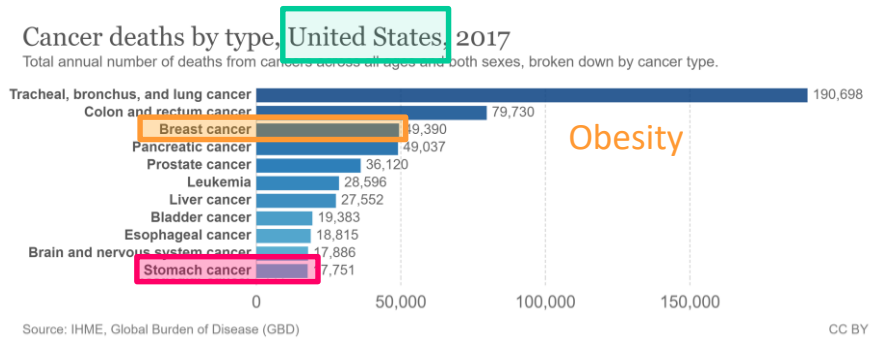
- A high fraction of cancers are potentially preventable
- The risk for developing cancer is modified by interactions between environmental exposures and genetic variants

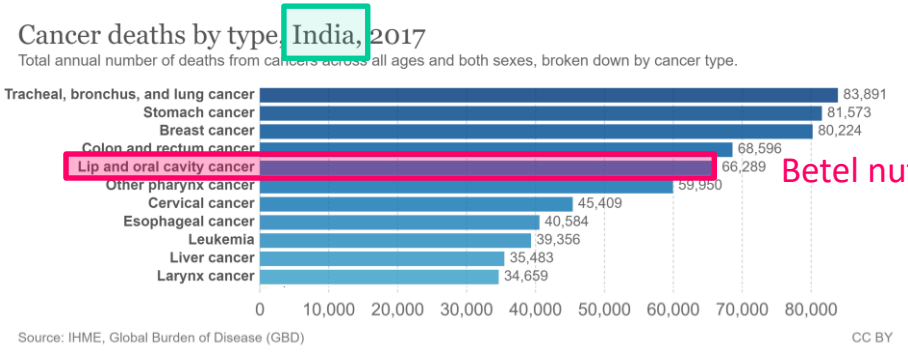


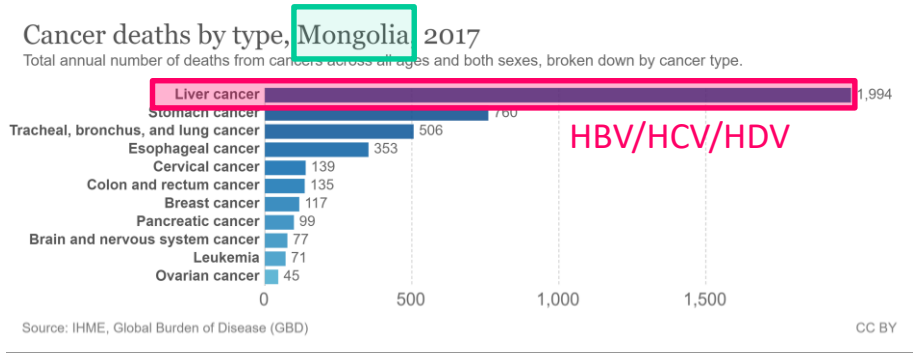
Environmental factors - Dominant risk factors

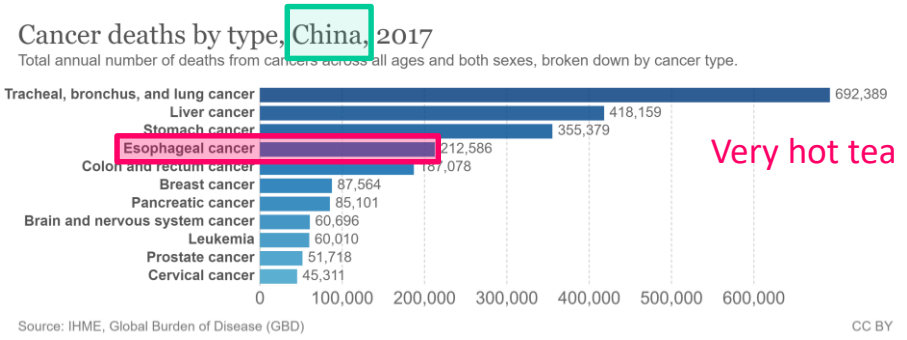
Supported by the geographic variation in death rates from specific forms of cancer

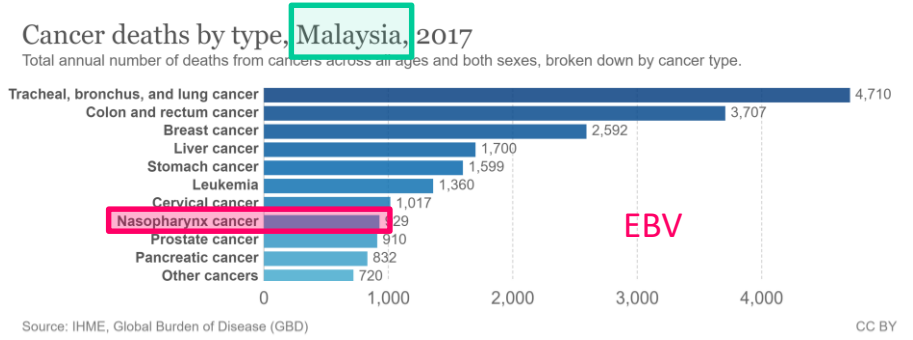










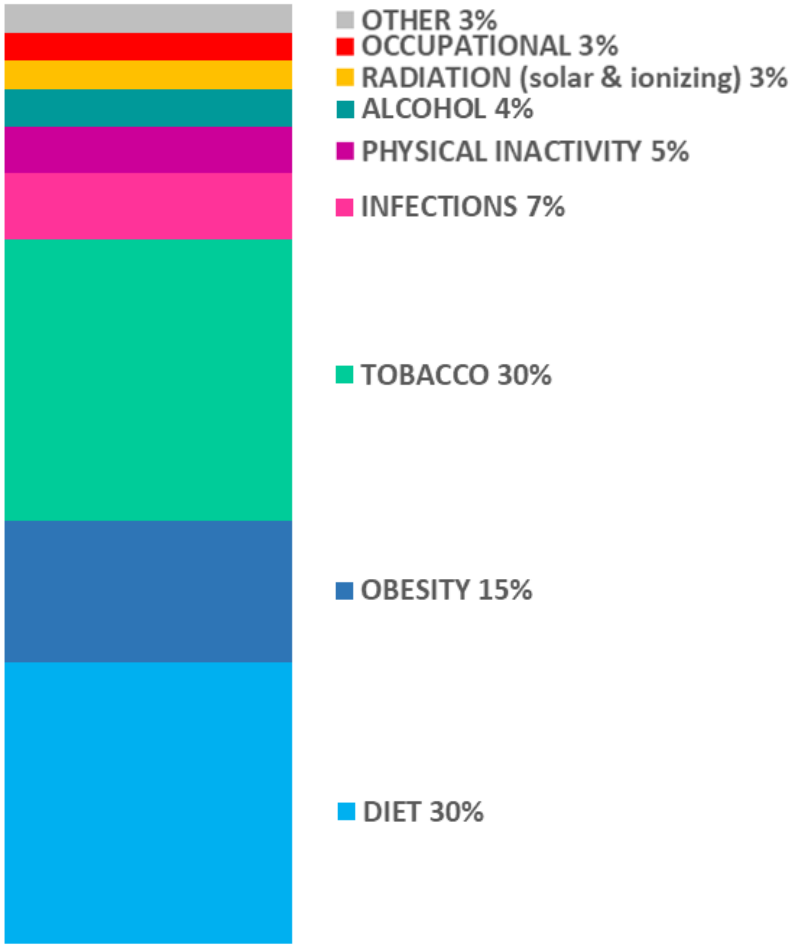


The most important environmental factors linked to cancer

- Diet
  - Obesity - a modestly increased risk for developing many different cancers
  - Low consumption of fruits and vegetables, red and processed meat consumption, low dietary fiber, salt
- Smoking
  - Cancers of the lung, mouth, pharynx, larynx, esophagus, pancreas and bladder
- Alcohol
  - Cancers of the oropharynx, larynx, esophagus and liver
- Reproductive history
  - Lifelong cumulative exposure to estrogen stimulation (if unopposed by progesterone) increases the risk for developing cancers of the endometrium and breast
- Infectious agents
  - Cause approximately 15% of cancers worldwide

Rate of different environmental factors in the development of cancer

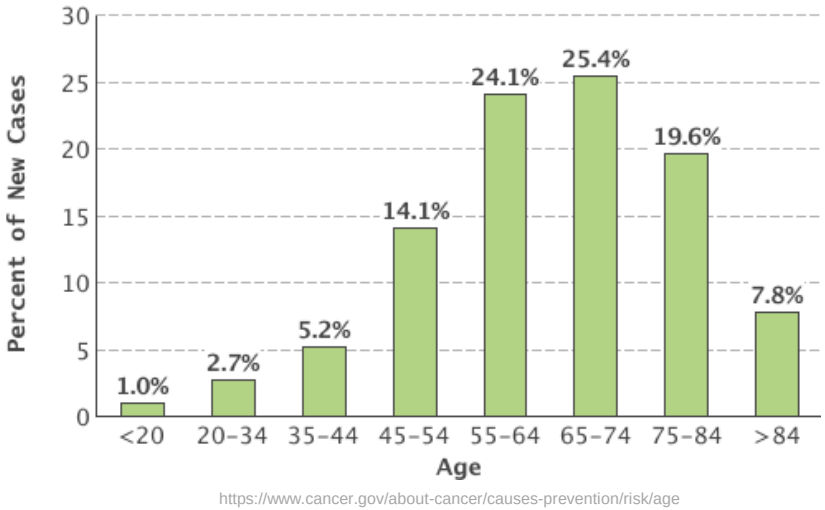
US data



Data from: https://doi.org/10.1146/annurev-publhealth-031912-114350

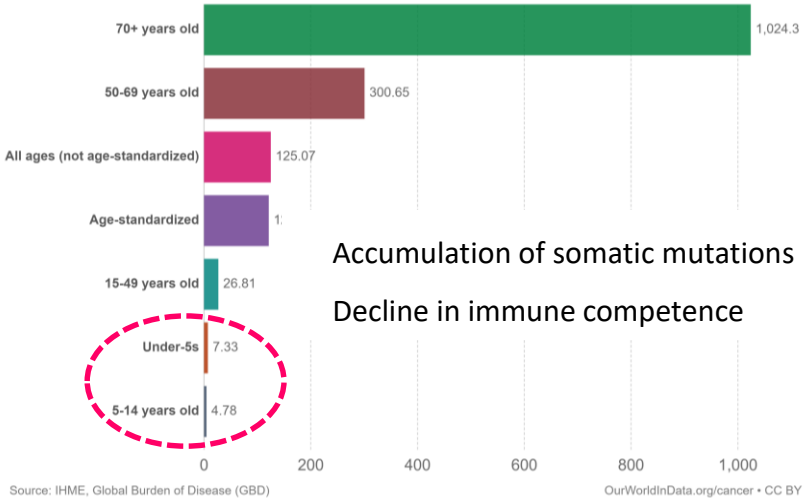
Age and cancer

The frequency of cancer increases with age



https://www.cancer.gov/about-cancer/causes-prevention/risk/age

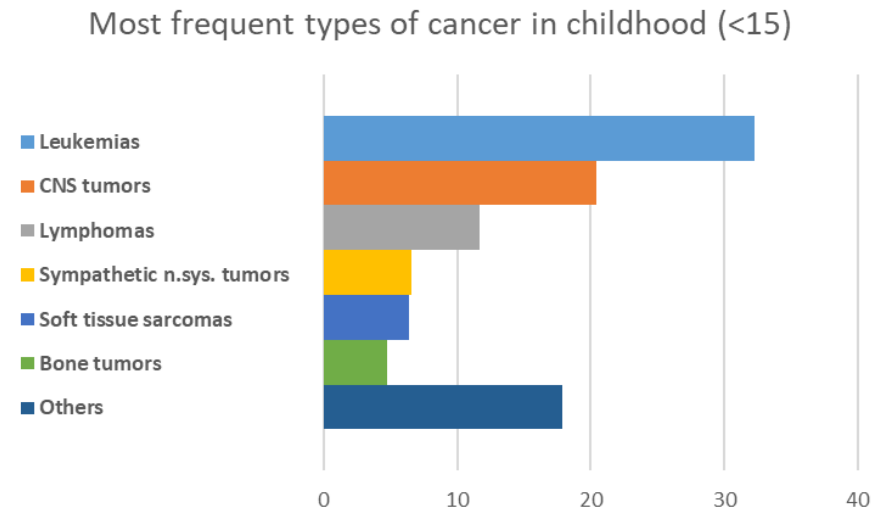
Most cancer deaths: 55-75 years of age

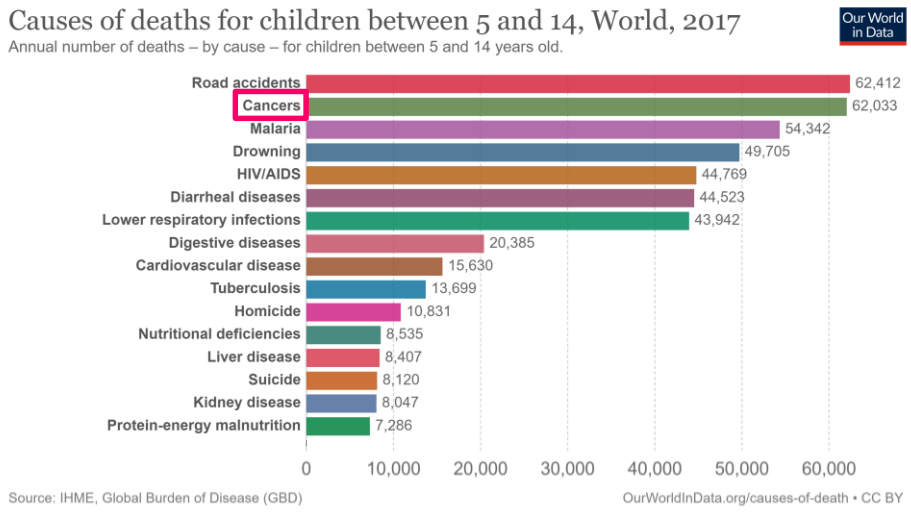


Accumulation of somatic mutations

Decline in immune competence

Cancer is responsible for ~10% of all deaths among children (<15 ys)

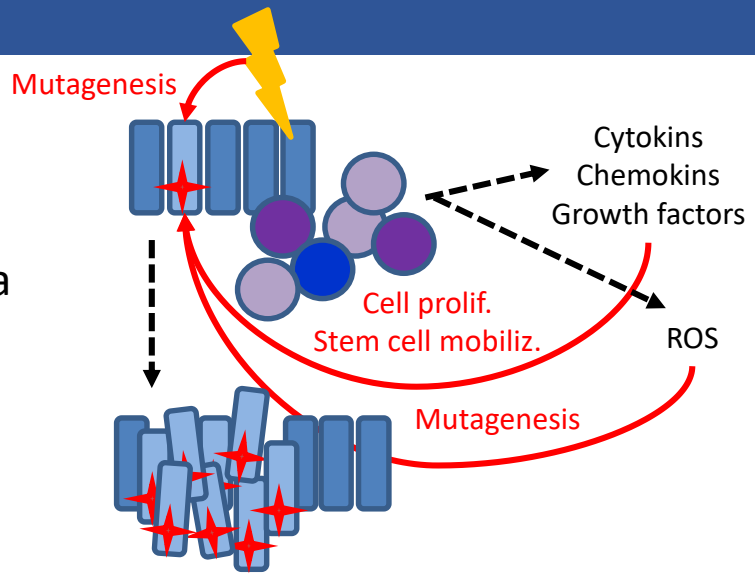




Acquired conditions that predispose to cancer

1. **Chronic inflammatory disorders**, e.g.:

- Inflammatory bowel disease → Colorectal carcinoma
- Gastritis / ulcers → Gastric adenocc., MALT lymphoma
- Viral hepatitis → Hepatocellular carcinoma
- Chronic pancreatitis → Pancreatic carcinoma
- Hashimoto thyreoiditis → MALT lymphoma



2. **Immunodeficiency states**, e.g.:

- EBV → NHL, HL
- HHV8 → Kaposi sarcoma
- HPV → Planocellular carcinoma

<u>Secondary IDs (90%)</u>
HIV, CMV, EBV
Lymphoma/Leukaemia
Prematurity/Old age
Drugs
Malnutrition
Diabetes
Splenectomy
Chronic renal disease

<u>Primary IDs (10%)</u>
Antibody deficiencies
Combined cellular & antibody deficiencies
Phagocytic cell deficiencies
Cellular deficiencies
Complement deficiencies

3. **Precursor lesions**

- Localized disturbances of (epithelial) cell differentiation
- Represent a stage in the multistep carcinogenesis
- May progress / be stable / regress
- Not all malignant tumors have precursor lesions

Lecture outline

1. Epidemiology of cancer

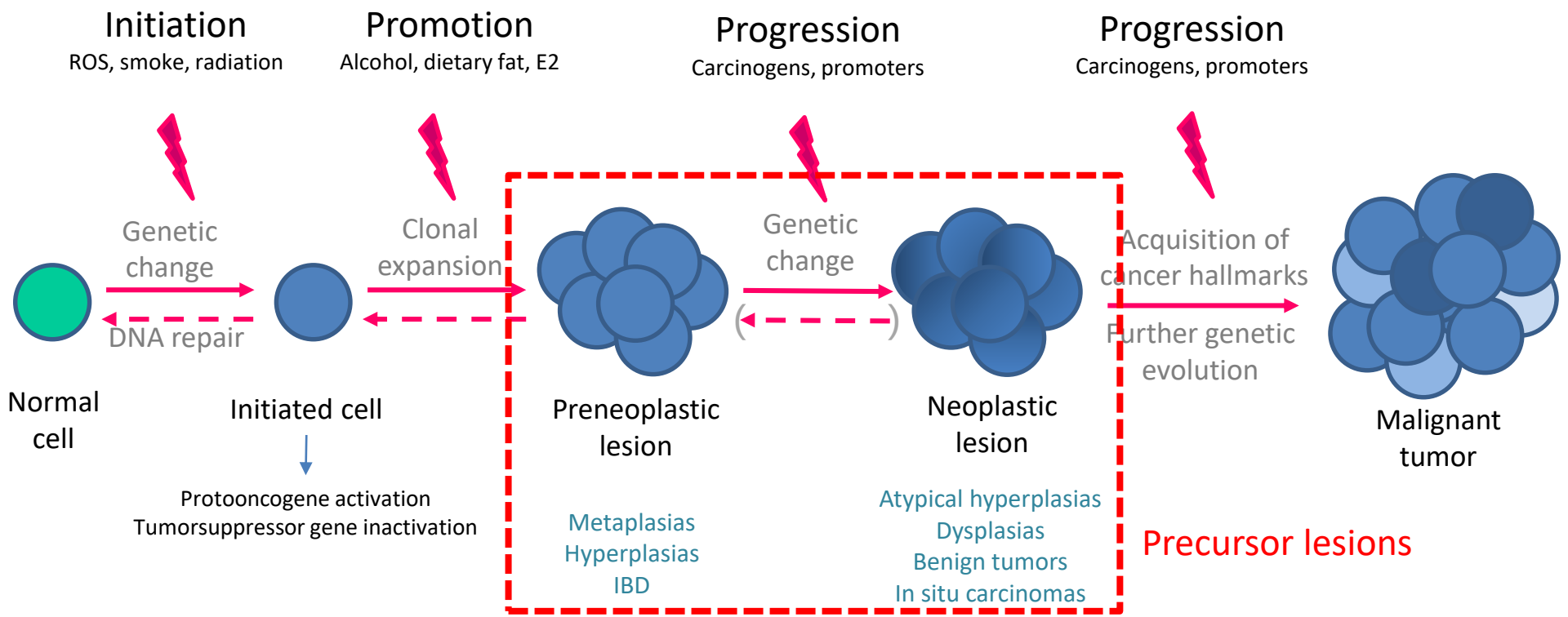
2. Preneoplastic disorders / precursor lesions

3. Effects of tumor on host

4. Grading and staging of cancer

Preneoplastic disorders / precursor lesions

- Preneoplastic = NOT neoplastic (not capable of autonomous growth), reversible
- Premalignant = precancerous = precursor lesions:
  - Preneoplastic lesions
  - Some benign tumors (different level of risk for malignant change)
    - colon adenoma - colon adenocarcinoma (up to 50%)
    - leiomyoma of the uterus - extremely rare malignant transformation
  - In situ carcinomas, dysplasias, atypical hyperplasias

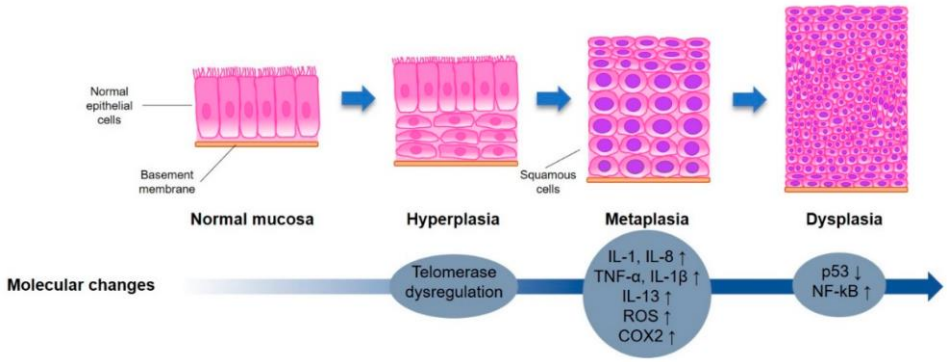


Precursor lesions

Organ	Precursor lesion	Malignant tumor
Lung	Squamous metaplasia and dysplasia	Squamous cell carcinoma
	Atypical adenomatous hyperplasia	Adenocarcinoma
Breast	Flat epithelial atypia (Chr. 1 gain, Vhr. 16 loss)	
	Atypical ductal hyperplasia (ADH) (Chr. 1 gain, Vhr. 16 loss, PIK3CA mut.)	
	Ductal carcinoma in situ (DCIS) (Chr. 1 gain, Vhr. 16 loss, PIK3CA mut.)	Invasive (ductal) carcinoma ER+ HER2 - (Chr. 1 gain, Vhr. 16 loss, PIK3CA mut.)
	Atypical apocrine adenosis (TP53 mut. HER2 amplif.) → DCIS (TP53 mut. HER2 amplif.)	Invasive (ductal) carcinoma HER2 + (TP53 mut. HER2 amplif.)
	? → DCIS (TP53 mut. BRCA inactivation)	Invasive (ductal) carcinoma ER-, HER2 - (TP53 mut. BRCA inactivation)
	Atypical lobular hyperplasia (ALH)	
	Lobular carcinoma in situ (LCIS)	Invasive lobular carcinoma
Prostate	High-grade prostatic intraepithelial neoplasia (HG-PIN)	Adenocarcinoma
Colon	Adenomas	Adenocarcinoma
	Serrated adenomas	Serrated adenocarcinoma
Stomach	Chronic gastritis (H. pylori) → atrophy → intestinal metaplasia → dysplasia	Intestinal type adenocarcinoma
	Adenoma	Intestinal type adenocarcinoma
	Inflammatory and hyperplastic polyps with dysplasia	Intestinal type adenocarcinoma
Bladder	Noninvasive papillary tumor	Invasive urothelial carcinoma
	Urothelial carcinoma in situ	Invasive urothelial carcinoma
Uterus	Endometrial hyperplasia and dysplasia (E2↑)	Endometrioid endometrial carcinoma
	Serous intraepithelial carcinoma (TP53 mut.)	Invasive serous carcinoma (TP53 mut.)
Uterine cervix	Cervical intraepithelial neoplasia (CIN) / Squamous intraepithelial lesion (SIL) (HPV)	Squamous cell carcinoma
Oral cavity	Leukoplakia	Squamous cell carcinoma
	Erythroplakia	Squamous cell carcinoma
Esophagus	Barrett esophagus	Adenocarcinoma
Liver	HBV-induced chronic liver disease (cirrhosis) → high-grade dysplastic nodules	Hepatocellular carcinoma
	Alcoholic liver disease (cirrhosis) → high-grade dysplastic nodules	Hepatocellular carcinoma
	Adenoma	Hepatocellular carcinoma
Pancreas	Pancreatic intraepithelial neoplasia (PanIN).	Adenocarcinoma
	Mucinous cystic neoplasms	Adenocarcinoma
	Intraductal Papillary Mucinous Neoplasms (IPMN) (GNAS mut.)	Adenocarcinoma (Colloid adenocc.)
Kidney	Nephrogenic rests	Wilms tumor
Vulva	Vulvar intraepithelial neoplasia (VIN) (HPV) (Leukoplakia)	Squamous cell carcinoma (poorly differentiated)
	Differentiated vulvar intraepithelial neoplasia (dVIN) (Leukoplakia)	Squamous cell carcinoma (well-differentiated, keratinizing)
Vagina	Vaginal intraepithelial neoplasia (VAIN) (HPV)	Squamous cell carcinoma
	Vaginal adenosis	Clear cell adenocarcinoma
Penis	Penile intraepithelial neoplasia (PeIN) (Bowen disease, in situ carcinoma) (HPV)	Squamous cell carcinoma
	Leukoplakia (HPV)	Squamous cell carcinoma
Ovarium	Benign and borderline serous/mucinous tumors	Low-grade serous carcinomas (KRAS mut.)/Mucinous carcinoma (KRAS mut.)
	Serous tubal intraepithelial carcinoma (STIC) (TP53 mut.)	High-grade serous carcinomas (TP53 mut.)
	Benign and borderline endometrioid tumors, endometriosis	Endometrioid carcinoma (PTEN mut.)
Fallopian tube	Serous tubal intraepithelial carcinoma (STIC) (TP53 mut.)	Invasive serous carcinoma (TP53 mut.)
Testis	Germ cell neoplasia in situ (Chr. 12 aberrations)	Germ cell tumors (Chr. 12 aberrations)
Bone marrow	Clonal hematopoieis of indeterminant prognosis (CHIP)	Acute myeloid leukemia
	CHIP → Myelodysplastic syndromes (MDS)	Acute myeloid leukemia
Bone	Paget disease	Osteosarcoma
Skin	Actinic keratosis (TP53 mut)	Squamous cell carcinoma (TP53 mut)
Salivary gland	Pleomorphic adenoma	Carcinoma ex pleomorphic adenoma (malignant mixed tumor)
Peripheral nerve	Plexiform neurofibroma	Malignant peripheral nerve sheath tumor

Lung – squamous metaplasia and dysplasia

- Smoking (and other environmental factors)
- Nearly linear correlation between the frequency of lung cancer and pack-years of cigarette smoking

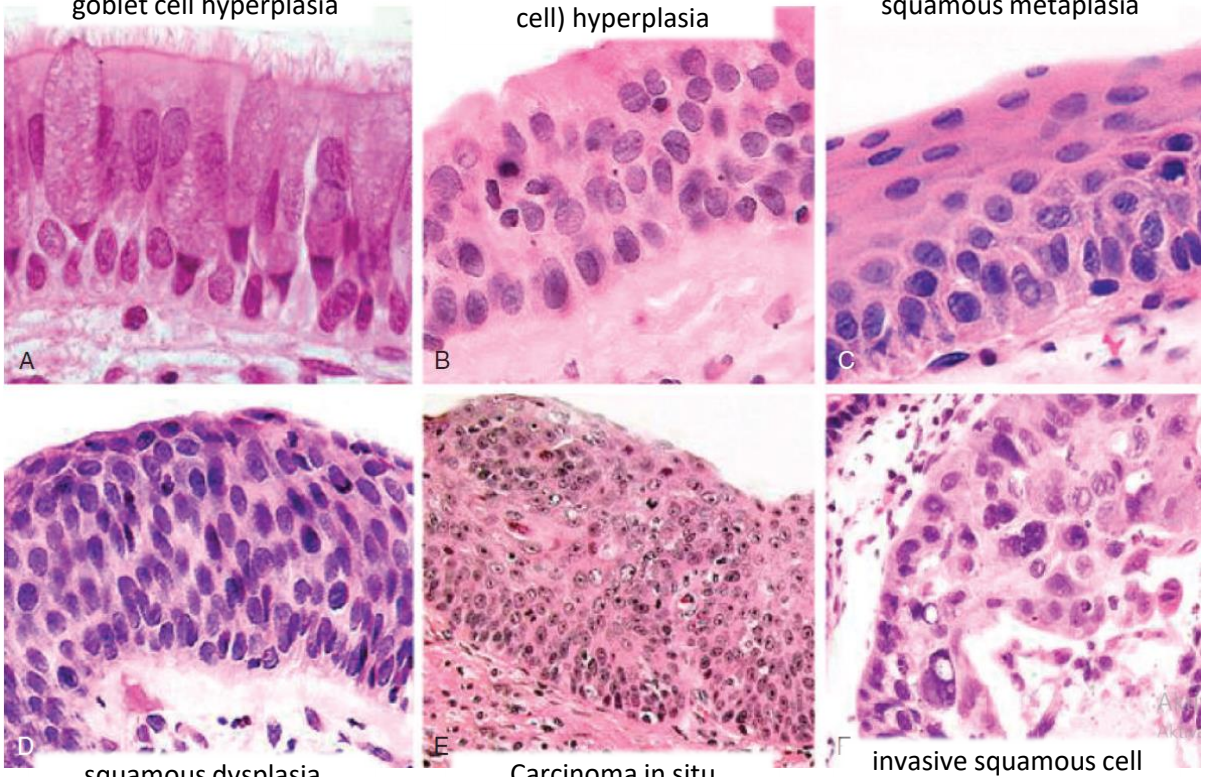


Cancers 2020, 12(5), 1265; https://doi.org/10.3390/cancers12051265

goblet cell hyperplasia

basal cell (or reserve cell) hyperplasia

squamous metaplasia



squamous dysplasia

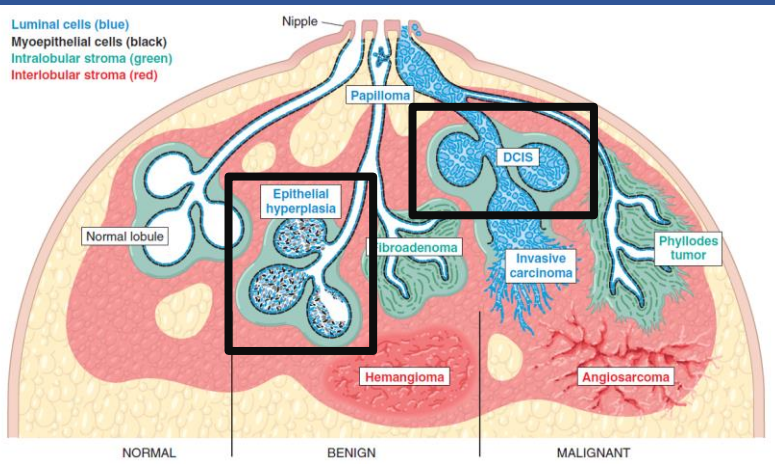
Carcinoma in situ

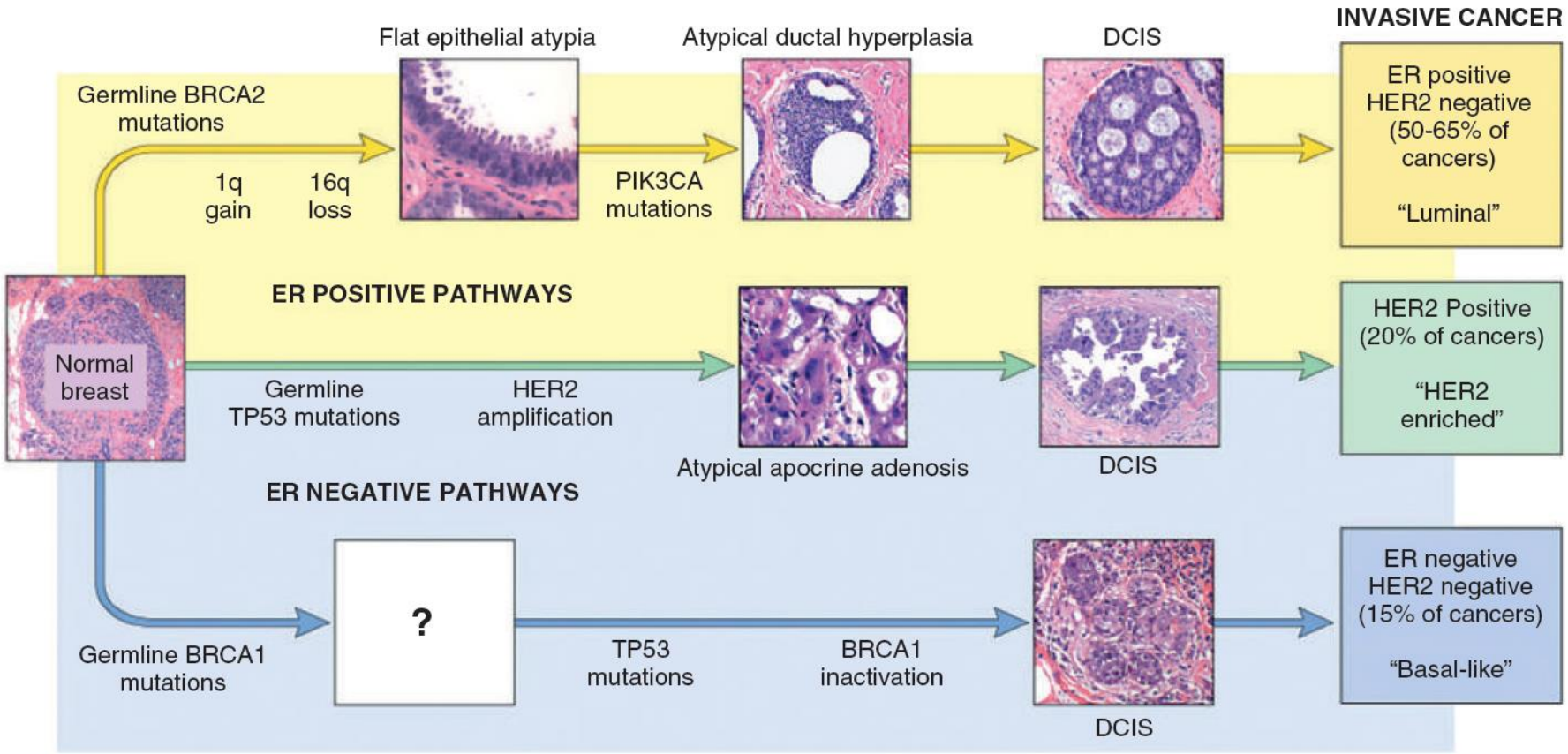
invasive squamous cell carcinoma

(A to E, Courtesy of Dr. Adi Gazdar, Department of Pathology, University of Texas Southwestern Medical School, Dallas, Texas. F, Reproduced with permission from Travis WD, Colby TV, Corrin B, et al, editors: World Health Organization histological typing of lung and pleural tumors, *Heidelberg, 1999, Springer.)*

Breast – DCIS (and FEA, ADH, AAA)

- Hormonal factors (E2 excess) and inherited susceptibility (BRCA 1 / 2 mutation)

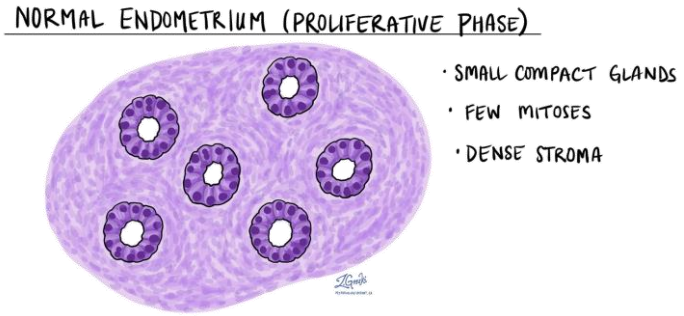




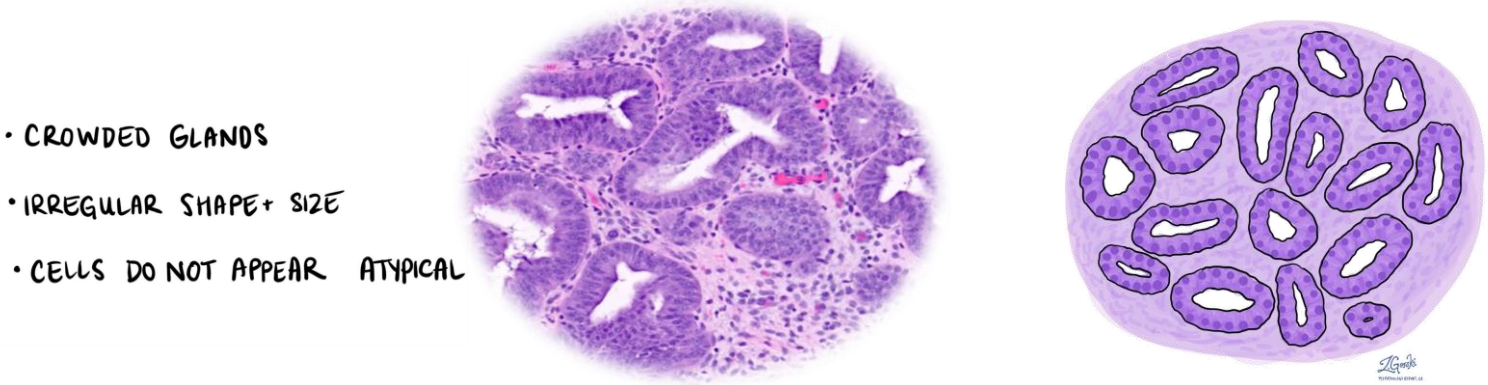
Robbins, Basic Pathology, 10th e. Elsevier

Uterus – endometrial hyperplasia & dysplasia

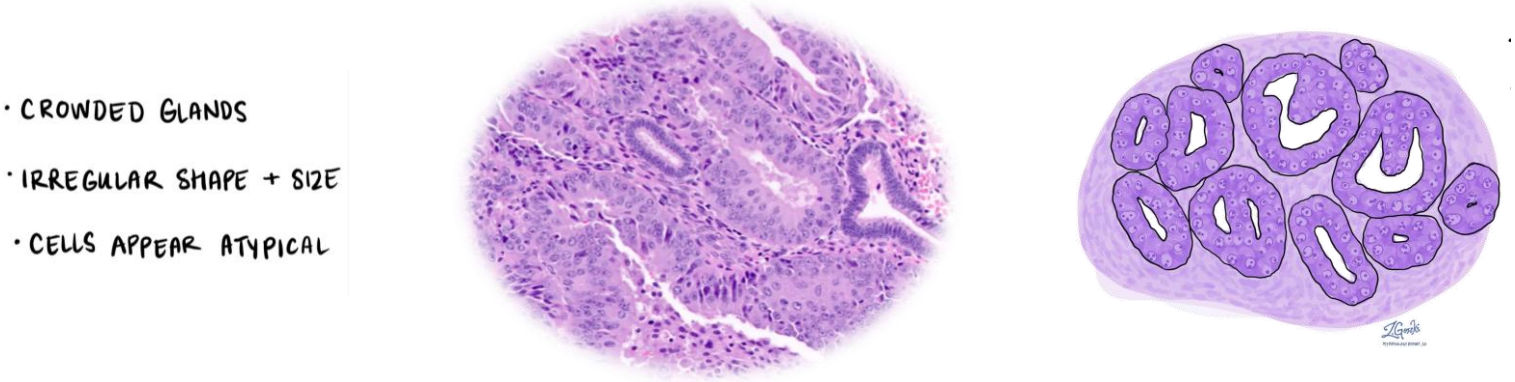
- Estrogen excess (obesity, failure of ovulation, prolonged admin. of estrogenic steroids without counterbalancing progestin, estrogen producing ovarian lesions: PCO, granulosa-theca cell tumors).



Hyperplasia without atypia – low risk



Hyperplasia with atypia (= endometrial intraepithelial neoplasia, EIN) – high risk



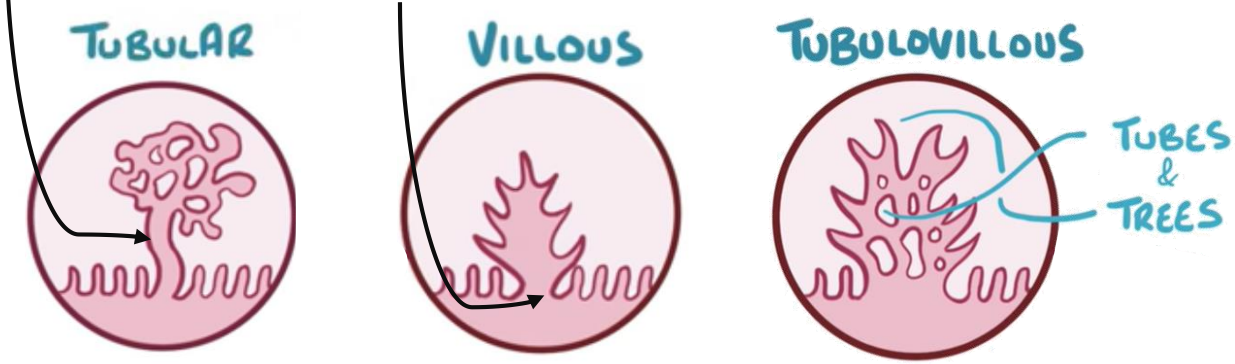
Colon – Adenomas

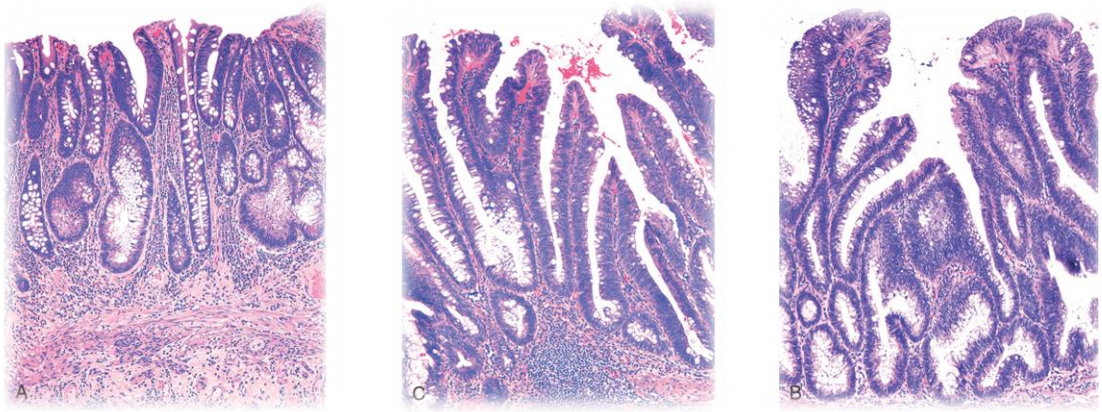
- Villous and sessile polyps more often show malignant transformation
- Size and high-grade dysplasia shows better association with malignant transf.

Adenomatous polyps

Pedunculated (has stalk)

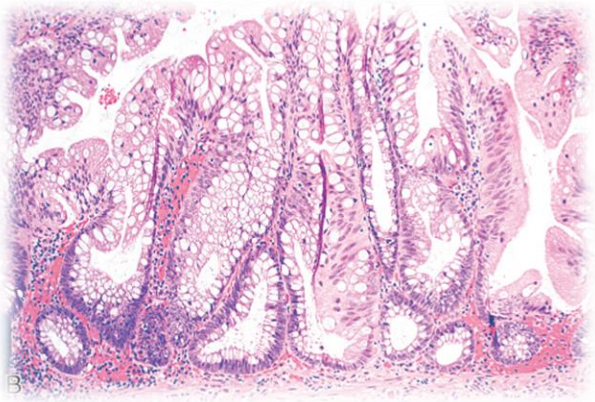
Sessile (firmly attached)





Serrated polyps

Hyperplastic polyps
Sessile serrated adenoma
Traditional serrated adenoma
Mixed



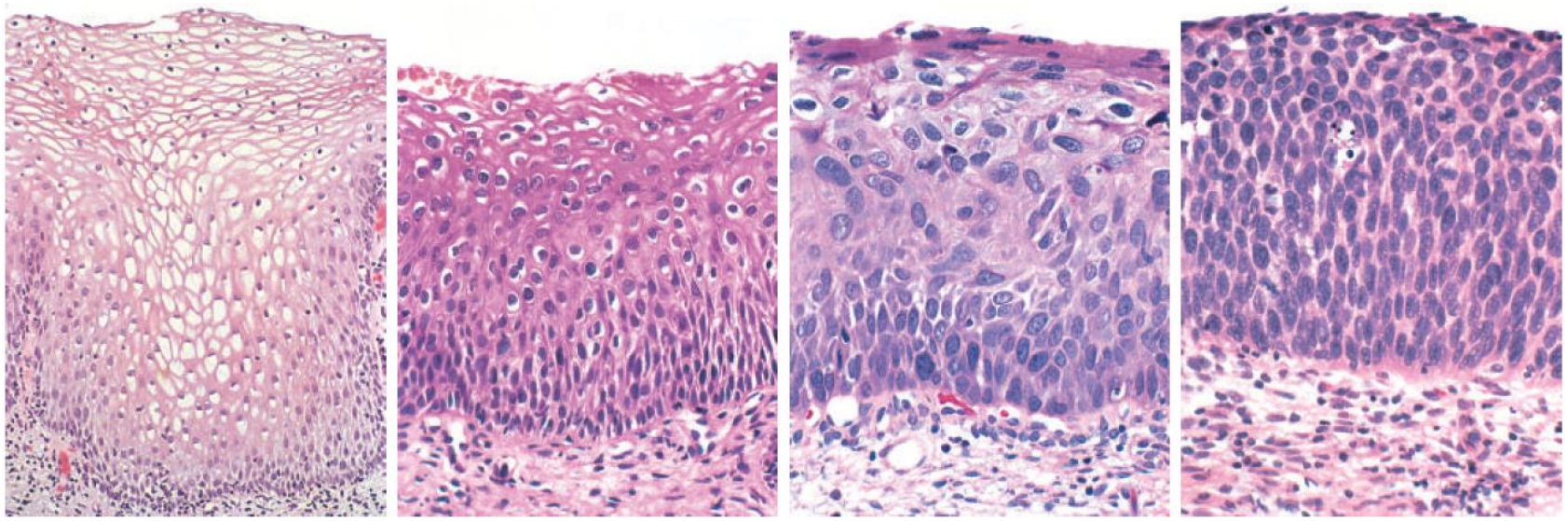
Cervix – SIL / CIN

- HPV (high risk, e.g. 16, 18)
- Formerly – Cervical intraepithelial neoplasm I-III
- At present – Low-grade / High-grade **squamous intraepithelial lesion**

Natural history of SILs

Lesion	Regress	Persist	Progress
LSIL (CIN I)	60%	30%	10% (to HSIL)
HSIL (CIN II, III)	30%	60%	10% (to carcinoma)[a]

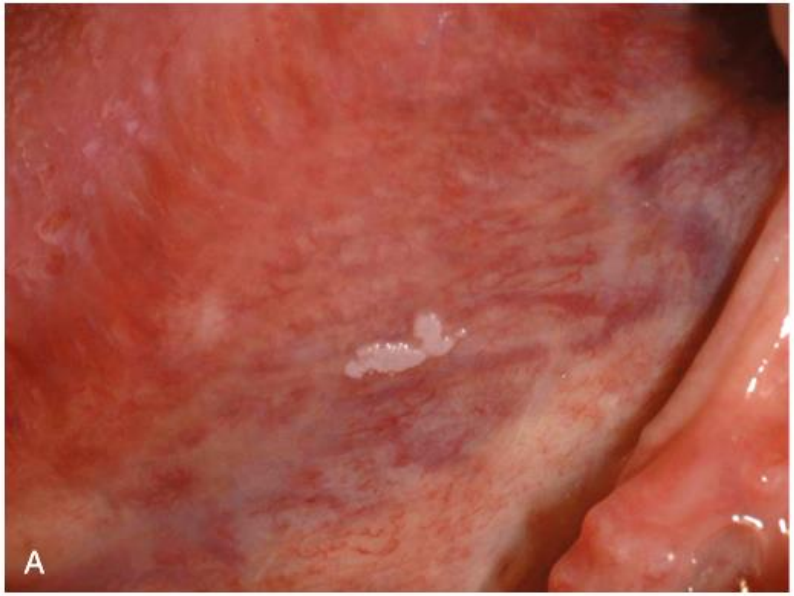
[a]Progression within 10 years.
LSIL, Low-grade SIL; HSIL, high-grade SIL.

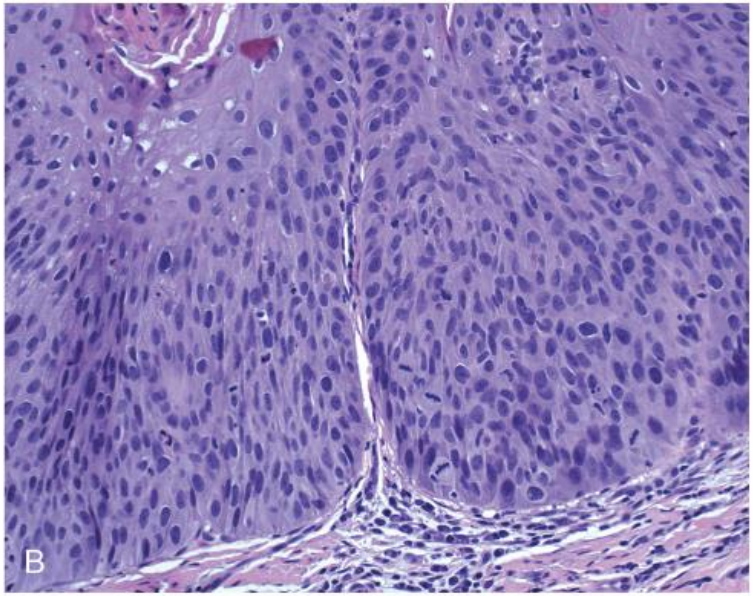


Robbins, Basic Pathology, 10th e. Elsevier

Oral cavity, vulva, penis – Leukoplakia

- A white patch or plaque that cannot be scraped off and cannot be characterized clinically or pathologically as any other disease
- Tobacco use / HPV are the most common risk factors
- Hyper- /parakeratosis, basal cell hyperplasia, and dysplastic epithelium in a proportion of cases (biopsy!)





Inherited syndromes that predispose to cancer

Inherited Predisposition	Gene(s)	Malignant tumor(s)
Autosomal Dominant Cancer Syndromes		
Retinoblastoma	*RB*	Retinoblastoma
Li-Fraumeni syndrome (various tumors)	*TP53*	Breast cc, sarcomas, glioblastoma, leukemia, lymphoma, adrenocortical
Melanoma	*CDKN2A*	Melanoma
Familial adenomatous polyposis/colon cancer	*APC*	Colon adenocarcinoma
Neurofibromatosis 1 and 2	*NF1, NF2*	MPNST, glioma, leukemia
Breast and ovarian tumors	*BRCA1, BRCA2*	Breast and ovarian carcinomas
Multiple endocrine neoplasia 1 and 2	*MEN1, RET*	Pit, parathy, pancr, phaeochr, medull
Hereditary nonpolyposis colon cancer	*MSH2, MLH1, MSH6*	Colon adenocarcinoma
Nevoid basal cell carcinoma syndrome	*PTCH1*	Basal cell carcinoma, medullobl.
Autosomal Recessive Syndromes of Defective DNA Repair		
Xeroderma pigmentosum	Diverse genes involved in nucleotide excision repair	Basal cell carcinoma, squamous cell carcinoma, melanoma
Ataxia-telangiectasia	*ATM*	Leukemia, lymphoma, breast cc
Bloom syndrome	*BLM*	Wide variety of cancer types
Fanconi anemia	Diverse genes involved in repair of DNA cross-links	Leukemia, MDS, liver cc and other solid tumors

Lecture outline

1. Epidemiology of cancer

2. Preneoplastic disorders / precursor lesions

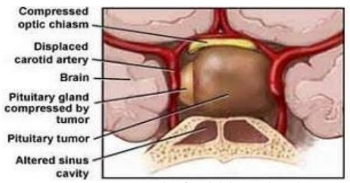
3. Effects of tumor on host

4. Grading and staging of cancer

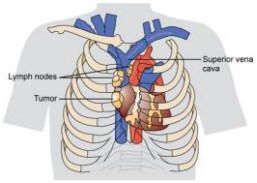
Effects of tumor on host

1. Local effects – location is crucial for both benign & malignant neoplasms

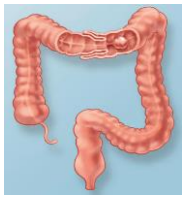
- Mass effect
  - Compression
  - Mechanical obstruction
    - ➢ infarction
- Tissue destruction
- Uceration → bleeding, secondary infection

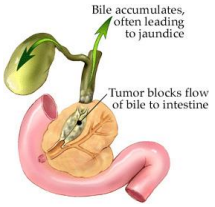


Mayo Foundation for Medical Education and Research.

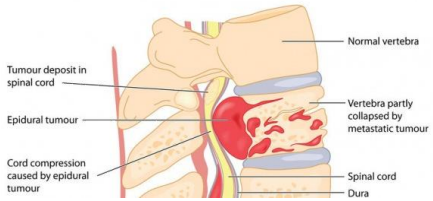


https://littlefighterscancertrust.wordpress.com/side-effects-of-childhood-cancer/superior-vena-cava-syndrome-in-childhood-cancer/

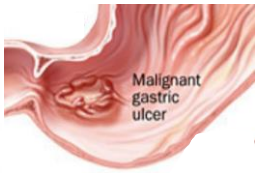

https://samadimd.com/common-diseases/what-is-intussusception



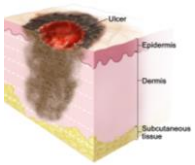
http://www.uhnj.org/specialized_services/livertransplant/html/liverandliverdiseases/treatoptions.htm



123rf.com

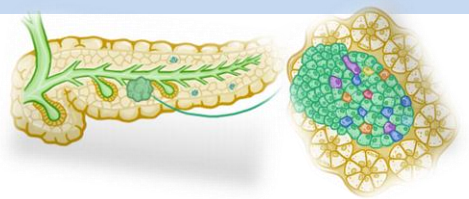


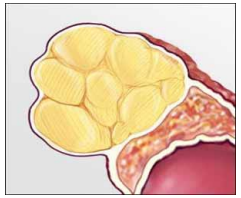
https://www.hopkinsmedicine.org/gastroenterology_hepatology/_pdfs/esophagus_stomach/peptic_ulcer_disease.pdf



2. Systemic effects

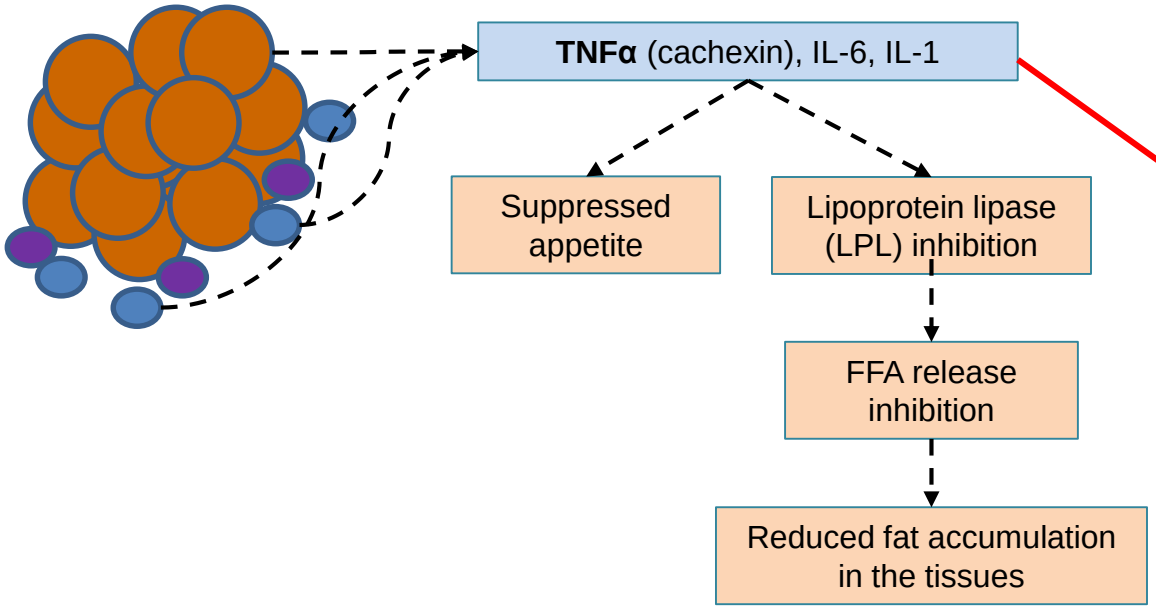
- Hormonal effects (more likely with benign tu.)
  - Endocrine gland tumors (e.g. Pituitary adenomas, Islets of Langerhans tu. = insulinoma, Adrenocortical tu.)
- Cachexia
- Paraneoplastic syndromes

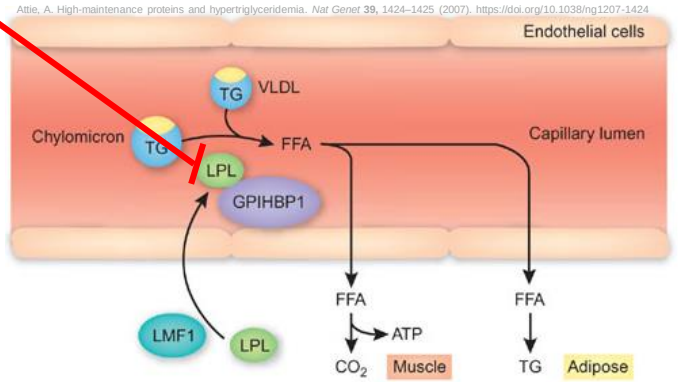

https://www.youtube.com/watch?v=_A6GbgUnEZc


https://speciality.medicaldialogues.in/rare-case-of-boy-with-adrenal-adenoma-presenting-as-ventricular-tachycardia-a-report/?infinitescroll=1

Cachexia – Greek, *kakos* = bad things & *hexis* = state of being

- Progressive loss of body mass (skeletal muscle & fat)
- Profound weakness, anorexia, and anemia
- Pathogenesis – not fully understood
  - Reduced food intake
  - Complex metabolic aberrations: elevated energy expenditure, excess catabolism and inflammation





- No satisfatory treatment (only to remove the tumor)
- Cancer cachexia is now considered a systemic paraneoplastic phenomenon

Paraneoplastic syndromes

- Symptom complexes of cancer patients (10-15%) NOT related to local or metastatic expansion of the tumor, or hormonal elaboration of endocrine gland tumors
- May represent the earliest manifestation of an occult neoplasm
- May be associated with significant clinical illness / be lethal.

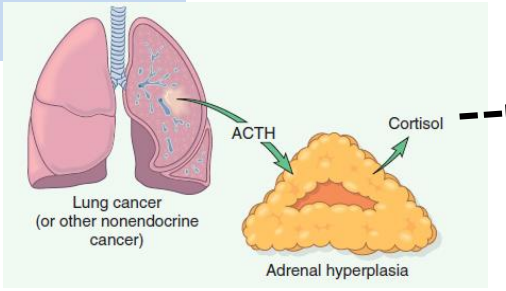
Clinical Syndrome	Major Forms of Neoplasia	Causal Mechanism(s)/Agent(s)
Endocrinopathies		
Cushing syndrome	Small cell carcinoma of lung Pancreatic carcinoma Neural tumors	ACTH or ACTH-like substance
Syndrome of inappropriate anti-diuretic hormone secretion	Small cell carcinoma of lung; intracranial neoplasms	Anti-diuretic hormone or atrial natriuretic hormones
Hypercalcemia	Squamous cell carcinoma of lung Breast carcinoma Renal carcinoma Adult T cell leukemia/lymphoma	Parathyroid hormone–related protein, TGF-α
Hypoglycemia	Fibrosarcoma Other mesenchymal sarcomas Ovarian carcinoma	Insulin or insulin-like substance
Polycythemia	Renal carcinoma Cerebellar hemangioma Hepatocellular carcinoma	Erythropoietin
Nerve and Muscle Syndrome		
Myasthenia	Bronchogenic carcinoma, thymoma	Immunologic
Disorders of the central and peripheral nervous systems	Breast carcinoma, teratoma	Immunologic
Dermatologic Disorders		
Acanthosis nigricans	Gastric carcinoma Lung carcinoma Uterine carcinoma	Immunologic; secretion of epidermal growth factor
Dermatomyositis	Bronchogenic and breast carcinoma	Immunologic
Osseous, Articular, and Soft-Tissue Changes		
Hypertrophic osteoarthropathy and clubbing of the fingers	Bronchogenic carcinoma	Unknown
Vascular and Hematologic Changes		
Venous thrombosis (Trousseau phenomenon)	Pancreatic carcinoma Bronchogenic carcinoma Other cancers	Tumor products (mucins that activate clotting)
Nonbacterial thrombotic endocarditis	Advanced cancers	Hypercoagulability
Anemia	Thymoma	Immunologic
Others		
Nephrotic syndrome	Various cancers	Tumor antigens, immune complexes

Mnemonic:
MEN DOVVN

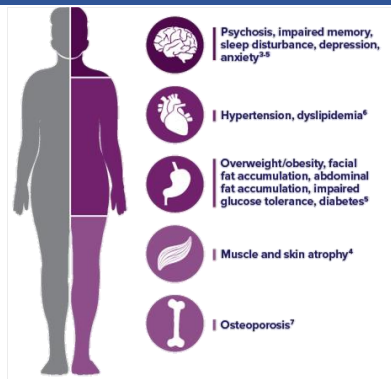
Endocrinopathies & Muscle syndrome

1. Cushing syndrome - ACTH

- Small cell lung carcinoma
- Pancreatic neuroendocrine tumors
- Pheochromocytoma
- Thyroid medullary carcinoma



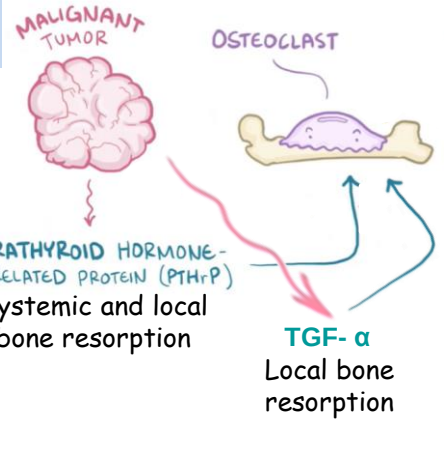
Robbins, Basic Pathology, 10th e. Elsevier

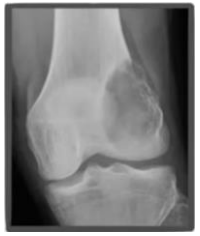


https://www.strongbridgebio.com/therapeutic-focus/endogenous-cushings-syndrome/

2. Hypercalcemia – PTH-related protein, TGF-α

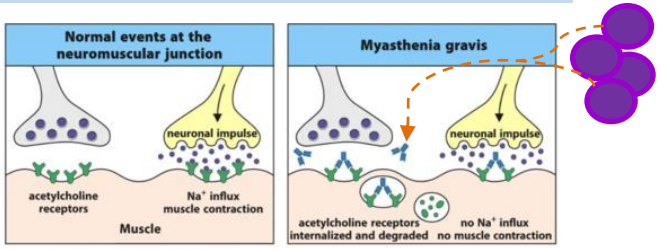
- Squamous cell lung carcinoma
- Breast carcinoma
- Renal cell carcinoma
- Adult T-cell leukemia / lymphoma

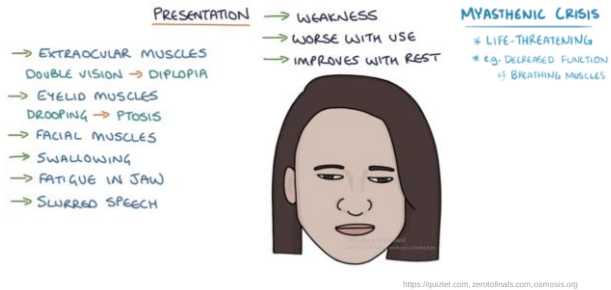




3. Myasthenia – Postsynaptic acetylcholine receptor (AChR) antibody

- Lung carcinoma
- Thymoma



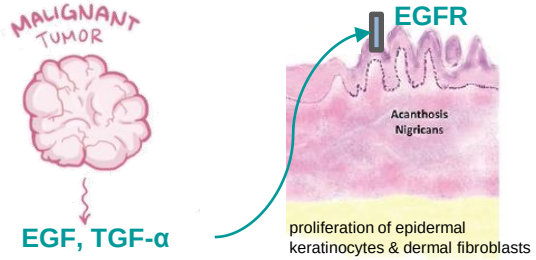


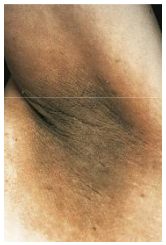
https://quizlet.com, zerotofinals.com, osmosis.org

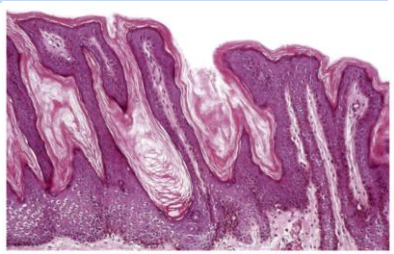
Dermatologic & Osseus & Vascular-Hematologic

1. Acanthosis nigricans – EGF, TGF-α

- Gastric carcinoma
- Lung carcinoma
- Uterine carcinoma



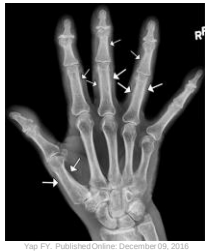




McKee's Pathology of the skin, Elsevier

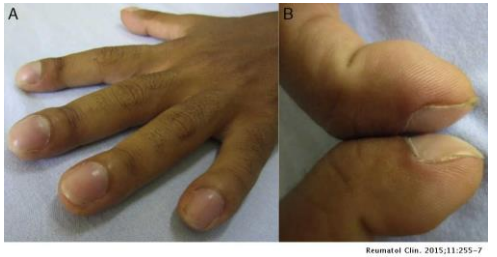
2. Hypertrophic osteoartropathy & clubbing of the fingers - ?PDGF, PGE2, VEGF

- Lung carcinoma
  - Painful artropathy due to proliferative periostitis
  - Proliferation of connective tissue beneath the nail matrix



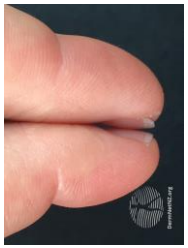
Yap FY. Published Online: December 09, 2016 https://doi.org/10.1148/rg.2017160052

Clubbing and positive Schamroth's sign



Reumatol Clin. 2015;11:255–7

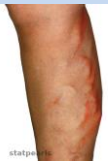
Schamroth window



3. Venous thrombosis (Trousseau phenomenon / migratory thrombophlebitis)

- Pancreatic carcinoma
- Lung carcinoma

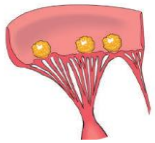
Procoagulant factors e.g. mucin, tissue factor

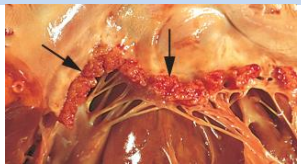


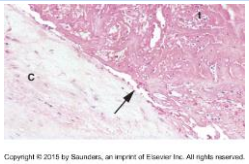
Multiple venous thrombosis in different and changing sites

4. Nonbacterial thrombotic (marantic) endocarditis – hypercoagulable state

- Advanced cancers
- Mucin producing adenocc.







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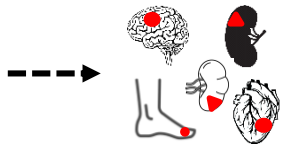


Lecture outline

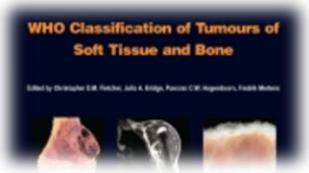
1. Epidemiology of cancer
2. Preneoplastic disorders / precursor lesions
3. Effects of tumor on host
4. Grading and staging of cancer

Grading and staging of cancer

- To predict clinical behavior, aggressivity
- To set up prognostic groups for common therapy
- To establish criteria for therapy

1. Grading – level of differentiation of a tumor, based on microscopic features

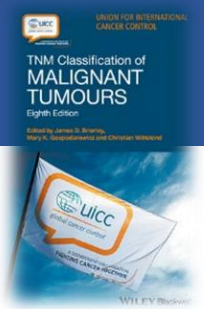
- The degree of differentiation of tumor cells ± No of mitoses ± presence of certain architectural features (semi-quantitative)
- Criteria for the individual grades vary in different types of tumors
- 2 - 4 categories: Low-grade, High-grade; Grade I, II, III, IV
- Correlation with biologic behavior is not very good → well / poorly differentiated



2. Staging – extent of spread of a tumor, based on clinical, radiological, surgical and histological criteria

- Prognostic value
- TNM classification (developed and maintained by the Union for International Cancer Control (UICC); also used by the American Joint Committee on Cancer (AJCC)
  - Used for solid tumors (except CNS tu.)
- Lymphomas / Leukemias have different staging system

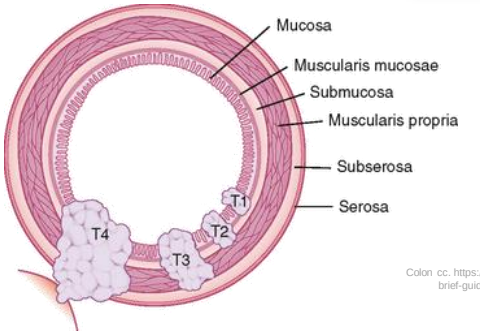
TNM classification of solid tumors



TNM staging varies for specific forms of cancer

T: size or direct extent of the primary tumor

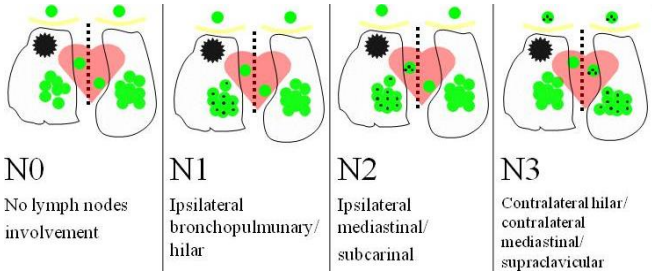
- Tx: tumor cannot be assessed
- Tis: carcinoma in situ
- T0: no evidence of tumor
- T1, T2, T3, T4: size and/or extension of the primary tumor



Colon cc. https://radiologykey.com/a-brief-guide-to-cancer-imaging/

N: degree of spread to regional lymph nodes

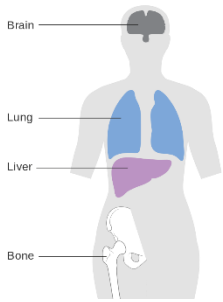
- Nx: lymph nodes cannot be assessed
- N0: no regional lymph nodes metastasis
- N1: regional lymph node metastasis present
- N2: tumor spread to an extent between N1-N3
- N3: tumor spread to more distant or numerous regional lymph nodes



Lung cc.; http://www.thebestoncologist.com/Cancer_Diseases/Lung_Cancer/Staging_of_Lung_Cancer.html

M: presence of distant metastasis

- M0: no distant metastasis
- M1: metastasis to distant organs

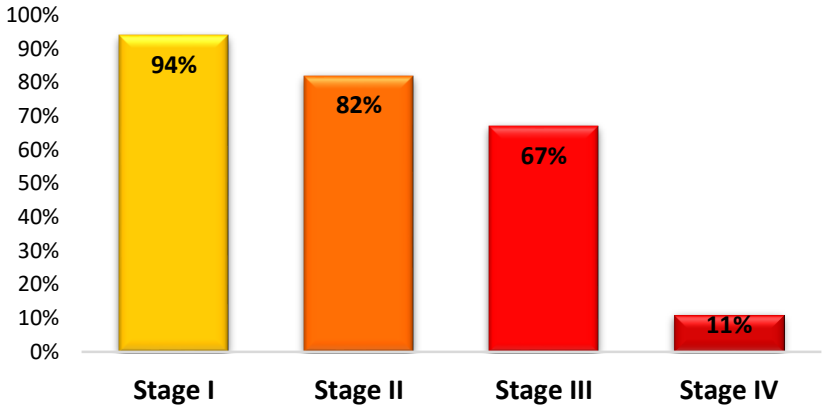


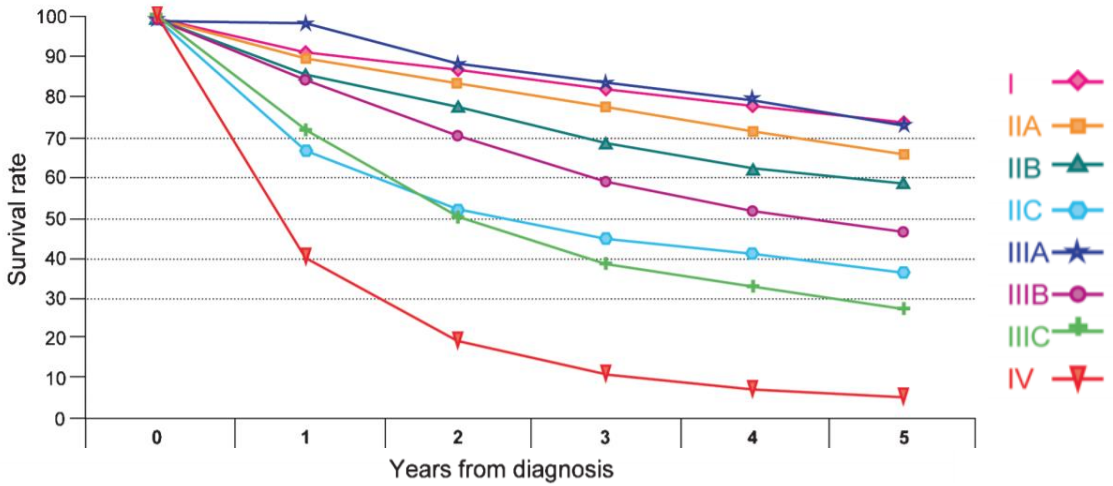
Breast cc. By Cancer Research UK - Original email from CRUK, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=34333556

Prognostic value of TNM staging (e.g. colon cancer)

STAGE	T	N	M
Stage 0	Tis	No	Mo
Stage I	T1, T2	No	Mo
Stage II	T3, T4	No	Mo
Stage IIA	T3	No	Mo
Stage IIB	T4a	No	Mo
Stage IIC	T4b	No	Mo
Stage III	Any T	N1, N2	Mo
Stage IIIA	T1, T2	N1	Mo
	T1	N2a	Mo
Stage IIIB	T1, T2	N2b	Mo
	T2, T3	N2a	Mo
	T3, T4a	N1	Mo
Stage IIIC	T3, T4a	N2b	Mo
	T4a	N2a	Mo
	T4b	N1, N2	Mo
Stage IV	Any T	Any N	M1
Stage IVA	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b
Stage IVC	Any T	Any N	M1c

5 year survival rate for colon carcinoma





Observed survival rates for 28,491 cases with adenocarcinoma of the colon. Data from the SEER 1973–2005 Public Use File diagnosed in years 1998–2000. Stage I includes 7,417; Stage IIA, 9,956; Stage IIB, 997; Stage IIC, 725; Stage IIIA, 868; Stage IIIB, 1,492; Stage IIIC, 2,000; and Stage IV, 5,036.

Colon and Rectum At-A-Glance, Springer, 2010

Other staging systems

1. **Ann Arbor classification**
   - Clinical staging system of Hodgkin and Non-Hodgkin lymphomas
2. **Rai and Binet classifications**
   - Similar clinical staging systems of chronic lymphocytic leukemia
3. **International Neuroblastoma Risk Group Staging System**
   - Clinical staging systems of neuroblastoma
4. **Children's Oncology Group/National Wilms Tumour Study Group (NWTSG) classification and International Society of Paediatric Oncology (SIOP) classification**
   - Clinical staging systems of Wilms tumor
5. **Modified Chang's Staging of Medulloblastoma**
   - Clinical staging system of medulloblastoma