CANCER PREVENTION
A COMPREHENSIVE APPROACH

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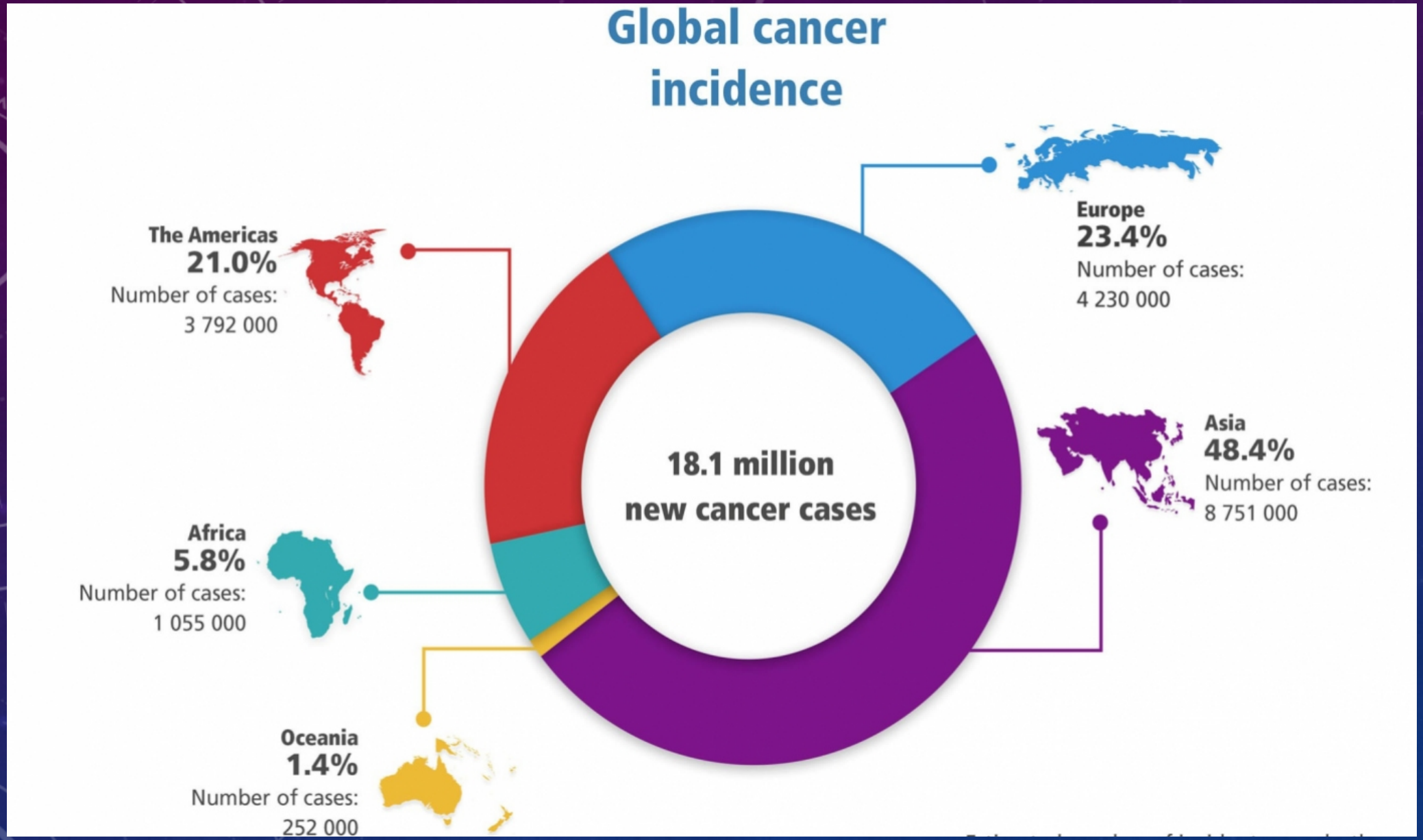
CANCER PREVENTION -A COMPREHENSIVE APPROACH

- Objectives:
  1. Global impact of cancer
  2. Enhance the early diagnosis of cancer through age appropriate screening
  3. Lifestyle Risk factors and modification
  4. Public Awareness and Education about cancer risks, preventive measures such as vaccines.
  5. Challenges in prevention such as global disparities, access to vaccines, and screenings.

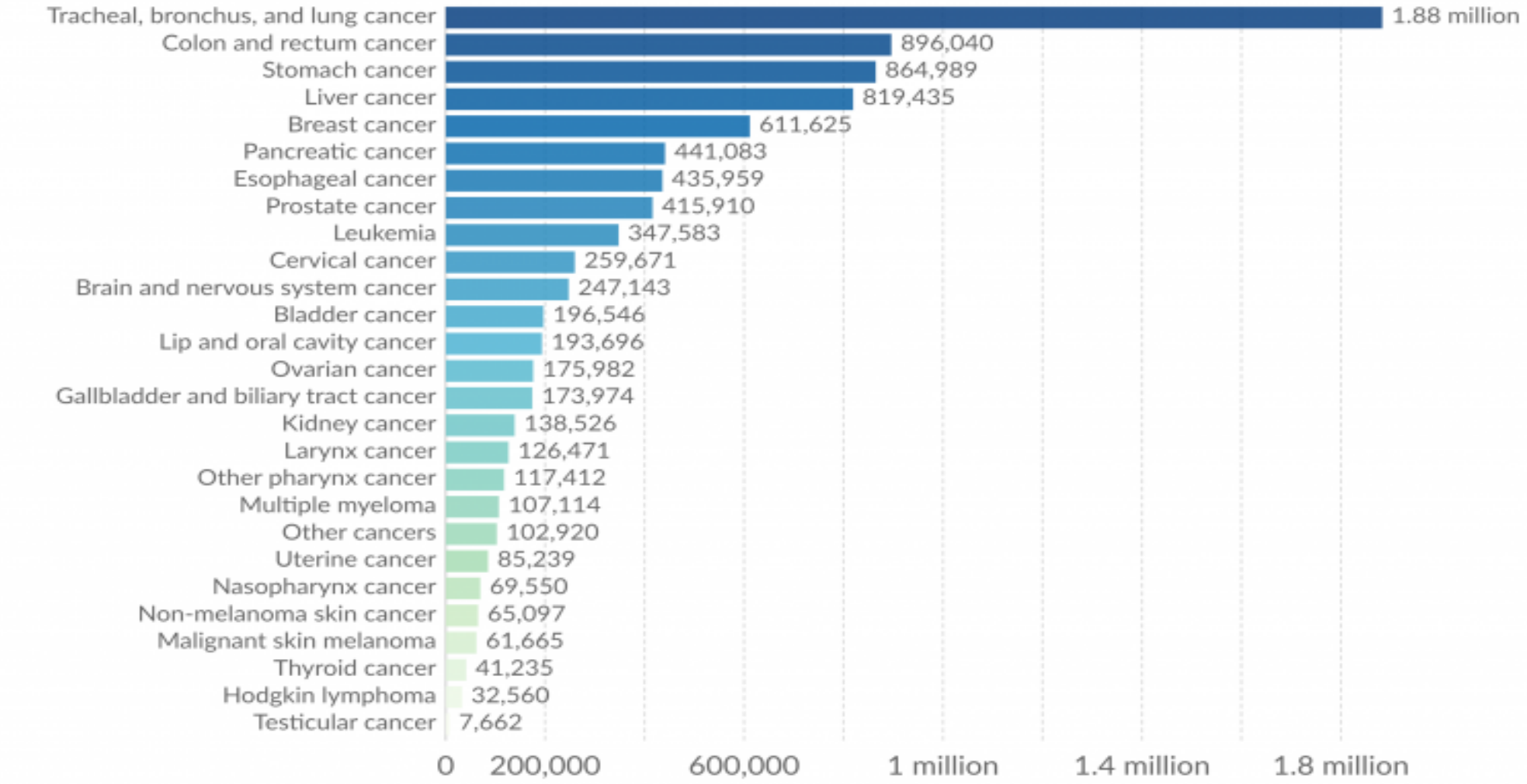
Global cancer incidence



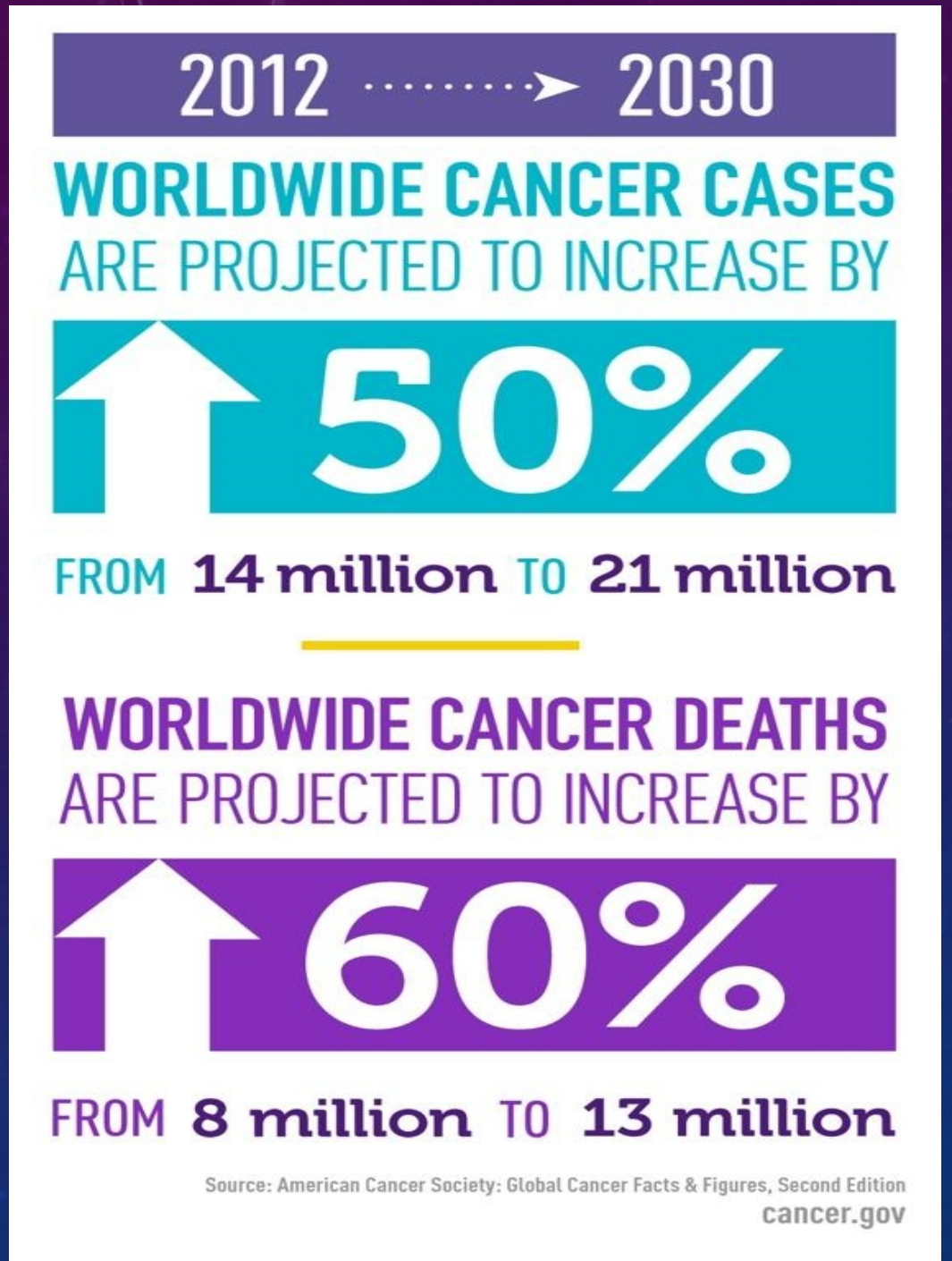
Cancer deaths by type, World, 2017

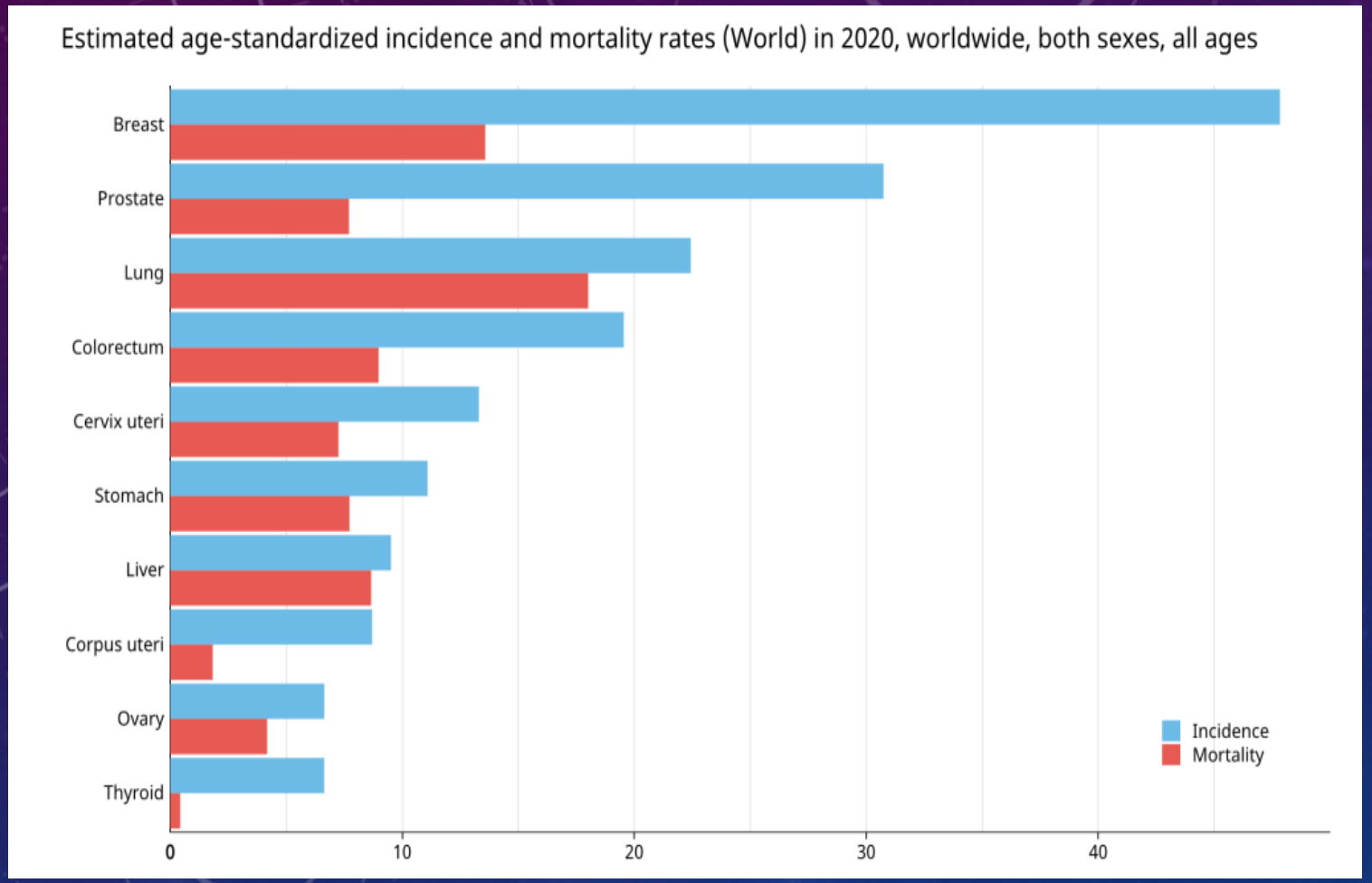
Total annual number of deaths from cancers across all ages and both sexes, broken down by cancer type.

Our World in Data



Source: IHME, Global Burden of Disease (GBD)


2012 2030
WORLDWIDE CANCER CASES
ARE PROJECTED TO INCREASE BY
50%
FROM 14 million TO 21 million
WORLDWIDE CANCER DEATHS
ARE PROJECTED TO INCREASE BY
60%
FROM 8 million TO 13 million
Source: American Cancer Society: Global Cancer Facts & Figures, Second Edition
cancer.gov


Estimated age-standardized incidence and mortality rates (World) in 2020, worldwide, both sexes, all ages
Breast
Prostate
Lung
Colorectum
Cervix uteri
Stomach
Liver
Corpus uteri
Ovary
Thyroid
0
10
20
30
40
Incidence
Mortality

CHROMOSOMES, DNA, AND GENES

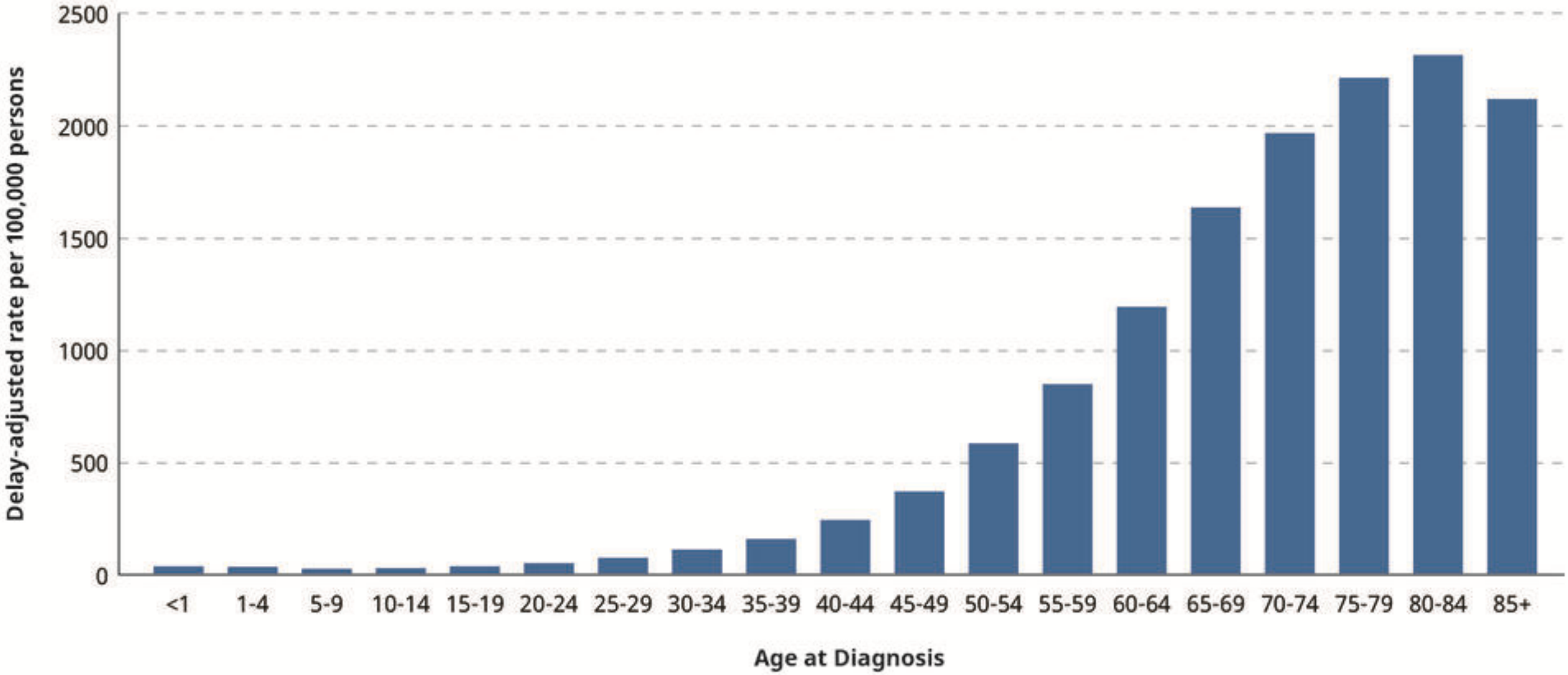
CANCER- RISK FACTORS

Non modifiable risk factors

Modifiable risk factors- Life-style related, Environmental

WHAT ARE THE RISK FACTORS?

- Age
- Genetic or Family History
- Auto-Immune Disorders
- Immunodeficiency


Delay-adjusted rate per 100,000 persons
2500
2000
1500
1000
500
0
<1
1-4
5-9
10-14
15-19
20-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
65-69
70-74
75-79
80-84
85+
Age at Diagnosis

- Environmental:

- Exposure to Radiation
- Chemicals/Pesticides
- Asbestos
- Air Pollution and Diesel Exhaust
- Smoke from Cooking
- Radon

LIFESTYLE RISK FACTORS

- Smoking
- Alcohol
- Nutrition
- Obesity
- Physical Activity
- Stress
- Sunlight
- Viruses

SCREENING FOR CANCERS

- Mammogram- for women after 40 years
- Colonoscopy after 45 years
- PSA
- Pap Smear and HPV testing for cervical cancers
- Low dose CT scan for those who have smoking hx- =/>20 pack years

BREAST CANCER RISK FACTORS

- Personal history of breast, ovarian, tubal, or peritoneal cancer
- Family history of breast, ovarian, tubal, or peritoneal cancer
- Ancestry (eg, Ashkenazi Jewish) associated with *BRCA1* or *2* mutations
- Known carrier of a pathogenic mutation for a hereditary breast and ovarian cancer syndrome in self or relative
- Mammographic breast density
  Previous breast biopsy indicating high-risk lesion (atypical hyperplasia)
- Age of menarche, age at first live birth, number of pregnancies, and menopausal status
- Radiotherapy to the chest between age 10 and 30 years

- Average to Moderate Risk-
  - 15-20% lifetime risk of breast cancer

- High Risk-
  - >20% risk
  - BRCA1, 2 mutations
  - Prior chest radiation, or atypical hyperplasia

- Average or Moderate Risk- Mammography
- High Risk- MRI
- Ultrasound
- Clinical Breast Exam
- iBreast Exam

	ACR	ACS	ACOG	NCCN	USPSTF
Age	40	45	40-50	40	40
Age to stop	No limit	LE <10 yr	75 and then shared decision	Not stated	74 years
Interval	Annual	45-54 Annual 55 and older Every 1-2 year	1-2 yrs	Annual	Every 2 yrs
3D	Preferred	Preferred	Not stated	Preferred	Insufficient evidence

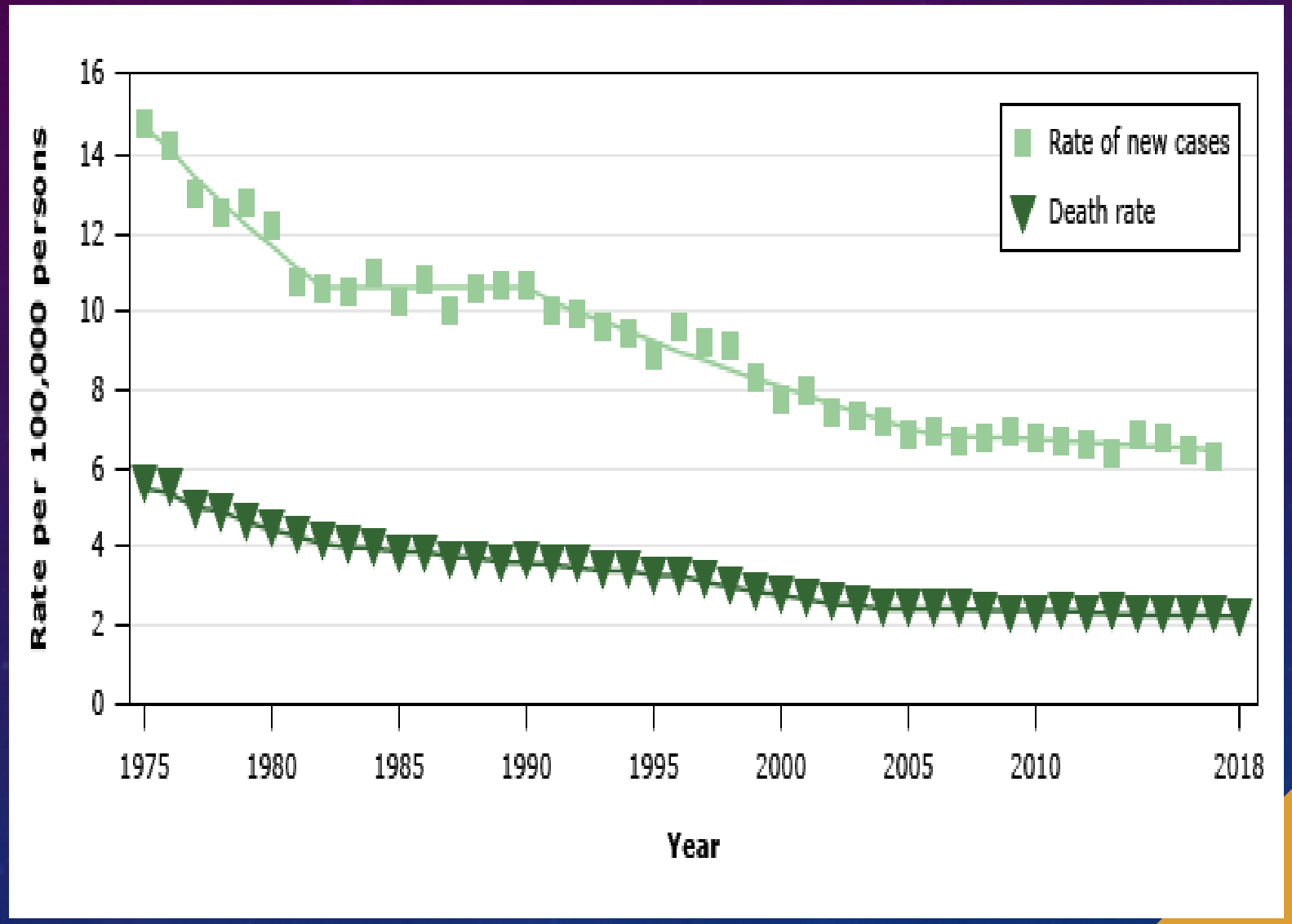

iBreastExam


REVIEW

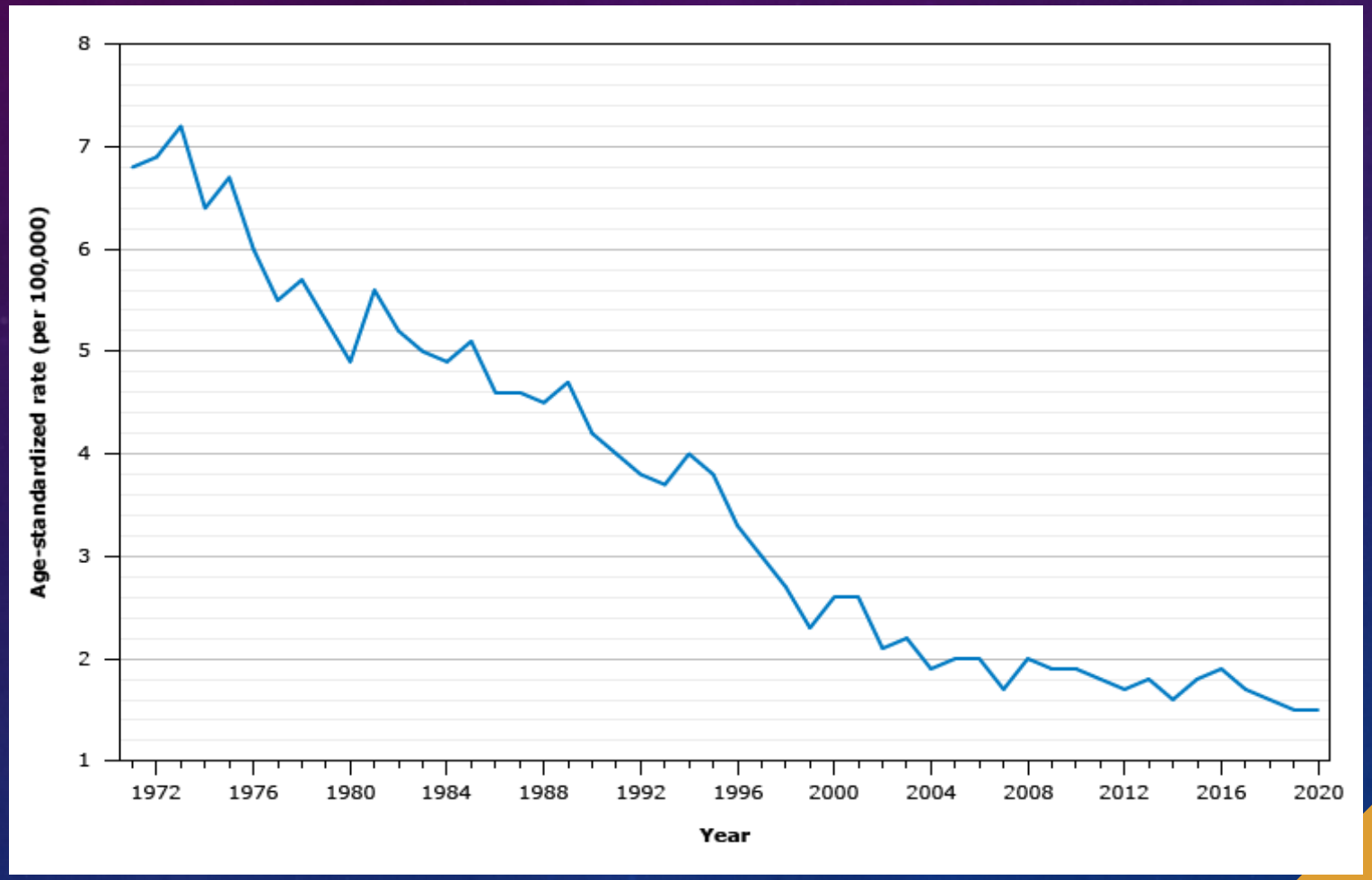
CERVICAL CANCER SCREENING

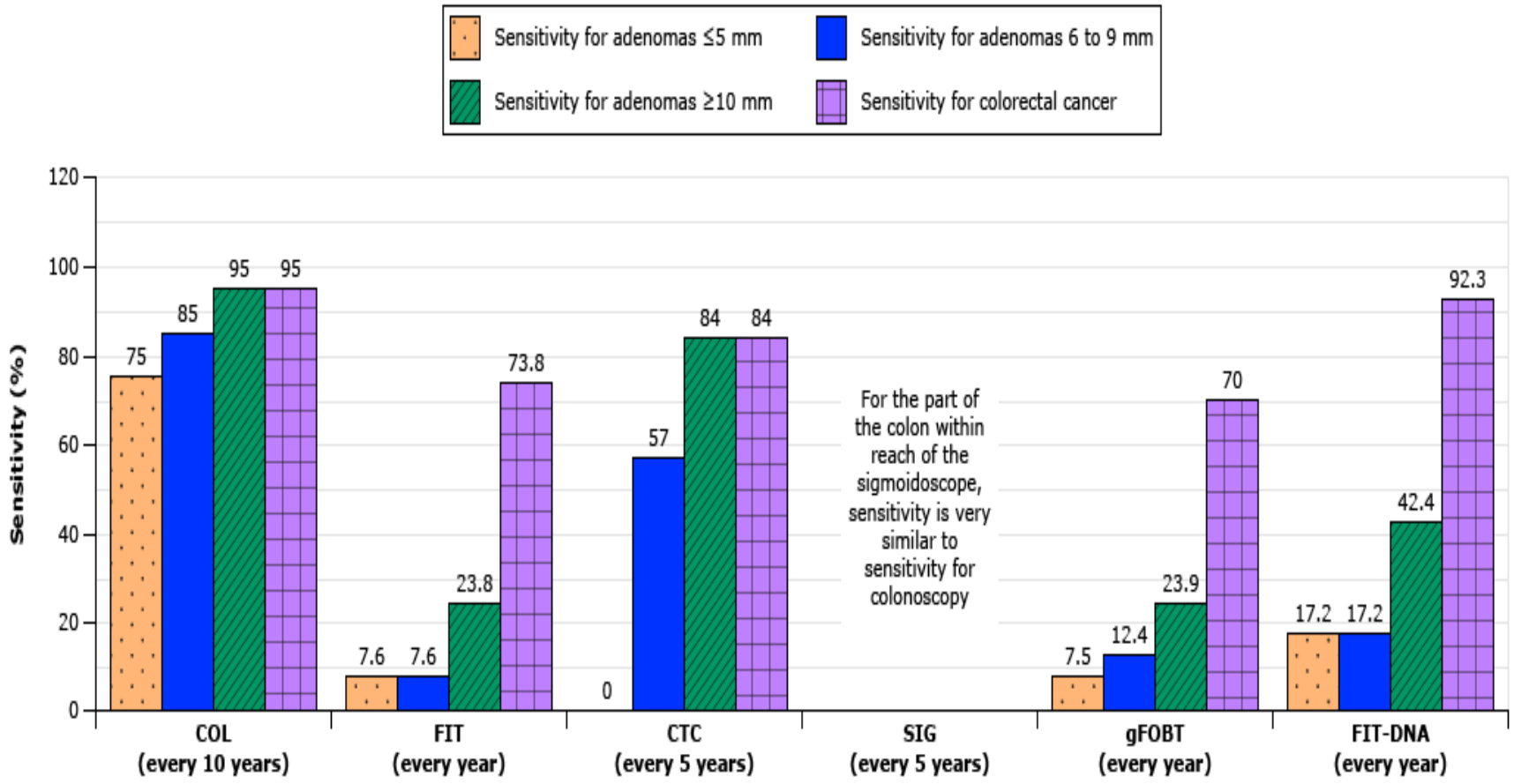
- Pap smear-
  - Starting at 21 years and stopping at 65 yrs
  - Every 3 years

- HPV testing
  - Every 5 years
  - Both together every 5 years
  - HPV vaccinated patients- Same recs.


Rate per 100,000 persons
16
14
12
10
8
6
4
2
0
1975
1980
1985
1990
1995
2000
2005
2010
2018
Year
Rate of new cases
Death rate

CERVICAL CANCER MORTALITY IN AUSTRALIA





Test specificity	86	96.4	88	87	92.5	89.8
Colorectal cancer deaths averted per 1000 40-year-olds (n)*	22 to 24	20 to 23	16 to 24	16 to 21	20 to 23	21 to 24

PROSTATE CANCER- PSA

- **Shared decision-making for most patients** –
- For average-risk males, many clinicians do not specifically advise in favor of or against screening.
- Males who are candidates for screening should be engaged in shared decision-making about whether they choose to be screened.

LUNG CANCER SCREENING

- More than 20 Pack year history
- 50-80 years
- Who quit within 15 years

- Low dose CT chest once a year
- Uptake rate is only 5-6%
- Checking Radon

PROSTATE CANCER- PSA

- **Age to begin screening** –
- Average-risk males, Initiate discussion of screening at age 50 years
- High risk
  - *BRCA1 o*r *BRCA2* genetic mutations or Lynch syndrome
  - Black Males and Family History
  - Initiate screening discussions as early as age 40 years

USE OF AI IN CANCER SCREENING

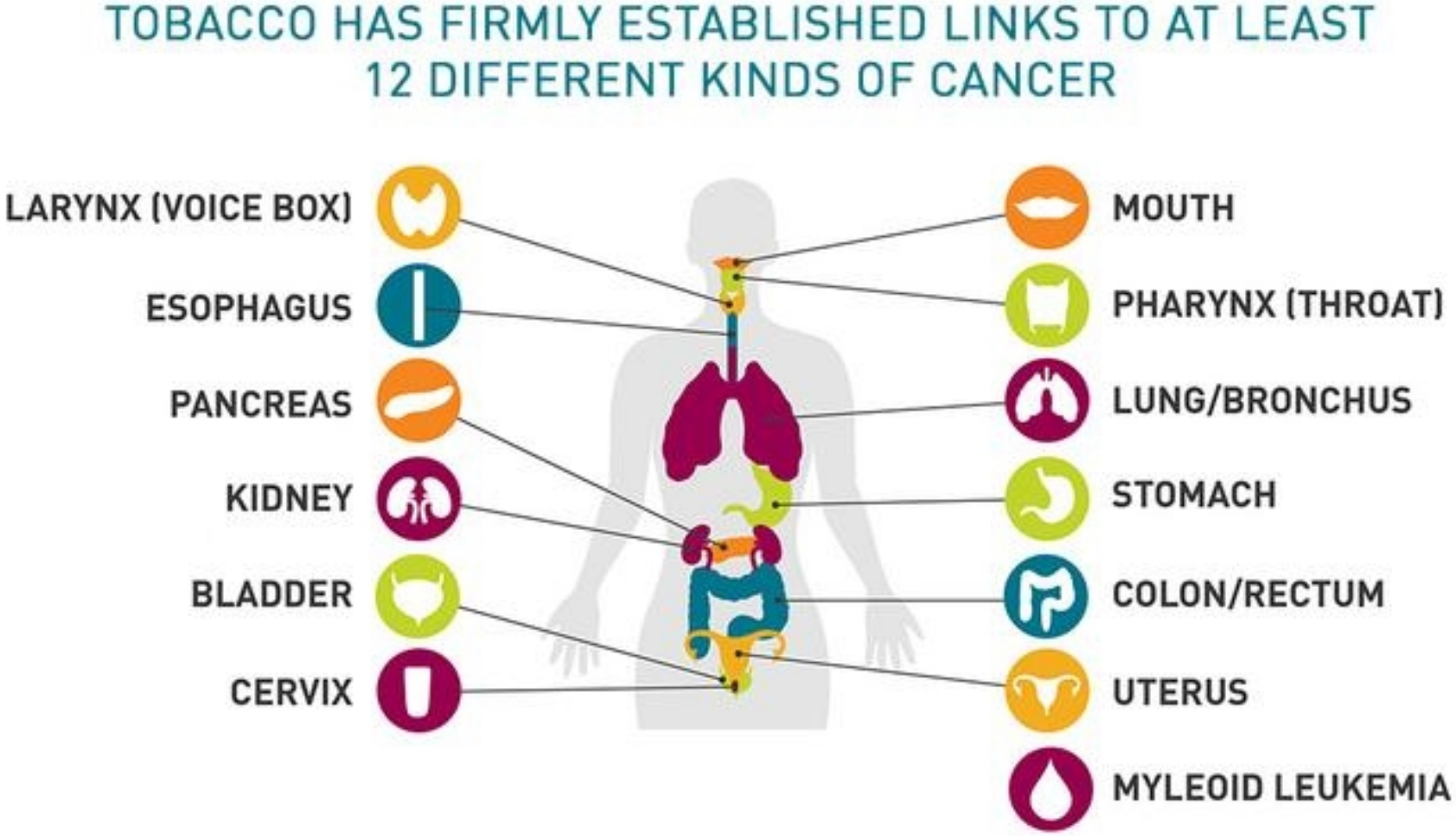
- Image analysis
  - AI can analyze medical images like mammograms, MRIs, x-rays, and sonograms to get more precise pictures and deeper analyses.
  - AI can identify subtle patterns and features that humans might miss.
- Breast cancer detection
  - AI can improve breast cancer detection on mammograms and help predict the risk of invasive breast cancer.
  - A June 2023 study found that AI was more accurate at predicting breast cancer risk than the Breast Cancer Surveillance Consortium (BCSC) risk model.
- Cervical cancer screening
  - AI can help detect precancerous cervical lesions from digital images.
-
- Pancreatic cancer screening
  - AI can identify patients at the highest risk of pancreatic cancer up to three years before a diagnosis.

HOME BASED CANCER GENE DETECTION

- 1 in 3 develop cancer
- Only few of more than hundred cancers have screening tests
- 70% of cancer deaths are from cancers without recommended screening options

- Cell free DNA technology (Blood test) Galleri- Rx required
- Saliva tests- Invitae

SMOKING- THE TRUE WEAPON OF MASS DESTRUCTION



SMOKING AND LUNG CANCER

- Cigarette smoking is estimated to account for approximately 90 percent of all lung cancers
- The cumulative lung cancer risk among heavy smokers may be as high as 30 percent
- Never smokers 1% or less
- The risk of lung cancer increases with
  - Number of cigarettes smoked per day
  - Duration of smoking
  - Age at onset of smoking
  - Degree of inhalation
  - Tar and nicotine content of the cigarettes
  - Unfiltered cigarettes
  - *Mattson ME, Pollack ES, Cullen JW. What are the odds that smoking will kill you? Am J Public Health 1987; 77:425.*

IS IT TOO LATE TO QUIT?

- Case-control studies show that former smokers who quit for more than 15 years had an 80 to 90% risk reduction in lung cancer compared with current smokers
- However, lung cancer risk still remains higher than in the never smoker, even after prolonged periods of complete abstinence
- In fact, for the individual, the risk of lung cancer continues to rise with age, even after smoking cessation
- Adults who quit smoking gained 6 to 10 years of life expectancy, depending upon the age at which they quit smoking.

Jha P, Ramasundarahettige C, Landsman V, et al. 21st-century hazards of smoking and benefits of cessation in the United States. N Engl J Med 2013; 368:341.

- Even if smokers are unable to quit, cutting down smoking can decrease risk of lung cancer.
- An observational study that included 19,714 adults found that smokers who continued to smoke but cut back by at least 50%reduced their risk of lung cancer by 27%
- Smoking cessation decreases the recurrence rates, new cancers and improve survival

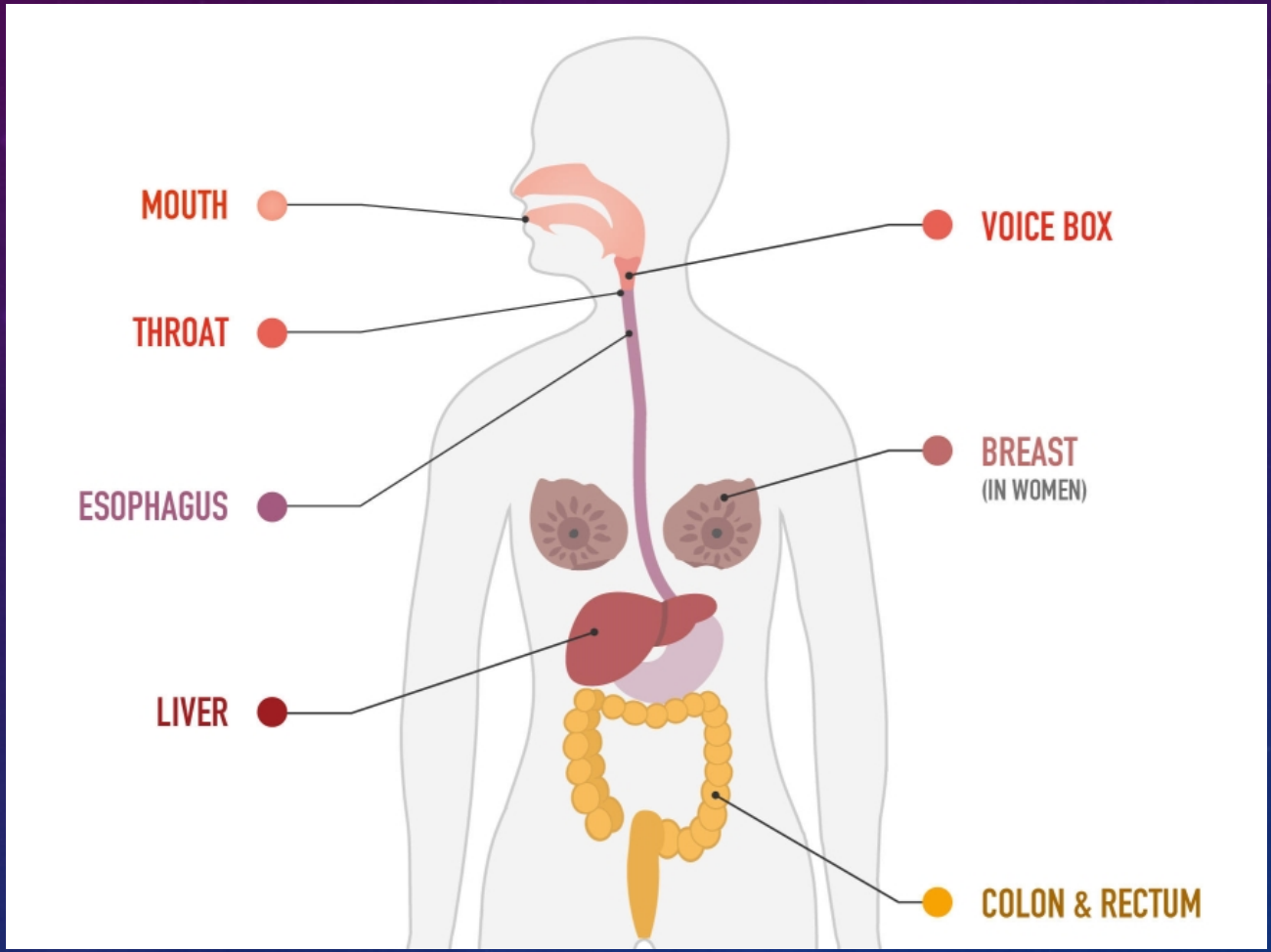
Godtfredsen NS, Prescott E, Osler M. Effect of smoking reduction on lung cancer risk. JAMA 2005; 294:1505.

Influence of smoking cessation after diagnosis of early stage lung cancer on prognosis: systematic review of observational studies with meta-analysis.AUParsons A, Daley A, Begh R, Aveyard P SOBMJ. 2010;340:b5569. Epub 2010 Jan 21.

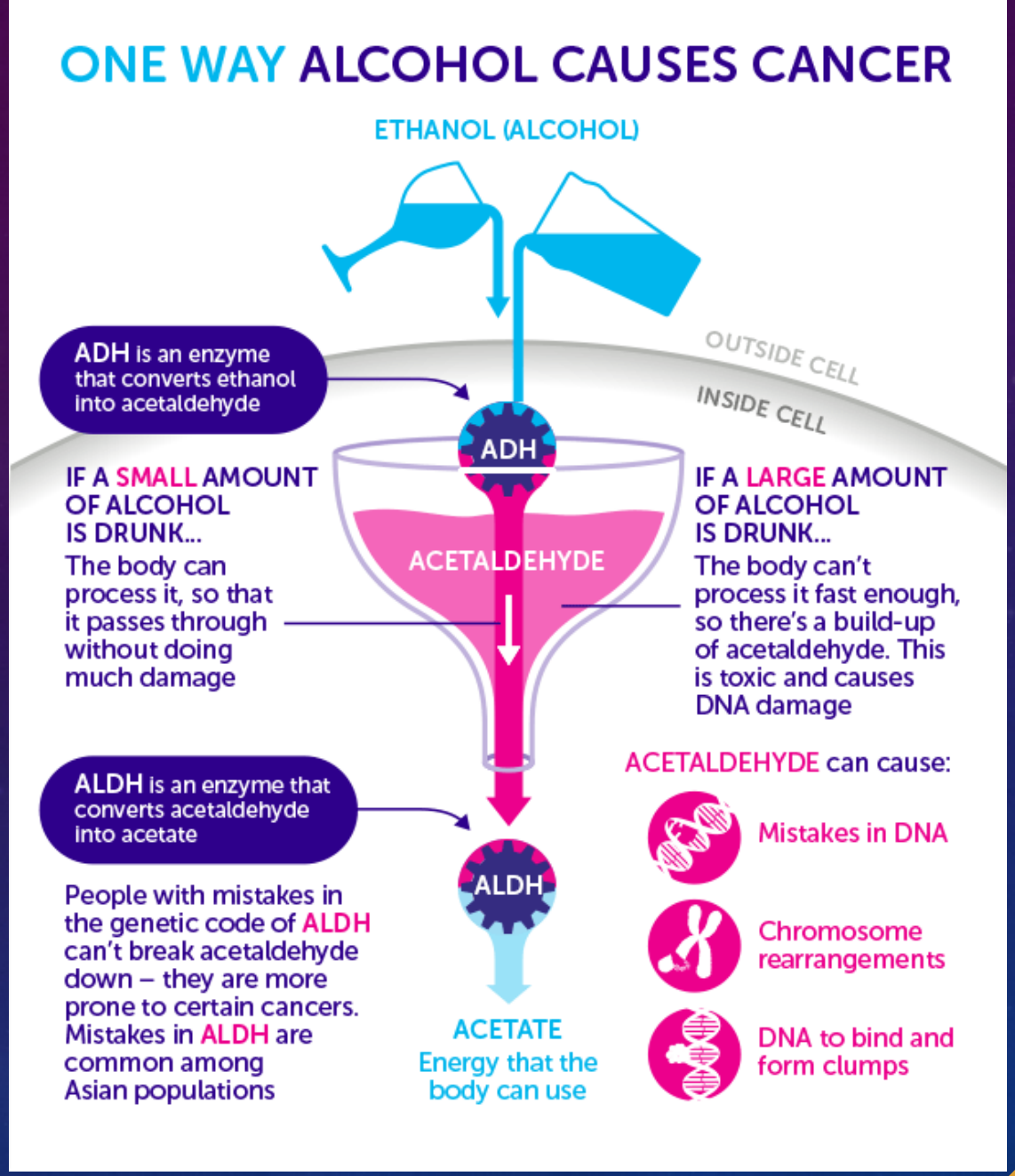
WHAT ABOUT VAPING?

- Can cause cancer in animals
- Not known in humans, but has many chemicals
  - Benzene
  - Acetaldehyde
  - Formaldehyde
  - Toxic metals, like cadmium and heavy metals (including lead, nickel and tin)
  - Acrolein, a weed killer known to cause permanent lung damage.
  - Diacetyl
  - Diethylene glycol
  - Propylene glycol

ALCOHOL


MOUTH
THROAT
ESOPHAGUS
LIVER
VOICE BOX
BREAST
(IN WOMEN)
COLON & RECTUM

ONE WAY ALCOHOL CAUSES CANCER



ALCOHOL AND BREAST CANCER

- There is a 10 percent increase in risk with each 10 grams per day of alcohol intake
- Mostly ER, PR and Her-2 Positive, but not associated with ER negative cancers.
- Hormone therapy in drinkers increases the risk even further
- In the United States, 2% breast cancers are related to alcohol intake
- In Italy, where alcohol intake is higher, alcohol accounts for 11% cases .
- In the European Prospective Investigation into Cancer and Nutrition (EPIC) study of over 250,000 females in 8 European countries, the attributable risk for breast cancer with alcohol was 5%

Ferrari P, Licaj I, Muller DC, et al. Lifetime alcohol use and overall and cause-specific mortality in the European Prospective Investigation into Cancer and nutrition (EPIC) study. BMJ Open. 2014;4(7):e005245. Published 2014 Jul 3. doi:10.1136/bmjopen-2014-005245

ALCOHOL AND BREAST CANCER

- Breast cancer risk is higher for individuals consuming both low (<1 drink per day) to high (≥3 drinks per day) levels of alcohol compared with abstainers.
- There seems to be a significant dose response relationship with alcohol

Light to moderate intake of alcohol, drinking patterns, and risk of cancer: results from two prospective US cohort studies. Cao Y, Willett WC, Rimm EB, Stampfer MJ, Giovannucci EL BMJ. 2015;351:h4238. Epub 2015 Aug 18.

Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, Scotti L, Jenab M, Turati F, Pasquali E, Pelucchi C, Galeone C, Bellocco R, Negri E, Corrao G, Boffetta P, La Vecchia C. Br J Cancer. 2015 Feb3;112(3):580-93. doi: 10.1038/bjc.2014.579. Epub 2014 Nov 25. PMID: 25422909; PMCID: PMC4453639.

ALCOHOL AND GI MALIGNANCIES

- **Esophageal** – The risk of squamous cell esophageal cancer increased, not adenocarcinoma
- **Colorectal** –Most of the studies report an association between moderate or heavy alcohol use and colorectal cancer, but not light drinking
- **Pancreatic** – Associated with Heavy drinking, but not mild to moderate drinking
- **Hepatocellular** –Much of this association may be due to cirrhosis

A large prospective study of middle-aged females found no increased risk for liver cancer with three to six drinks per week. However, risk was significantly increased by 70% among females consuming more than 14 drinks per week.

Moderate alcohol intake and cancer incidence in women. Allen NE, Beral V, Casabonne D, Kan SW, Reeves GK, Brown A, Green J, Million Women Study Collaborators J Natl Cancer Inst. 2009;101(5):296. Epub 2009 Feb 24.

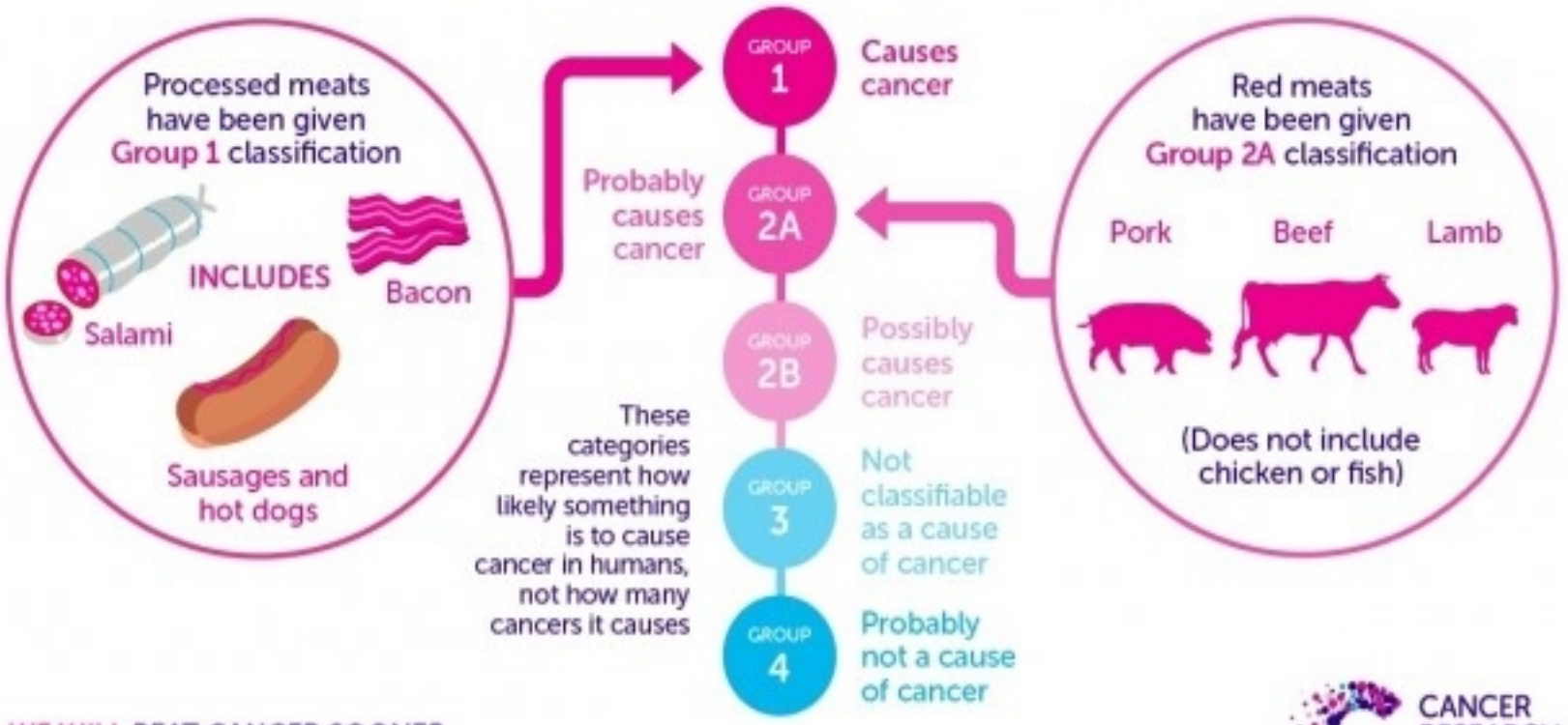
ALCOHOL & CANCER- RECOMMENDATIONS

- The American Society of Clinical Oncology advises that alcohol drinking is an established risk factor for several malignancies and is a potentially modifiable risk factor for cancer
- American Cancer Society, 2020 Guidelines recommend complete avoidance of alcohol for cancer prevention

CASE- 1

- A 28 yr old patient diagnosed to have rectal cancer. Underwent Chemoradiation, neoadjuvant chemo with FOLFOX, with plan to do surgery but colonoscopy showed no residual tumor. Ct DNA testing was negative. The surgeon decides to wait and monitor closely. Patient is under surveillance with colonoscopy every 6-12 months and comes for a follow-up visit. What are the additional recommendations?

MEAT AND CANCER HOW STRONG IS THE EVIDENCE?



WE WILL BEAT CANCER SOONER
cruk.org

CANCER RESEARCH UK

DIET AND CANCER

Meta-analyses of observational studies has shown that healthy dietary patterns are associated with a decreased risk of primary cancer development.

-A population study of 65,000 participants in England found that daily consumption of 7 or more servings of fruit and vegetables reduced cancer incidence by 25% (hazard ratio, 0.75; 95% CI, 0.59-0.96)

-Plant-based diets are associated with a decrease in cancer recurrence and improved outcomes in survivors. For instance, in survivors of stage III colon cancer, a diet consisting of more fruits, vegetables, whole grains, poultry, and fish, and less red meat, refined grains, and concentrated sweets improved cancer recurrence and death, and overall survival.

WHAT IS A HEALTHY DIET?

- In general, a healthy diet is rich in plant sources, such as fruit, vegetables, whole grains, legumes, avocados, seeds, and nuts.
- Fish and poultry are recommended, whereas red and processed meats/foods, and foods and beverages with added sugars or fats should be limited.

PHYSICAL ACTIVITY:

-Decreased physical activity is associated with an increased risk for cancer

-Increase in circulating levels of insulin, hormones, and other growth factors; impact on prostaglandin levels; altered immune function

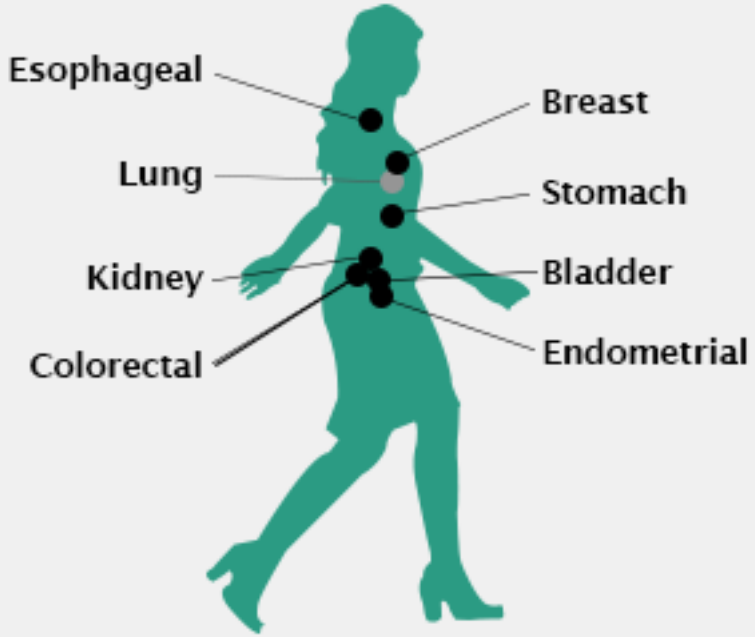
-Sedentary lifestyle is associated with up to 14 percent of cancer deaths- Independent risk factor

Physical Activity

is associated with

lower risk

of these cancers:



● strong evidence ● moderate evidence

RECOMMENDATIONS FROM ACSM

The general recommendation from ACSM…

30 minutes of exercise 3 times a week and resistance training at least twice weekly.

- Sedentary behavior, may be an independent risk for increased cancer risk in the general population and poor prognosis in cancer survivors.

- A meta-analysis of 14 studies including individuals with and without cancer demonstrated that sedentary behavior was associated with an increased risk of all-cause mortality 22%, cancer mortality 14%!

Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. Biswas A, Oh PI, Faulkner GE, Bajaj RR, Silver MA, Mitchell MS, Alter DA. Ann Intern Med. 2015;162(2):123.

-Can increase in physical activity reduce cancer risk or mortality?

- In a meta-analysis of 52 studies, there was a 24 % reduced risk of colon cancer when comparing the most versus the least active individuals (relative risk [RR] 0.76, 95% CI 0.72-0.81)

- Several studies have shown that increasing physical activity can improve the survival in certain cancers including breast, colon and prostate.

- Reduction in symptoms of anxiety, and depression, cancer induced fatigue, and improvement in quality of life.

American Institute for Cancer Research

PHYSICAL ACTIVITY AND CANCER: REDUCING YOUR RISK

GETTING REGULAR PHYSICAL ACTIVITY

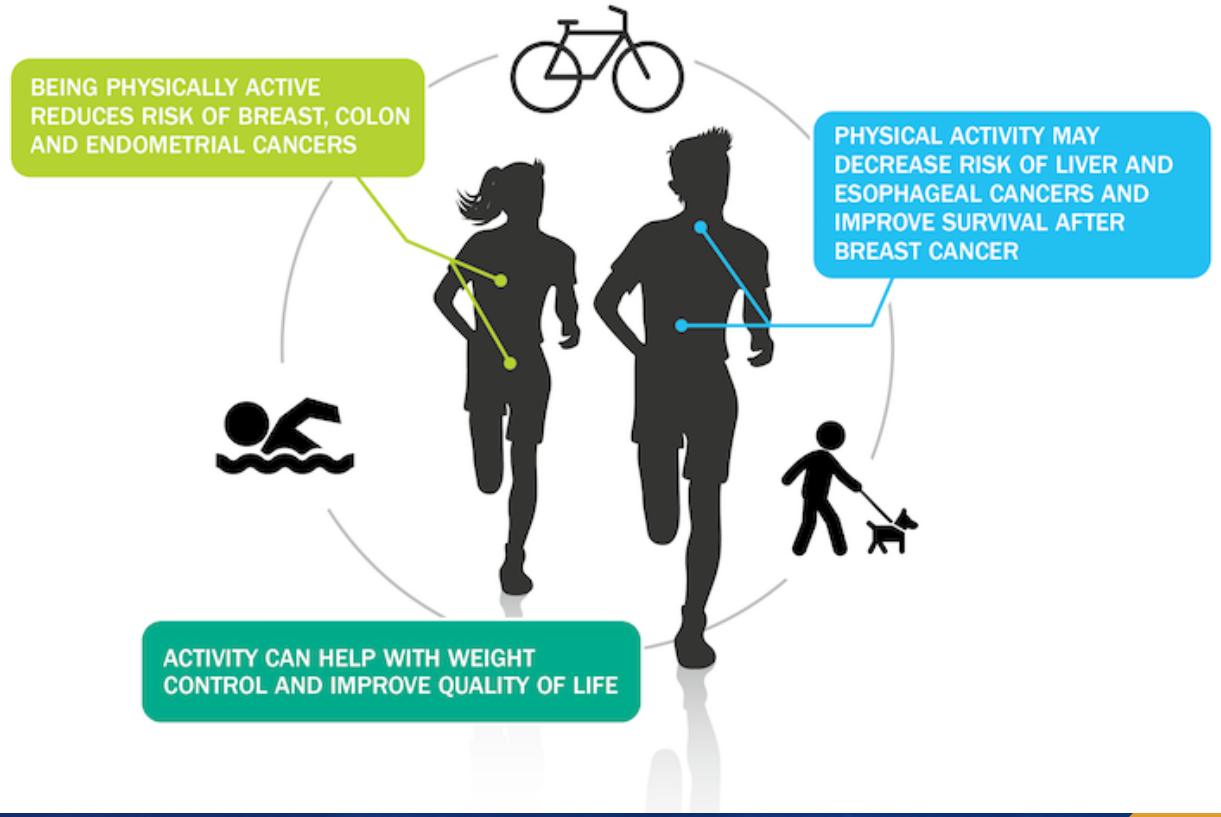
EVERY DAY IN ANY WAY

LOWERS RISK FOR CANCER

WALK MORE AND SIT LESS

AIM TO GET AT LEAST **150 MINUTES A WEEK**

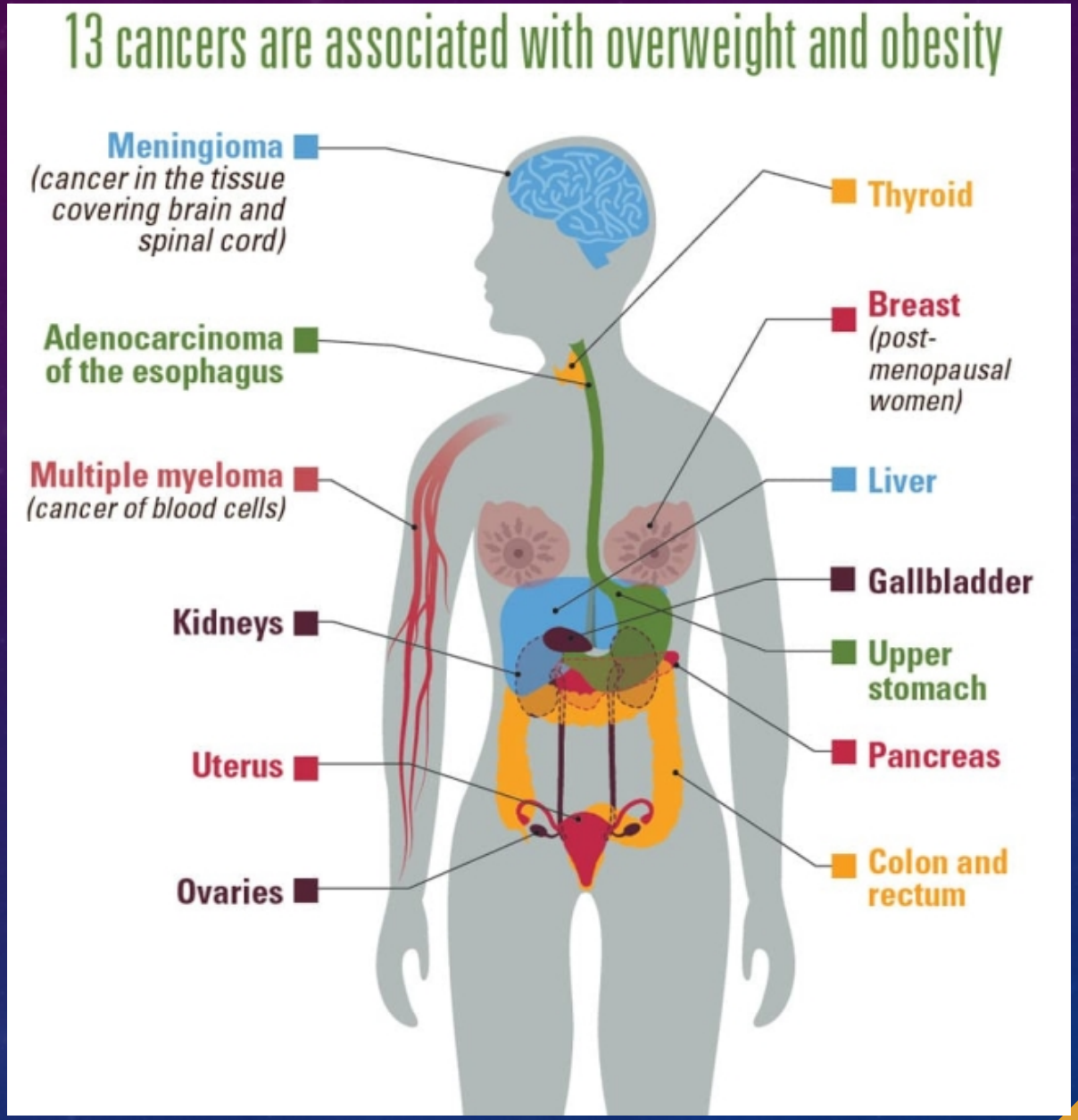
FOR MORE PROTECTION, BE ACTIVE FOR **45 - 60 MINUTES EVERY DAY**



HIGH BMI AND CANCER

It is estimated that 3.5% new cancers in men, and 9.5% new cancers in women are linked to high BMI.

Adipose tissue produces excess amounts of estrogen which may lead to increased chance of breast, endometrial, ovarian cancers, etc.


13 cancers are associated with overweight and obesity
Meningioma
(cancer in the tissue covering brain and spinal cord)
Adenocarcinoma of the esophagus
Multiple myeloma
(cancer of blood cells)
Kidneys
Uterus
Ovaries
Thyroid
Breast
(post-menopausal women)
Liver
Gallbladder
Upper stomach
Pancreas
Colon and rectum

HIGH BMI AND COLORECTAL CANCER

- In Europe, about 11% of colorectal cancers are attributed to overweight and obesity
- Epidemiological data suggest that obesity is associated with a 30%-70% increased risk of colon cancer
- Abdominal obesity and Visceral fat seems to be worse than subcutaneous fat obesity
- Obesity might increase the likelihood of recurrence or mortality of the primary cancer
- Despite a growing body of evidence linking obesity to CRC, many questions remain unanswered, including whether we should screen patients with obesity earlier or propose prophylactic bariatric surgery for certain patients with obesity.

Bardou, Marc et al. "Review article: obesity and colorectal cancer." Alimentary pharmacology & therapeutics vol. 56,3 (2022): 407-418. doi:10.1111/apt.17045

HIGH BMI AND MYELOMA

- Patients with multiple myeloma with high BMI are 50% more likely to die from the disease when compared to normal BMI

Teras LR, Kitahara CM, Birmann BM,et al. Body size and multiple myeloma mortality: a pooled analysis of 20 prospective studies. Br J Haematol. 2014 Sep;166(5):667-76. doi: 10.1111/bjh.12935. Epub 2014 May 23

IS IT ALL HIGH BMI THAT MATTERS?

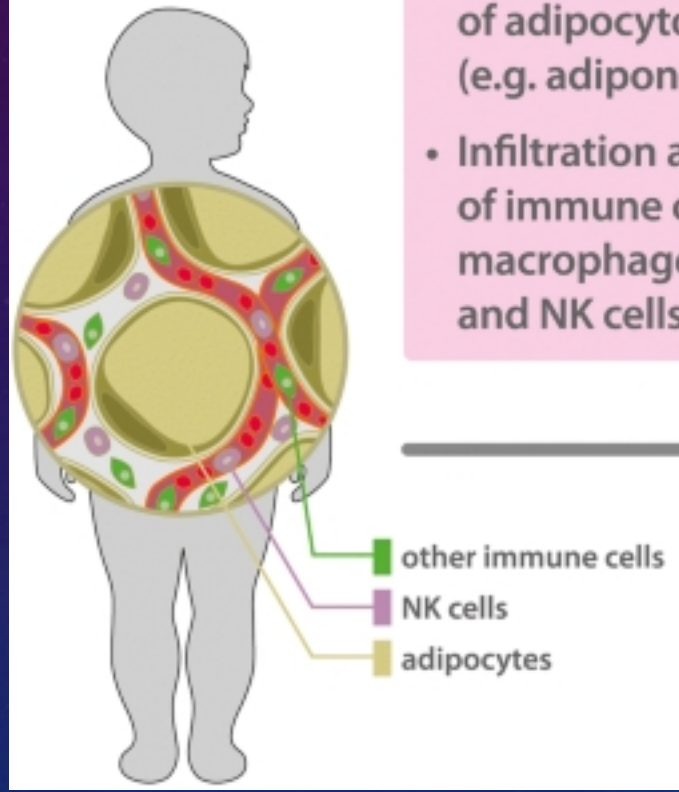
- BMI does not reflect muscle or fat distribution, and there are increasing data supportive of a protective effect of muscle for cancer patients
- In a pooled analysis of 44 observational studies that included 18,891 patients with CRC, over one-third of were found to be sarcopenic
- Sarcopenic patients also had lower overall survival (HR 1.83, 95% CI 1.57-2.14) and cancer-specific survival (HR 1.77, 95% CI 1.40-2.23) compared with nonsarcopenic patients.

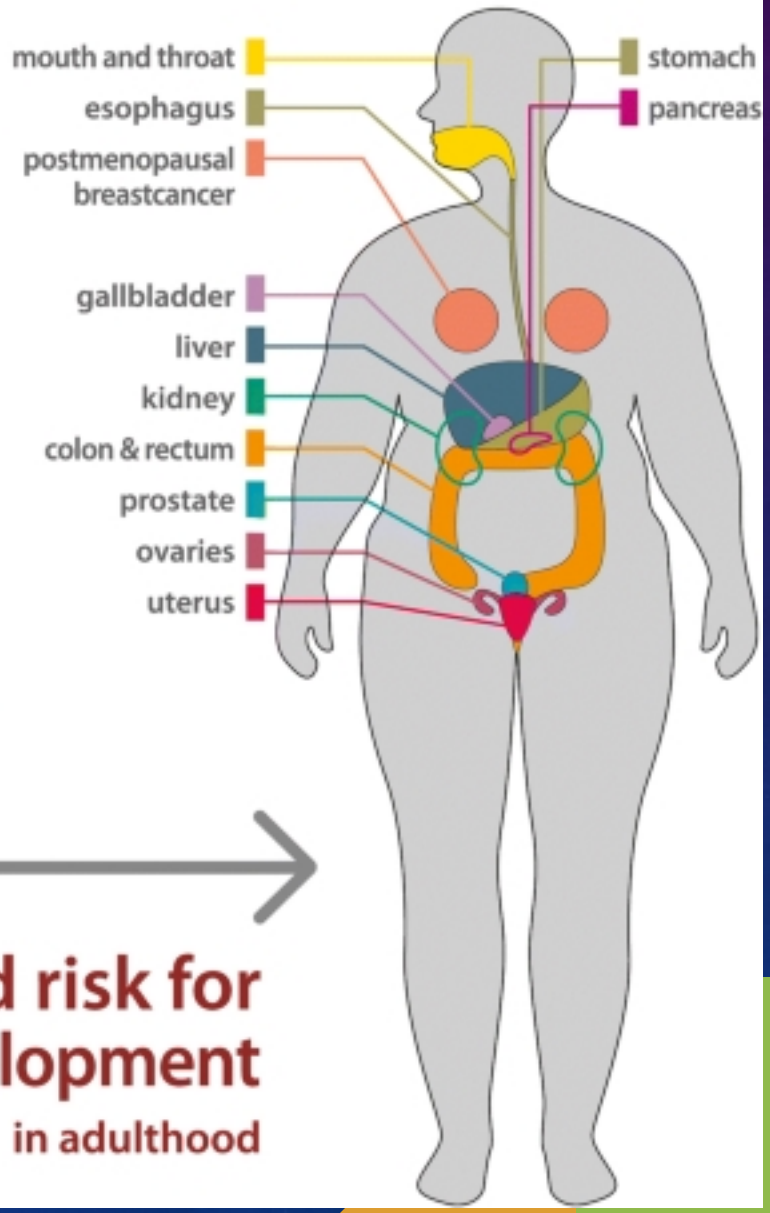
- *Sarcopenia predicts worse postoperative outcomes and decreased survival rates in patients with colorectal cancer: a systematic review and meta analysis. AUTrejo-Avila M, Bozada-Gutiérrez K, Valenzuela-Salazar C, Herrera-Esquivel J, Moreno-Portillo M SOInt J Colorectal Dis. 2021;36(6):1077. Epub 2021 Jan 22.*

Obesity
in childhood

„Metaflammation“

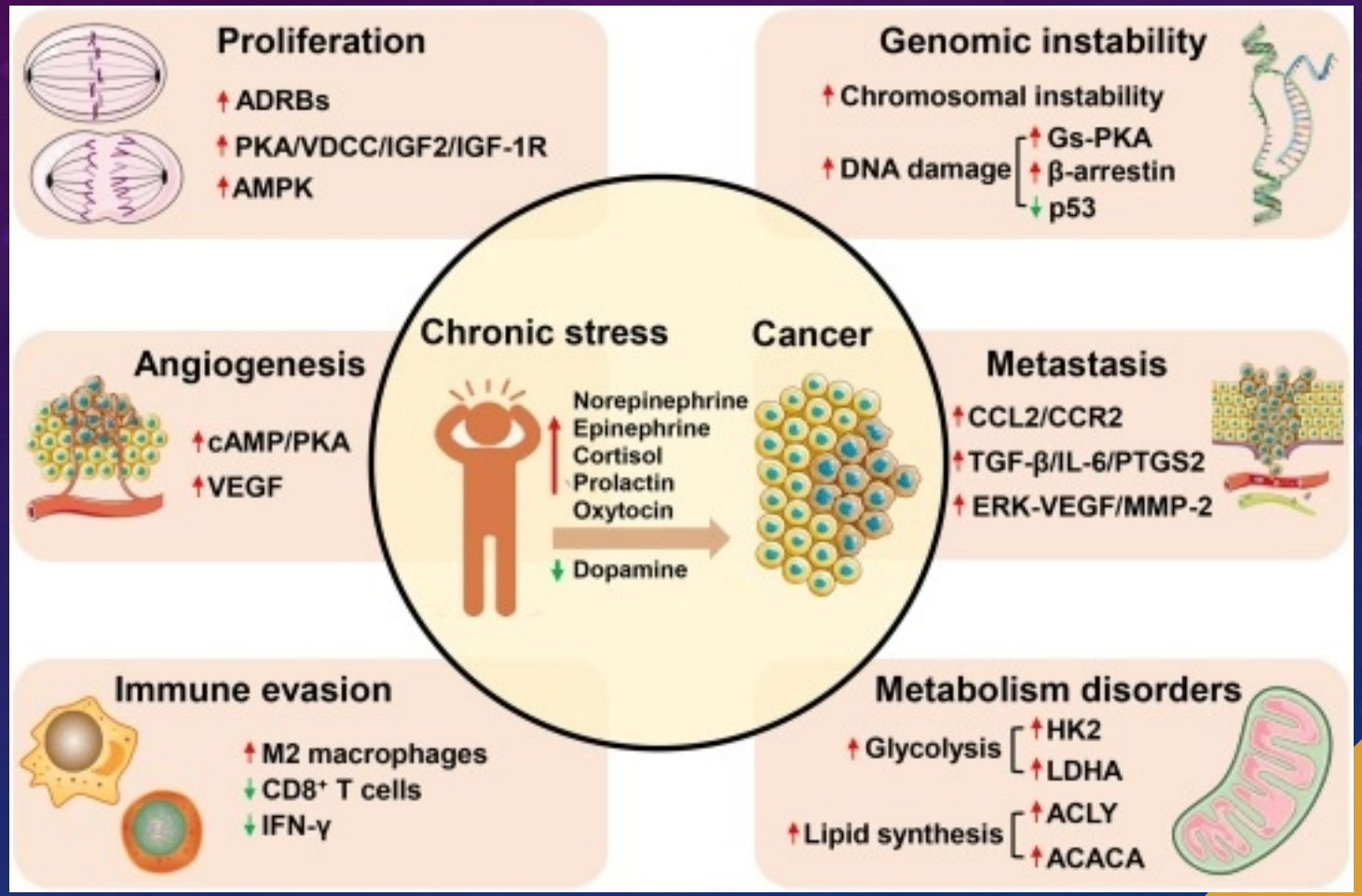
- Increased secretion of proinflammatory cytokines (IFN-γ, IL-6, TNF-α) and inflammatory markers (hsCRP)
- Dysregulated secretion of adipocytokines (e.g. adiponectin, leptin)
- Infiltration and dysfunction of immune cells (monocytes/ macrophages, T cells, B cells and NK cells)





Increased risk for tumor development
in adulthood

STRESS AND CANCER



SLEEP AND CANCER

- A meta-analysis including 8 cohort studies with more than 500,000 participants found a moderate 24% increased risk of cancer for participants with insomnia compared with those without insomnia
- Mostly breast cancer and prostate cancer patients were studied

Shi T, et al. Does insomnia predict a high risk of cancer? A systematic review and meta-analysis of cohort studies. J Sleep Res. 2020;29(1):e12876

Virus	Mechanism	Cancer
Hepatitis B and C	Increased Inflammation	Hepatocellular carcinoma
Epstein Barr Virus	Cell proliferation, inhibition of Apoptosis	Burkitt's Lymphoma Hodgkin's Lymphoma
HIV	Immunosuppression	Kaposi's, Lymphoma
Human Papilloma Virus	Inhibition of DNA damage response, decreased apoptosis	Cervical carcinoma, Anal and Head and Neck Ca
Human T cell Lymphotropic Virus	Immortalization and transformation of T cells	Adult T cell Leukemia and Lymphoma

COFFEE- CANCER RISK

COFFEE AND CANCER

- Colon cancer patients consuming 4 or more cups per day of caffeinated coffee during and six months after adjuvant chemotherapy experienced a reduced cancer recurrence or mortality risk compared with abstainers (HR 0.48, 95% CI 0.25-0.91)

- Coffee might reduce the risk of colon cancer recurrence and death through improved insulin sensitization and decreased hyperinsulinemia.

Coffee Intake, Recurrence, and Mortality in Stage III Colon Cancer: Results From CALGB 89803 (Alliance). Guercio BO, J Clin Oncol. 2015;33(31):3598. Epub 2015 Aug 17.

COFFEE AND CANCER

- Data suggest an association between coffee (both caffeinated and decaffeinated) and survival in patients with metastatic colorectal cancer.
- A prospective observational cohort study of 1171 patients with treatment-naïve metastatic CRC who participated in a randomized trial, increased consumption of coffee was associated with decreased risk of cancer progression and increased overall survival.

Association of Coffee Intake With Survival in Patients With Advanced or Metastatic Colorectal Cancer.AUMackintosh C, Yuan C, Ou FS, Zhang S, Niedzwiecki D, Chang IW, O'Neil BH, Mullen BC, Lenz HJ, Blanke CD, Venook AP, Mayer RJ, Fuchs CS, Innocenti F, Nixon AB, Goldberg RM, O'Reilly EM, Meyerhardt JA, Ng K SOJAMA Oncol. 2020;6(11):1713.

SOCIAL SUPPORT

- Higher levels of social support satisfaction had lower mortality risk than individuals reporting lower levels of satisfaction.
- The amount of support received, on the other hand, was not predictive of cancer survival.
- Individuals reported higher levels of social support satisfaction had lower levels of CRP, IL-6, and TNF-α and decreased mortality.

- *Boen CE, Barrow DA, Bensen JT, Farnan L, Gerstel A, Hendrix LH, Yang YC. Social Relationships, Inflammation, and Cancer Survival. Cancer Epidemiol Biomarkers Prev. 2018 May;27(5):541-549. doi: 10.1158/1055-9965.EPI-17-0836. Epub 2018 Feb 23. PMID: 29475966; PMCID: PMC5932225.*

CONCLUSIONS-LIFESTYLE AND CANCER

*Life style modifications are very important in preventing cancer and recurrence

*Quit smoking, Cut drinking

*Walk more, Worry less

*Eat right with less meat, more veggies and fruit

*Lose weight, Sleep tight

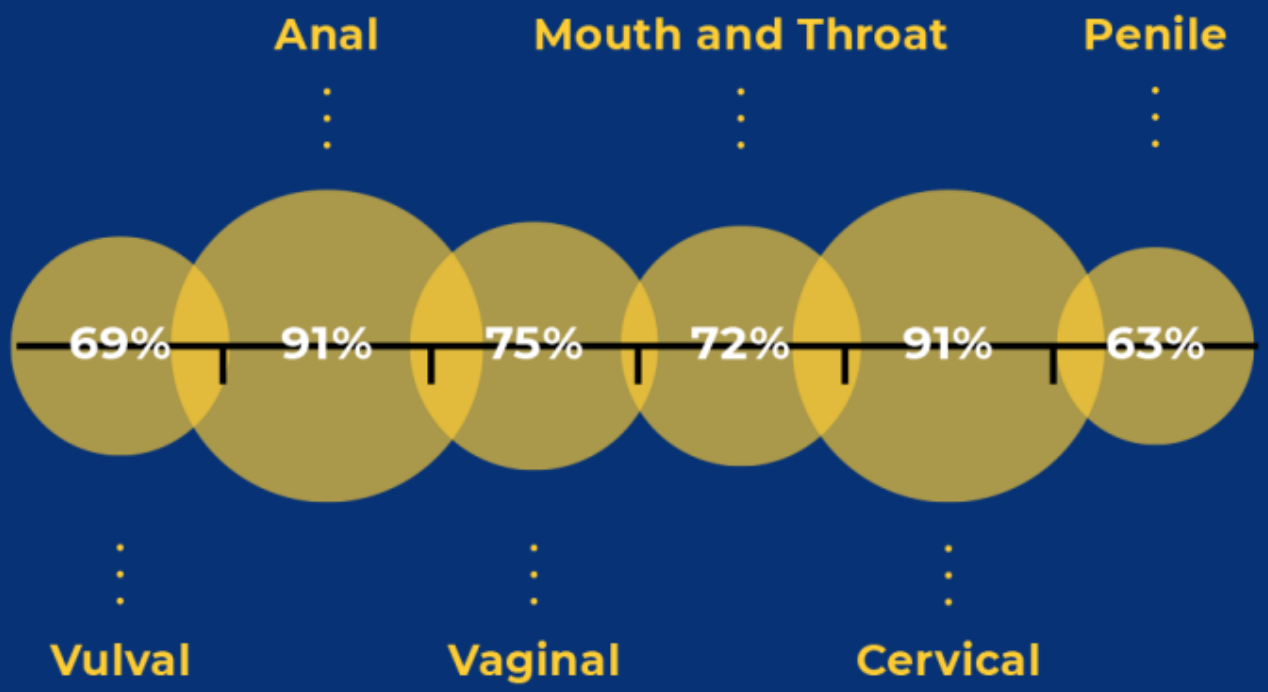
*Protect from sun as much as you can

*Beware of Viruses

You can’t change your genes, but you can change your life style!

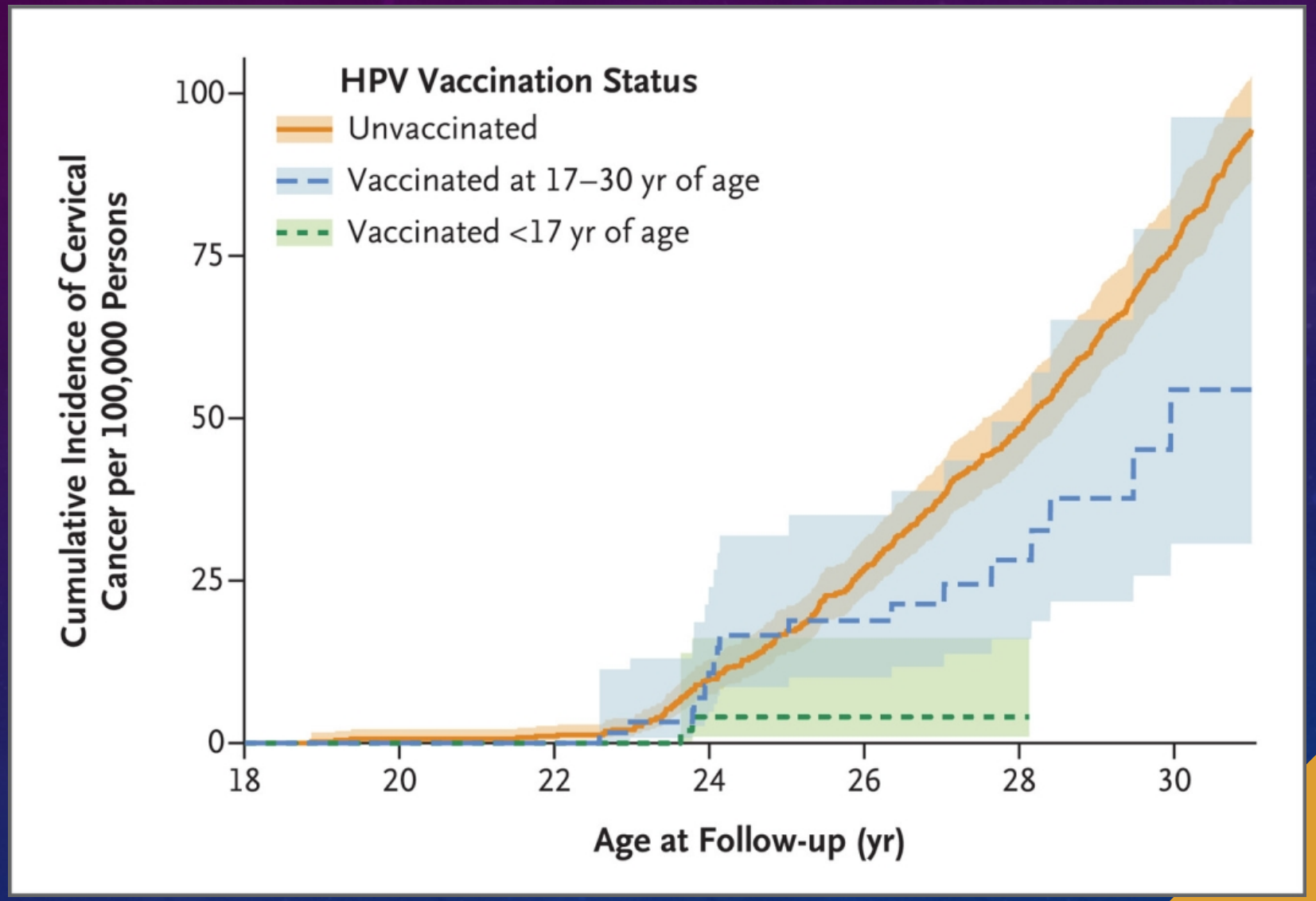
What cancers are caused by HPV?

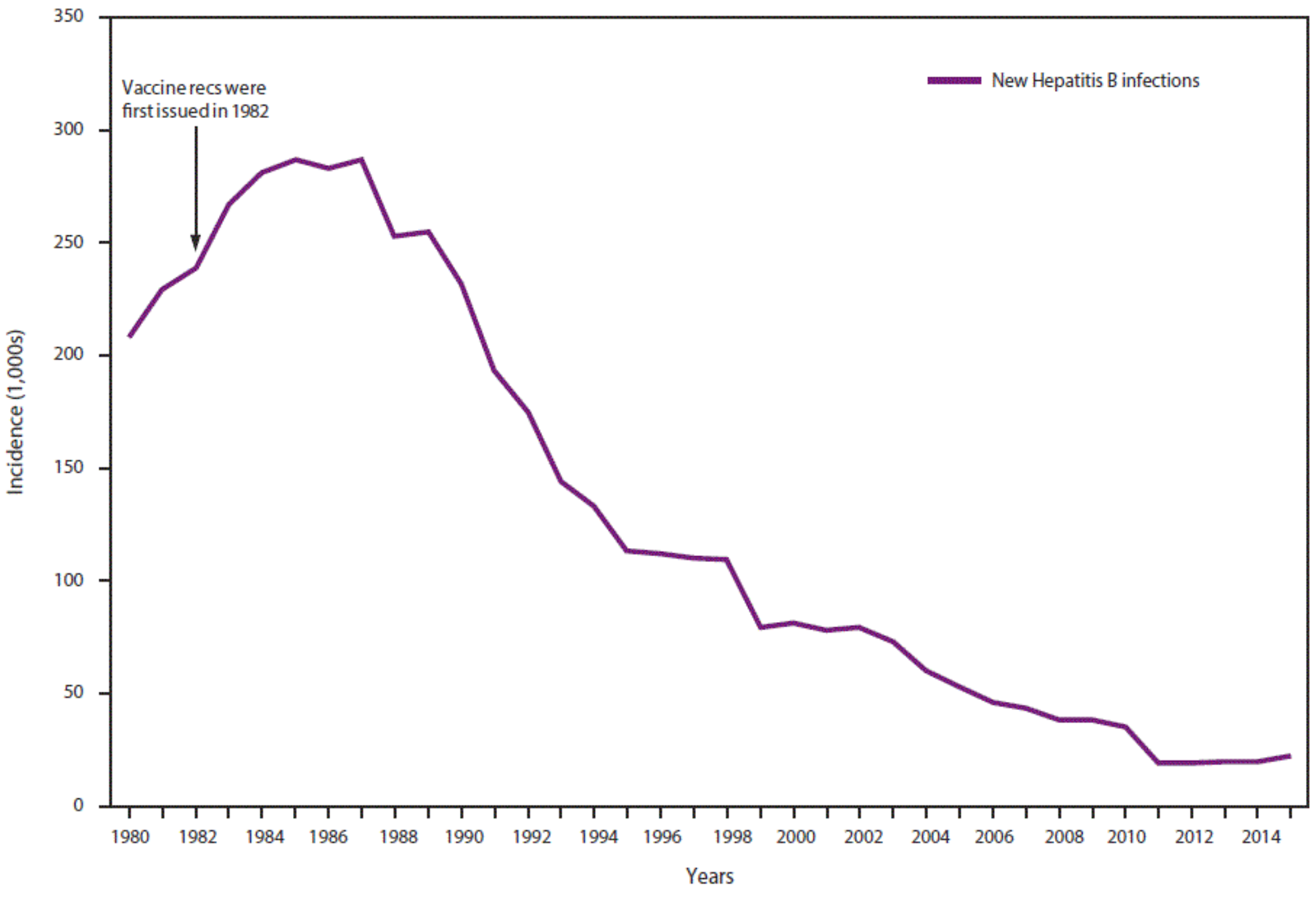
HPV causes the following percentages of six cancers.

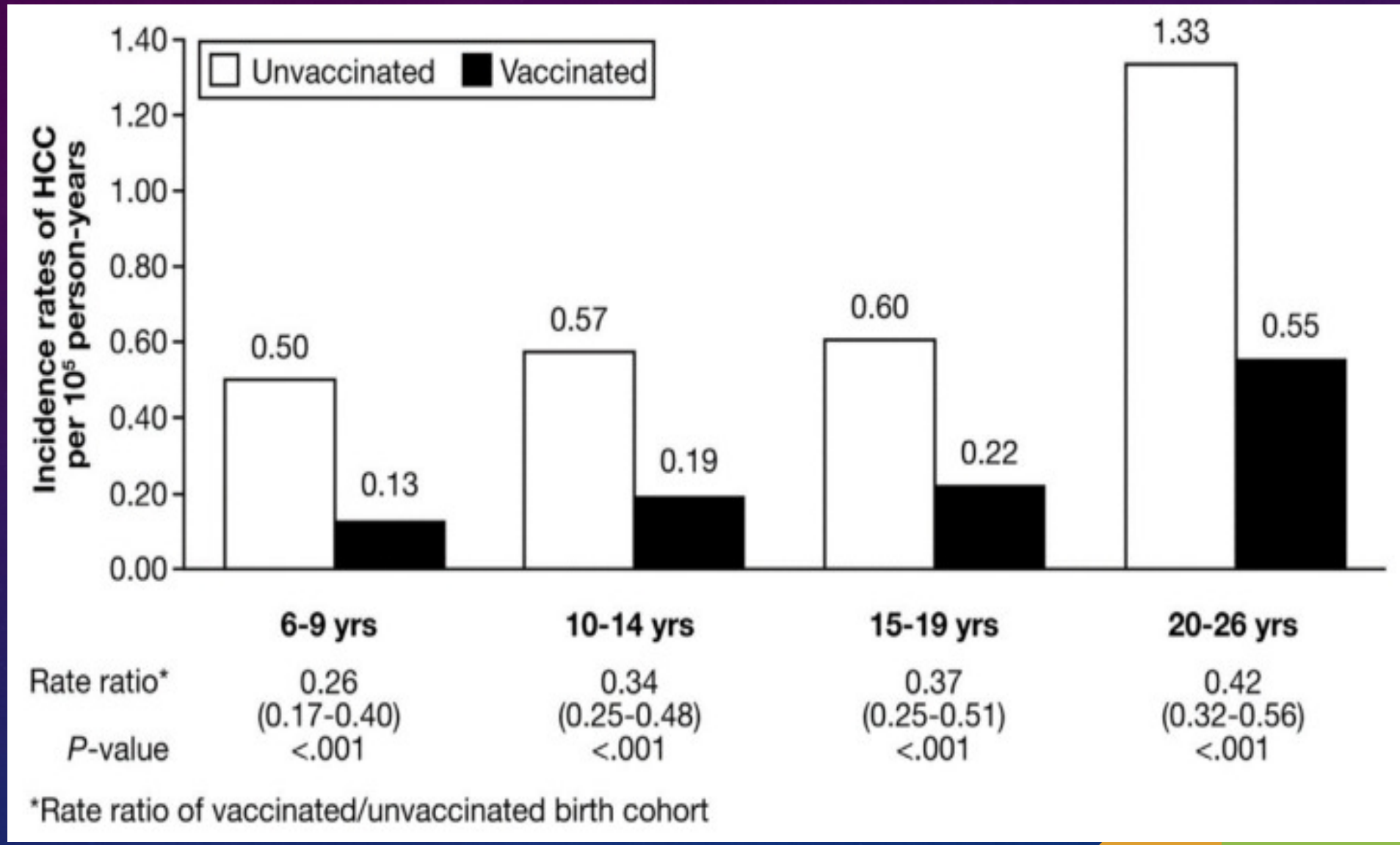


VACCINES

- HPV Vaccine
- HBV Vaccine

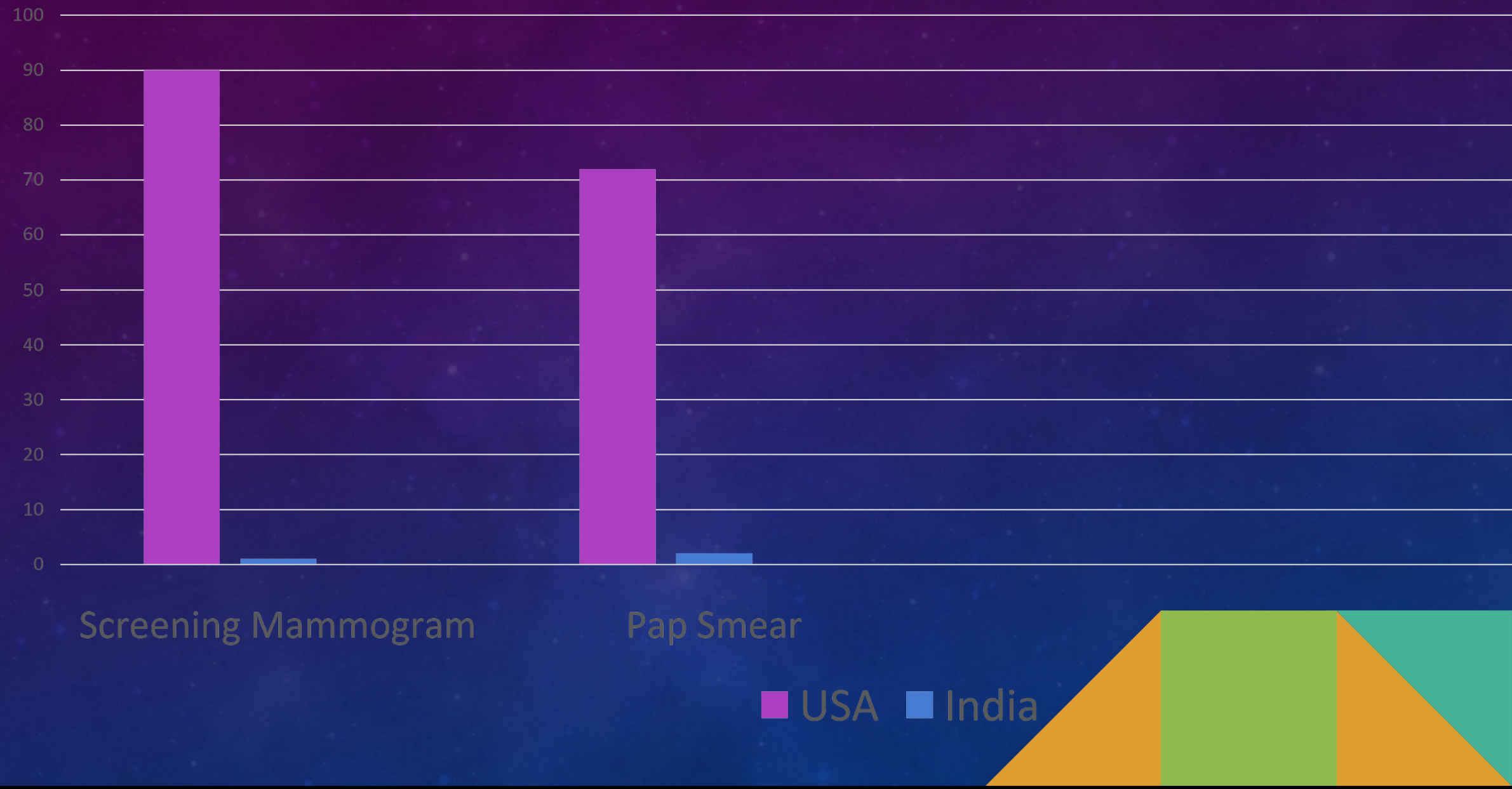

HPV Vaccination Status
Unvaccinated
Vaccinated at 17–30 yr of age
Vaccinated <17 yr of age
Cumulative Incidence of Cervical Cancer per 100,000 Persons
100
75
50
25
0
18
20
22
24
26
28
30
Age at Follow-up (yr)


Vaccine recs were first issued in 1982
New Hepatitis B infections
Incidence (1,000s)
350
300
250
200
150
100
50
0
1980
1982
1984
1986
1988
1990
1992
1994
1996
1998
2000
2002
2004
2006
2008
2010
2012
2014
Years


Unvaccinated
Vaccinated
Incidence rates of HCC per 10^5 person-years
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
0.50
0.13
0.57
0.19
0.60
0.22
1.33
0.55
6-9 yrs
10-14 yrs
15-19 yrs
20-26 yrs
Rate ratio*
0.26 (0.17-0.40)
0.34 (0.25-0.48)
0.37 (0.25-0.51)
0.42 (0.32-0.56)
P-value
<.001
<.001
<.001
<.001
*Rate ratio of vaccinated/unvaccinated birth cohort

CHALLENGES

- Increasing incidence in younger individuals
- Global Disparities
- Barriers to Lifestyle Changes
- Access to Vaccines and Screenings


100
90
80
70
60
50
40
30
20
10
0
Screening Mammogram
Pap Smear
USA
India

GLOBAL REDUCTION OF CANCER CAMPAIGN

- STOP 3 AND START 3
  - Stop 3- Smoking, Alcohol, Processed meat
  - Start 3- Physical activity, Screening, Vaccines