

M U N I
M E D

Primary prevention of cancer

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Causes of cancer

Although individual types of cancers have different causes, it is possible to express which main factors and to what extent they contribute to the overall mortality from tumors, or to the occurrence - the occurrence of tumors. The results of the analysis published by 1981 by Doll and Peto are still more or less valid, and do not differ fundamentally from other, later analyzes.

Analysis of the causes of cancer (Doll & Peto 1981):

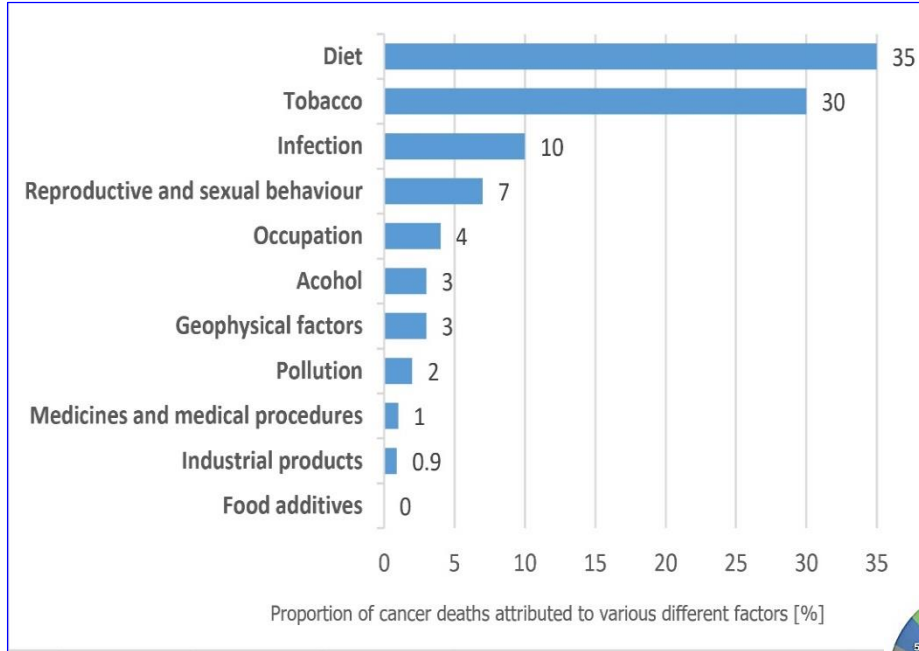


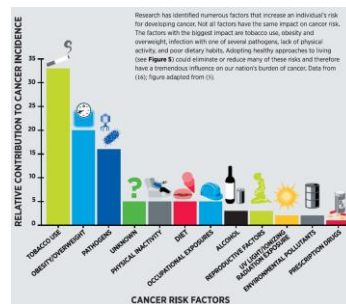
Table: Comparison with other similar analyzes

	Doll and Peto 1981	Anand 2008	AICR 2012	US	UK cancer research	AACR
Tobacco	30 (25-40)	25-30	33	30	19,4	33
Diet	35	30-35	5	30	9,2	5
Overweight and obesity		10-20	20	15	5,5	20
Infection	10? (1-?)	15-20	5	7		16
Alcohol	3 (2-4)	4-6	3	4	4	
Physical inactivity				5	1	5
Radiation (solar + ionizing)	3 (geofys.f.)		2	3	3,5	2
Occupational	4 (2-8)		5	3	3,7	
Environmental pollution	2 (-1-5)		2	1,5		
Prescriptions drugs and medical procedures	1 (0,5-3)		1	1,5	0,5	

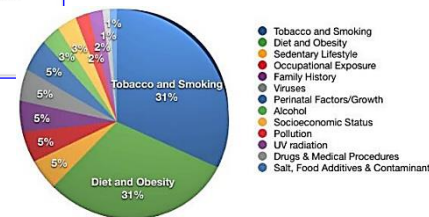
PREVENTABLE CAUSES OF CANCER

Among the factors with the biggest impact on cancer incidence in the United States are the following:

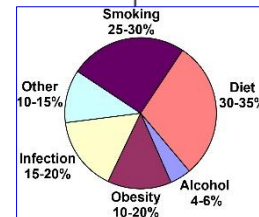
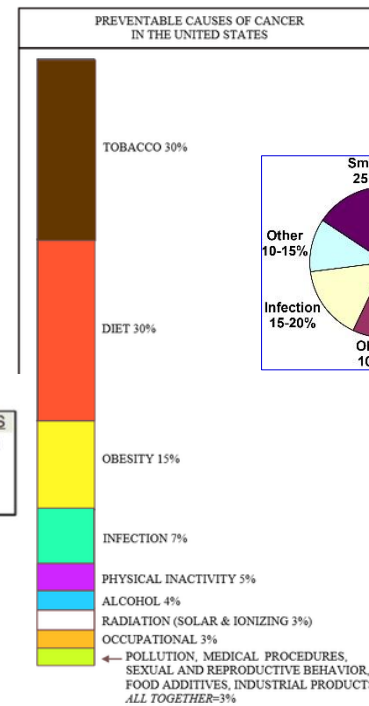
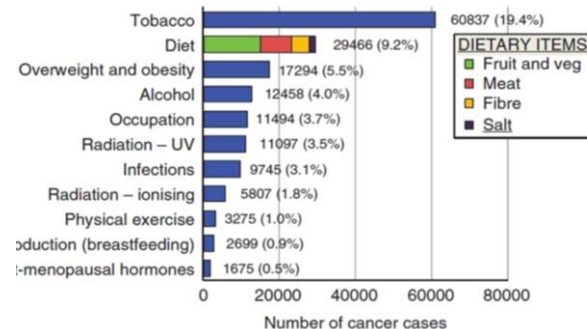
- ~33% of cancer diagnoses are caused by tobacco use.
- ~20% of cancer diagnoses are related to individuals being obese or overweight.
- ~16% of cancer diagnoses are related to infection with one of several cancer-causing pathogens.
- ~5% of cancer diagnoses are related to individuals getting insufficient physical activity.
- ~5% of cancer diagnoses are related to individuals having poor dietary habits.
- ~2% of cancer diagnoses are a result of exposure to ultraviolet light from the sun or tanning devices.



AICR/WCR 2007:

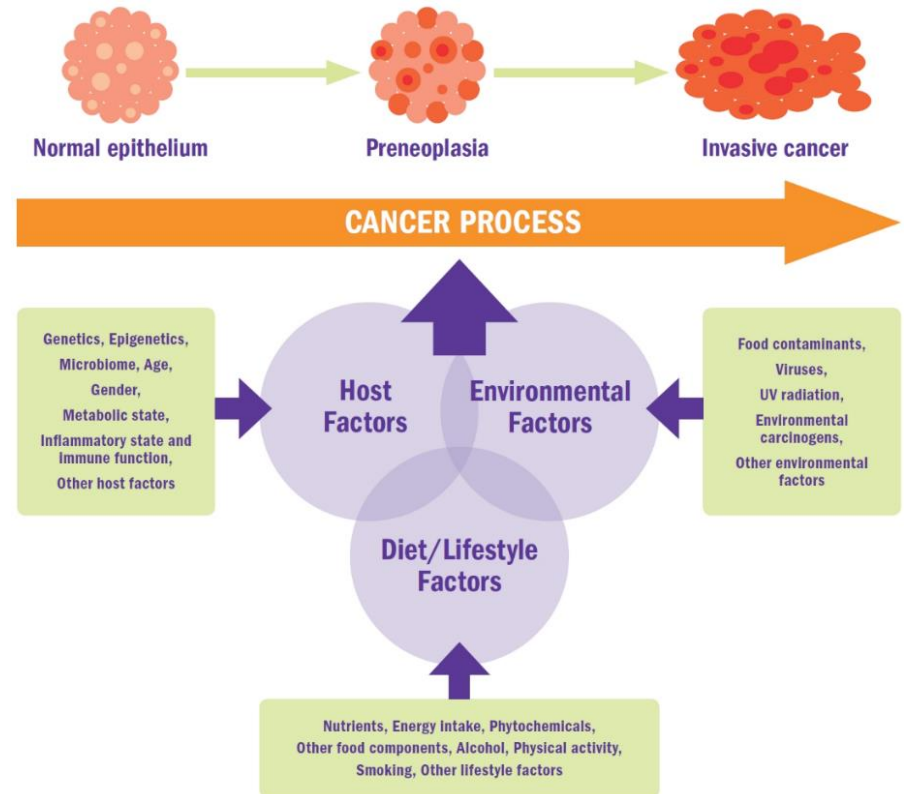


UK cancer research:



Carcinogens vs. factors affecting cancer risk

- **A carcinogen** is any factor (chemical, physical or biological agent - such as a virus, radionuclide or industrial process etc.) that causes cancerous cell proliferation, leading to the appearance of cancerous tumors.
- The official carcinogen database is maintained by the International Agency for Research on Cancer (IARC), which also categorizes them according to the level of scientific evidence on the association between exposure to a given factor and the incidence of cancer (see next slide).
- In contrast, "**Factors influencing cancer risk**" include both carcinogens (increasing the risk), but also protective factors that reduce the risk and protect against tumors.
- Furthermore, these or other factors can modify the risk by either influencing - modifying the action and effects of carcinogens, or influencing the action of protective substances, or directly resistance - the body's immunity.
- "Factors influencing cancer risk" are therefore a much broader concept than just carcinogens. For prevention, it is not enough just to know carcinogens and prevent their action, but it is necessary to know and be able to modify all the factors that determine the resulting risk of cancer.





Classification of carcinogens according to IARC – classes:

Category – group of carcinogenicity:	Group definition:	Number of agents
1	Carcinogenic to humans	121
2A	Probably carcinogenic to humans	82
2B	Possibly carcinogenic to humans	311
3	Not classifiable as to its carcinogenicity to humans	500

Realistic view of "carcinogens" - limits regarding use in primary prevention:

- The action of carcinogens is only one of the links in the chain of carcinogenesis. Whether or not tumors actually arise depends on a number of modifying factors. It can be environmental factors, lifestyle, or the state of the organism (immunity, obesity...)
- The IARC classification of carcinogens by its nature evaluates only risk factors - carcinogens. However, the factors determining the risk of tumors can also be protective, ie those that reduce the risk (for example, some nutritional factors, movement...)
- Many carcinogens pose only a specific risk to specific small groups that may be at risk. However, these findings are not always meaningfully useful for general recommendations on tumor prevention for the general population

Examples of IARC carcinogens:

Factor	Group
<i>Foods, alcohol:</i>	
• Acetaldehyde associated with consumption of alcoholic beverages	1
• Alcoholic beverages	1
• Aflatoxins	1
• Areca nut	1
• Ethanol in alcoholic beverages	1
• Salted fish, Chinese style	1
• Red meat (consumption of)	2A
• Processed meat (consumption of)	1
<i>Infection:</i>	
• Helicobacter pylori (infection with)	1
• Hepatitis B virus (chronic infection with)	1
• Hepatitis C virus (chronic infection with)	1
• Human immunodeficiency virus type 1 (infection with)	1
• Human papillomavirus	1
• Human T-cell lymphotropic virus type I	1
<i>Drugs - therapy:</i>	
• Estrogen therapy - postmenopausal	1
• Estrogen–progesteron menopausal therapy (combined)	1
• Estrogen-progesteron oral contraceptives (combined) (NB: There is also convincing evidence on protective effect against cancer in the endometrium and ovary)	1
• Androgenic (anabolic) steroids	2A
• Phenacetin	1
• Phenacetin, analgesic mixtures containing	1
<i>Radiation:</i>	
• Ionizing radiation (all types)	1
• X- and Gamma-radiation	1
• Ultraviolet radiation (wavelengths 100-400 nm, encompassing UVA, UVB and UVC)	1
• Ultraviolet-emitting tanning devices	1
<i>Other:</i>	
• Rubber manufacturing industry	1
• Nickel compounds	1
• Iron and steel founding (occupational exposure during)	1
• Wood dust	1

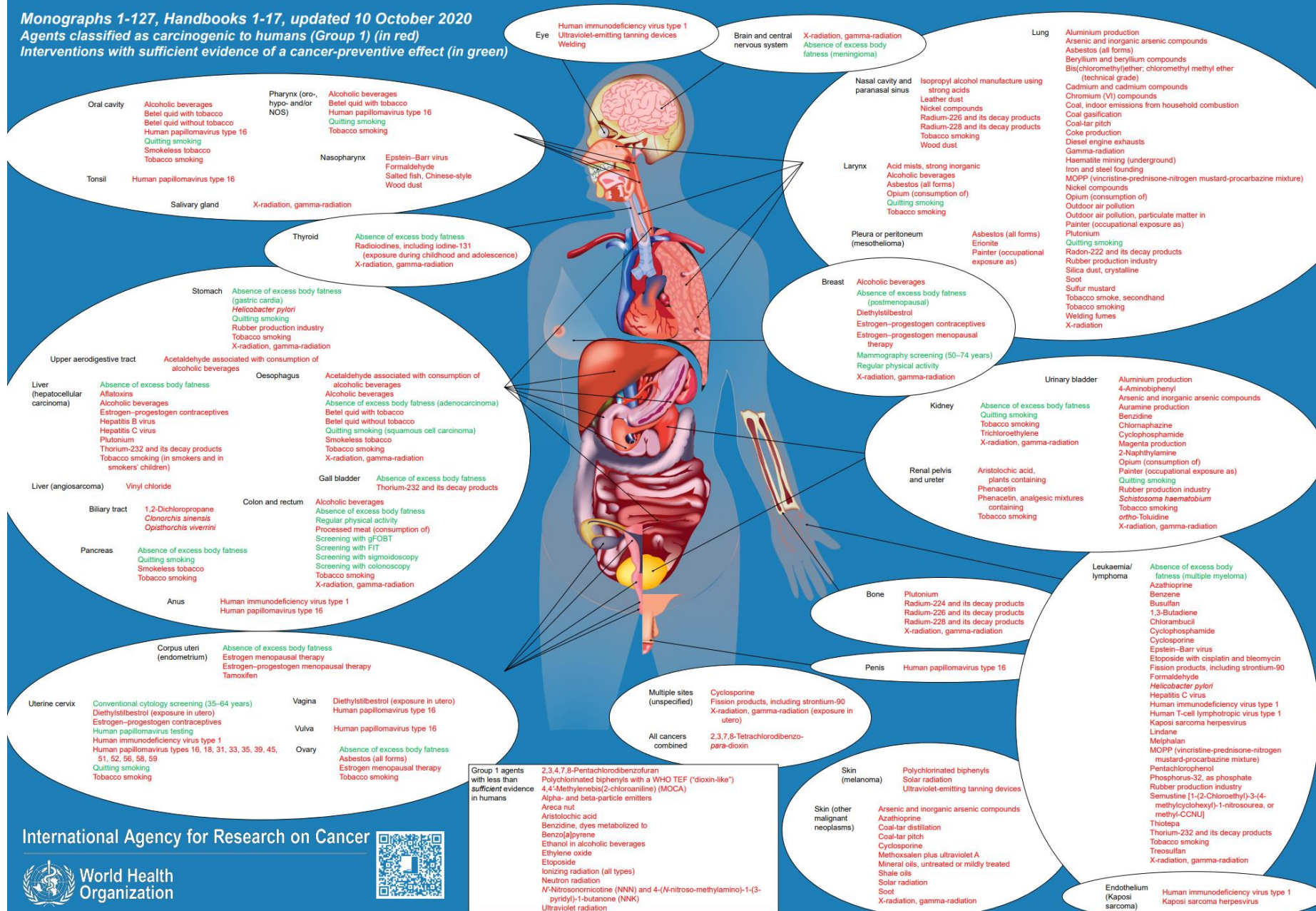
Human Cancer: Known Causes and Prevention by Organ Site

IARC Monographs on the Identification of Carcinogenic Hazards to Humans and Handbooks of Cancer Prevention

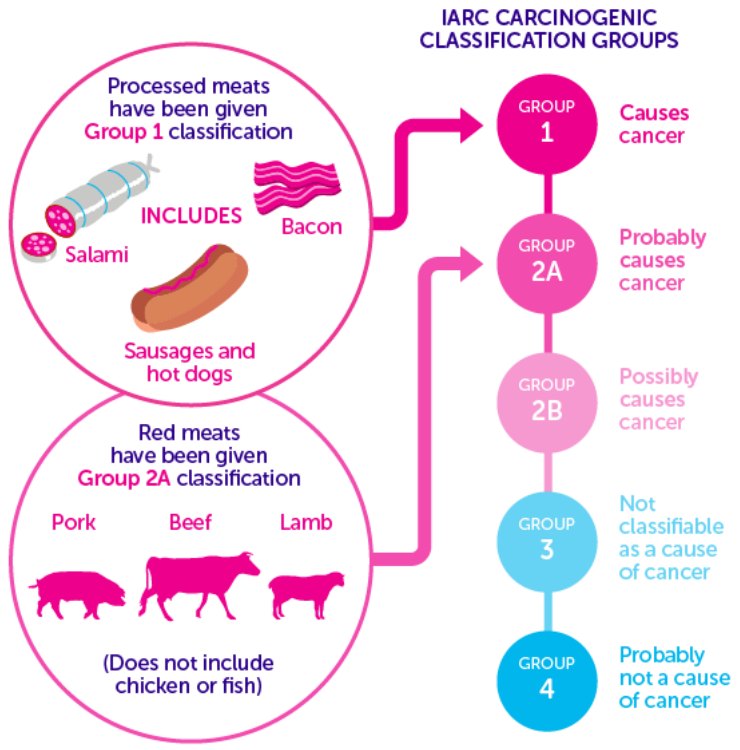
Monographs 1-127, Handbooks 1-17, updated 10 October 2020

Agents classified as carcinogenic to humans (Group 1) (in red)

Interventions with sufficient evidence of a cancer-preventive effect (in green)



MEAT AND CANCER HOW STRONG IS THE EVIDENCE?



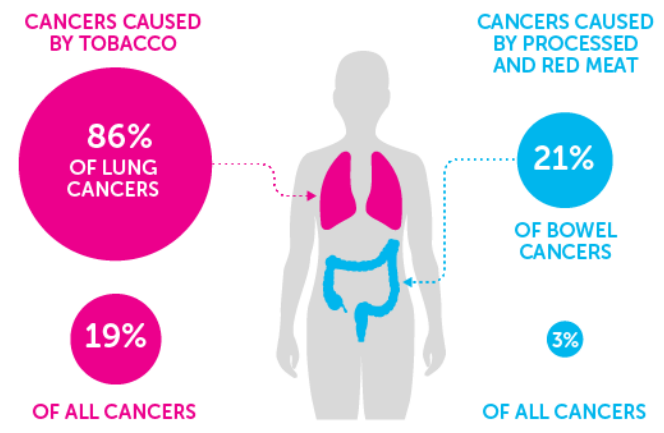
These categories represent how likely something is to cause cancer in humans, not how many cancers it causes.

WE WILL BEAT CANCER SOONER
cruk.org



TOBACCO vs MEAT WHAT'S THE RISK?

The **EVIDENCE** that processed meat causes cancer is as strong as the evidence for tobacco, but the **RISK** from tobacco is much higher...



THE NUMBER OF CANCERS PER YEAR IN THE UK THAT COULD BE PREVENTED IF...



Source: cruk.org/cancerstats

WE WILL BEAT CANCER SOONER
cruk.org



Cancer caused by tobacco use

Smoking causes:

30 % of all cancers

90 % of all lung and bronchus cancers

Cancer sites with a significant causal attribution of tobacco:

1. Lung and bronchus
2. Myeloid leukemia

Urogenital system:

3. Kidney
4. Ureter
5. Bladder
6. Ovary
7. Uterine Cervix

Head and Neck:

8. Oral cavity
9. Larynx
10. Hypopharynx
11. Nasopharynx
12. Oropharynx
13. Nasal cavity

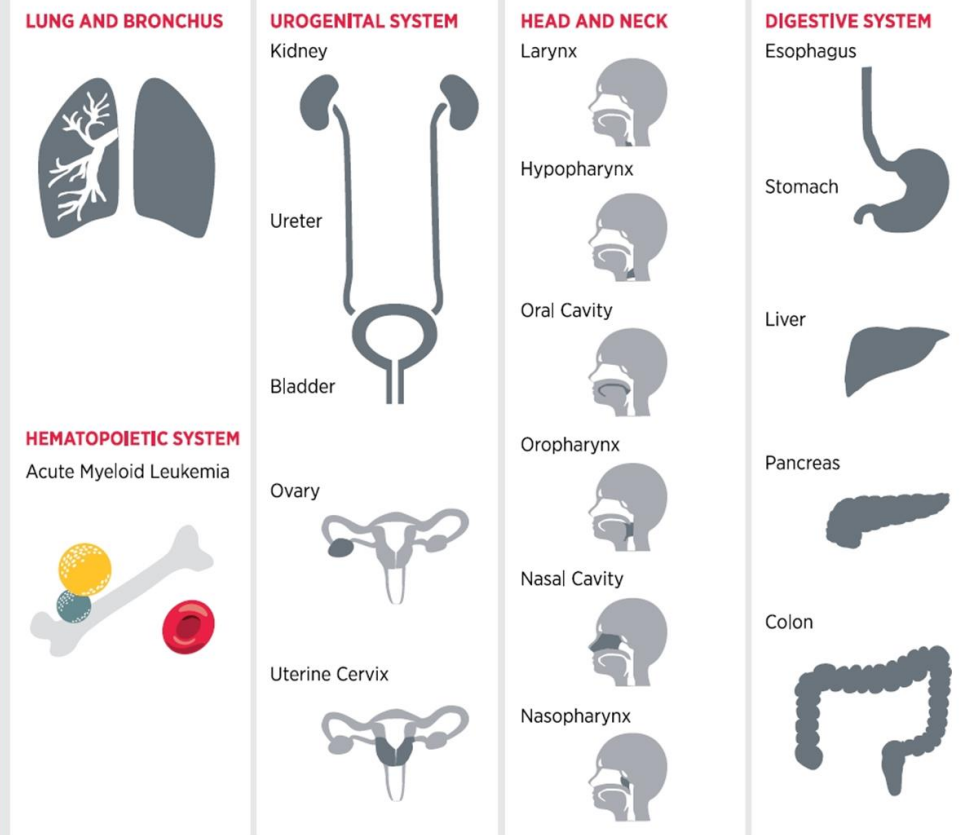
Digestive system:

14. Esophagus
15. Stomach
16. Liver
17. Pancreas
18. Colon

More:

19. Breast – limited evidence

FIGURE 6 | BEYOND THE LUNGS: CANCERS CAUSED BY TOBACCO USE

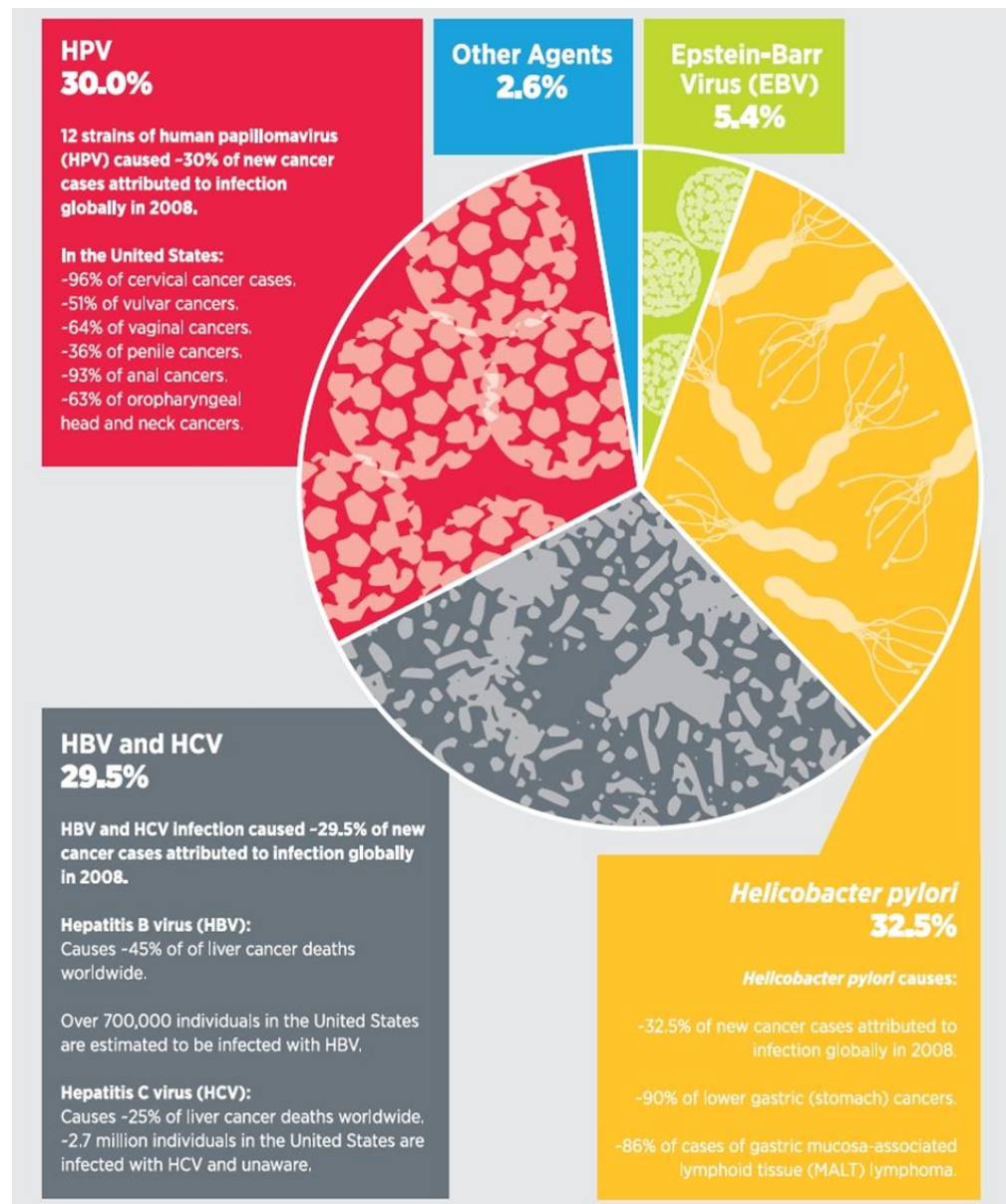


Tobacco use increases an individual's risk of developing not only lung cancer but also 17 other types of cancer (11). This explains why tobacco use will account for an estimated 30 percent of all cancer deaths in the United States in 2014 (1).

Influence of different infections on cancer risk

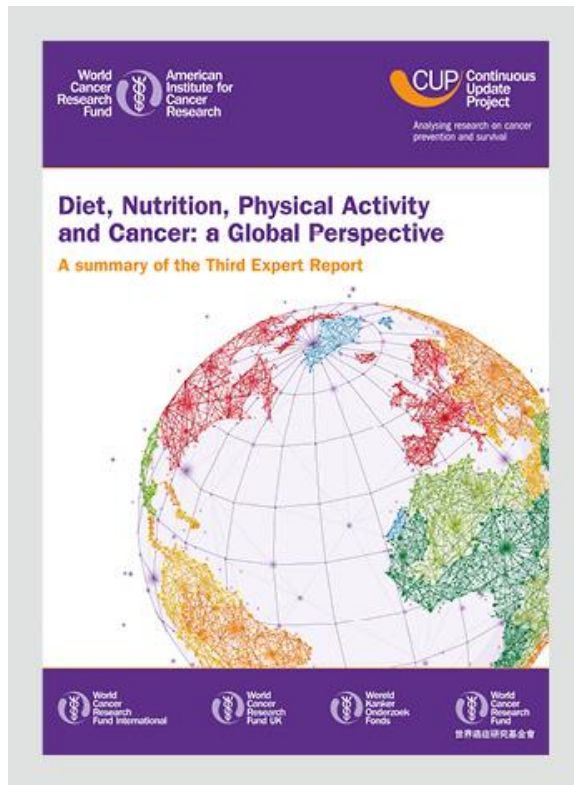
(% of all cancer cases attributed to infection globally)

- **Helicobacter pylori - 32.5 %**
- **HPV (Human Papillomavirus) - 30 %**
- **HBV a HCV (Hepatitis B+C) - 29.5 %**
- **EBV (Epstein-Barr) - 5.4 %**
- **Other agents - 2.6 %**

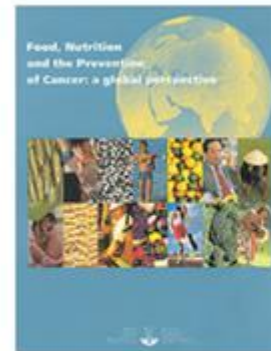


Influence of nutritional factors (and physical activity) on the risk of cancer

- The extensive report "**Diet, Nutrition, Physical Activity and Cancer: a Global Perspective - The Third Expert Report, 2018**" by an international panel of experts, based on a meta-analytical summary of more than 4,000 studies, provides the best and most comprehensive summary of the influence of nutritional factors (+ physical activity) on cancer risk.
- This is the third report in a row, they are published with a periodicity of approximately 10 years.
- Particular attention is paid to the quality of evidence. These are graded into classes, with clearly defined criteria, and any conclusions must be supported by sufficiently good evidence.



World Cancer Research Fund International: **Diet, Nutrition, Physical Activity and Cancer: a Global Perspective - The Third Expert Report**. London, UK: World Cancer Research Fund International; 2018 Available from: <https://www.wcrf.org/dietandcancer>



1997



2007



2018

Quality of evidence of effect

Grading the quality of evidence according to WCR / AICR - Diet, Nutrition, Physical Activity and Cancer: a Global Perspective:

EVIDENCE		Decreases risk	Increases risk
Strong evidence	Convincing	BASIS FOR RECOMMENDATIONS	
	Probable		
Limited evidence	Limited - suggestive	Cannot be used for recommendations	
	No conclusions		
Strong evidence	Substantial effect on risk unlikely		

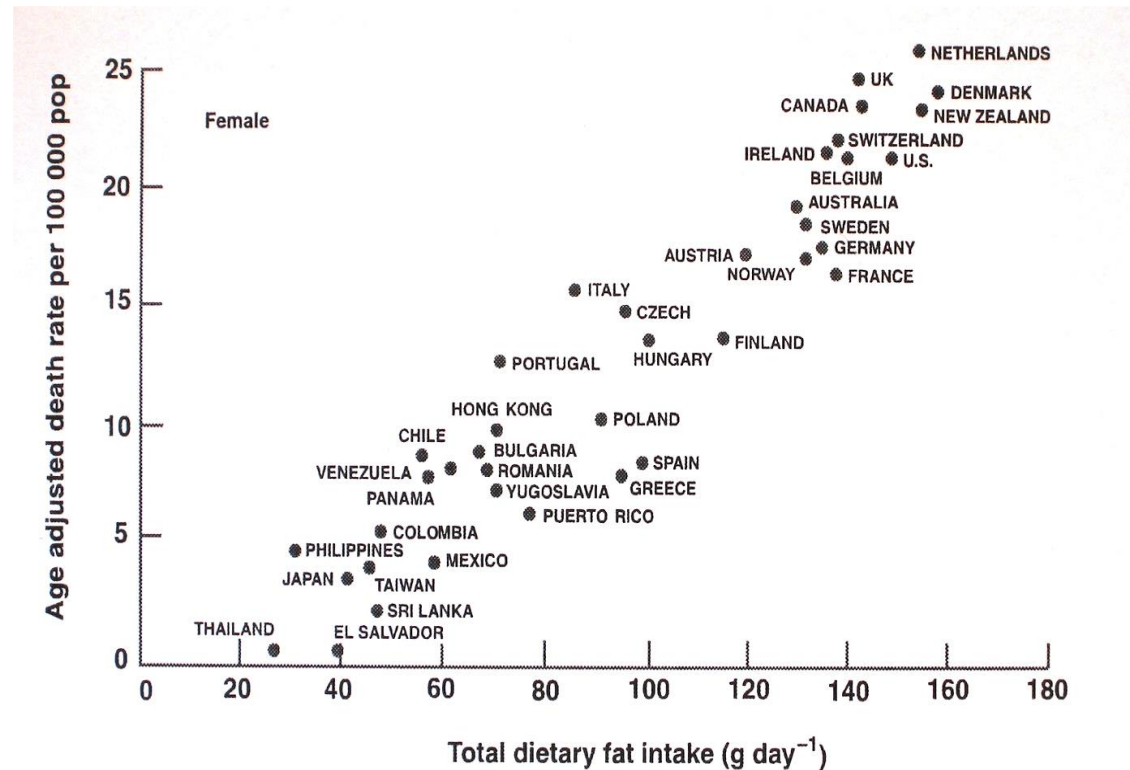
- In general, **epidemiological studies** are the only sufficient source for assessing the effect of a factor on cancer risk.
- They must therefore be performed on the human population and meet certain requirements. The results obtained from an in vitro experiment, on cell cultures, on animals cannot serve as sufficient evidence. These studies can be used to create - formulate hypotheses, but not to confirm them.
- Dosage - exposure - must correspond to real living conditions. Confirmation of carcinogenicity at extreme exposures says nothing about the real risk to the general population.
- The basic requirement is the confirmation of causality, the exclusion of **confounding** and **bias** factors. This is greatly aided by the adequate design of the study, which determines the final quality of the evidence and can eliminate the influence of different "biases". A distinction must be made between three basic types of epidemiological studies: 1) **correlation** studies, 2) **case-control** studies, and 3) **prospective** studies.
- The quality of the evidence is therefore determined by the type, quality of the design and the number of epidemiological studies performed

Correlations studies

An example of misleading results:

- The chart shows the correlation between total dietary fat intake and breast Ca mortality - a comparison of different countries.
- Based on the correlation, it was concluded that high fat consumption is a risk for cancer.
- Later, other epidemiological methods have shown that this conclusion is completely wrong, and the link is due to other, associated factors, which also vary from country to country, in addition to fat consumption...
- There is undoubtedly a significant correlation here, but not a causal one.

This impressive correlation is not a causal association!



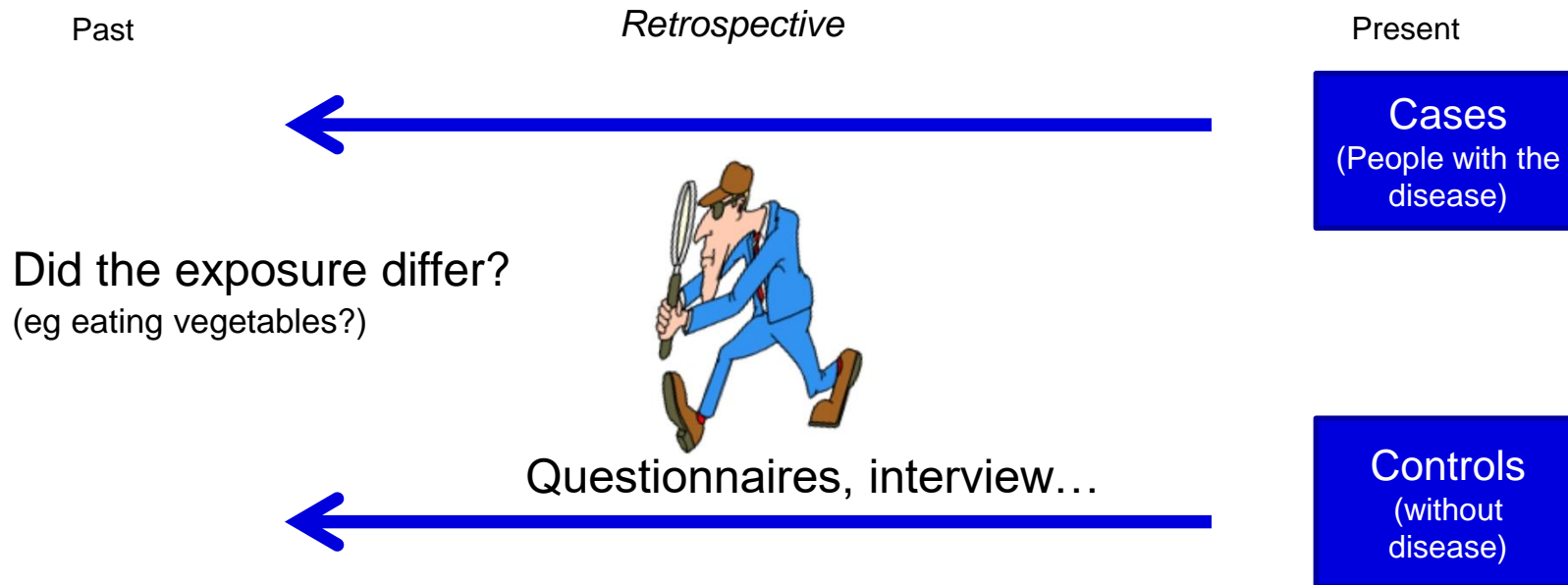
Advantages of correlation studies:

- Undemanding, easy, fast and cheap design.

Disadvantages - weaknesses of correlation studies:

- Data are not obtained on individuals, but in bulk, usually from national statistics or other aggregate results.
- Therefore, data on exposure and outcome cannot be directly related (especially causal), and the analysis is burdened with a large error and inaccuracies.
- They cannot be used at all to confirm hypotheses, but only to create them.

Case-control epidemiological studies



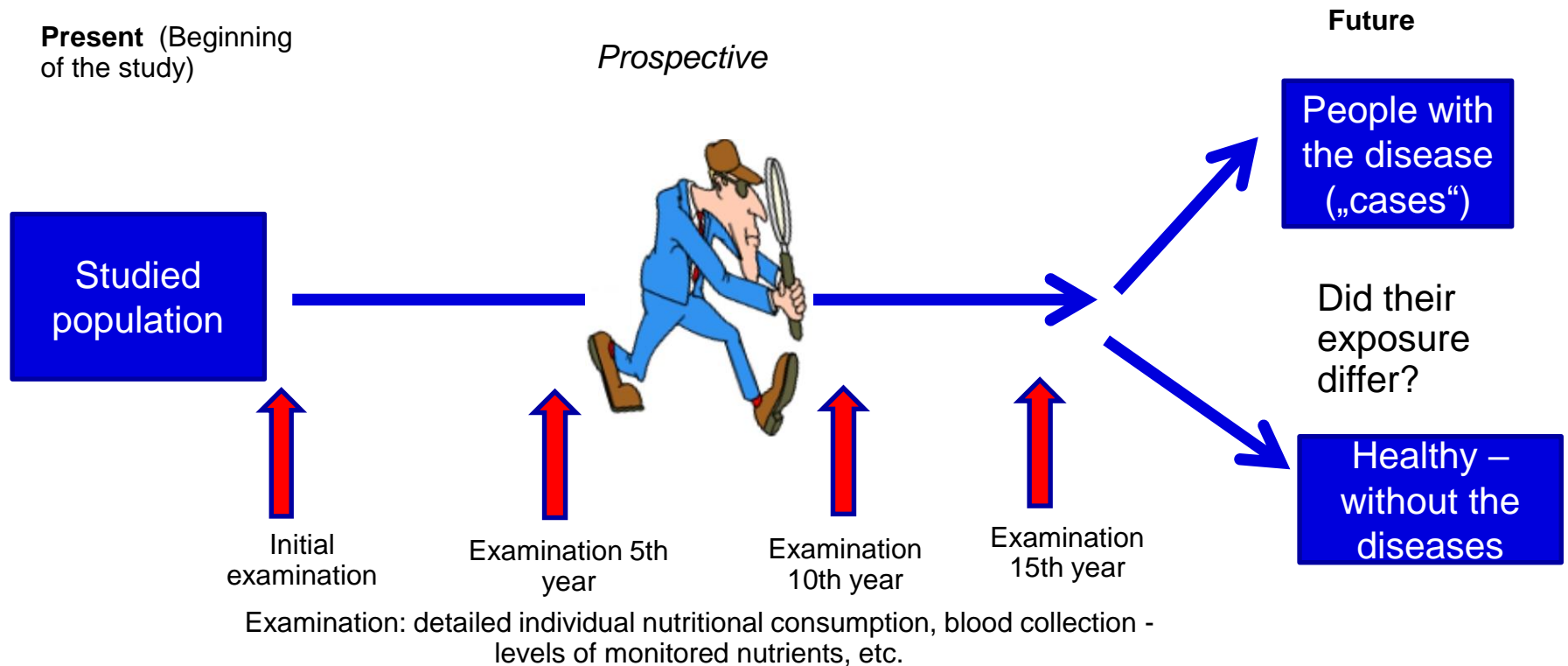
Advantages of case-control studies:

- Easy to carry out, data getting easily and quickly

Disadvantages - weaknesses of case and control studies:

- Data are obtained retrospectively, subjective reporting can be distorted and biased.

Prospective cohort study



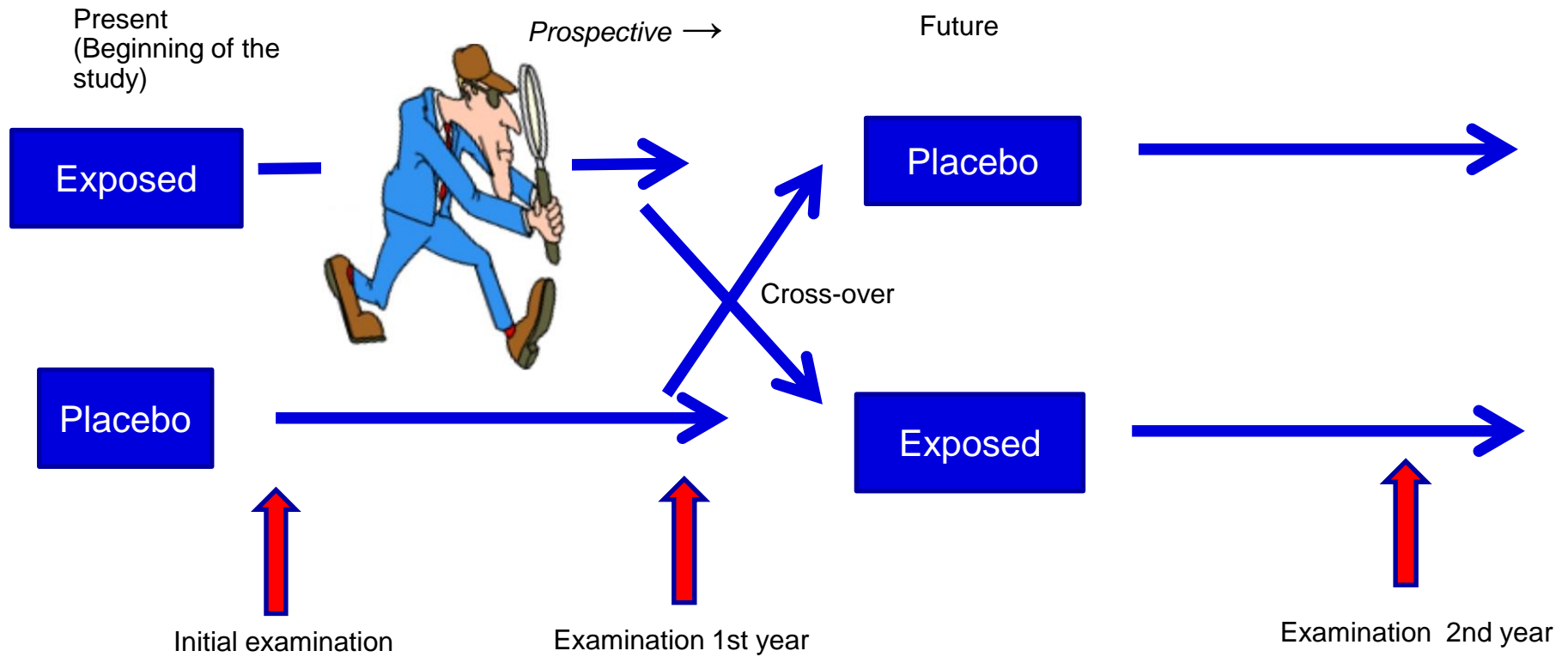
Advantages of a prospective cohort study:

- Data are collected in real time, continuously, it can also be an objective measurement. The results are not affected by the awareness of any observed diseases.
- This is the most accurate study, the only one that meets the current criteria for sufficient quality of evidence.

Disadvantages - weaknesses of the prospective cohort study

- Very demanding to carry out, very long duration, very large sample required

Randomized controlled trial (RCT)



Convincing (strong evidence)

Evidence strong enough to support a judgement of a convincing causal (or protective) relationship, which justifies making recommendations designed to reduce the risk of cancer. The evidence is robust enough to be unlikely to be modified in the foreseeable future as new evidence accumulates.

All of the following are generally required:

- Evidence from more than one study type
- Evidence from at least two independent cohort studies
- No substantial unexplained heterogeneity within or between study types or in different populations relating to the presence or absence of an association or direction of effect.
- Good-quality studies to exclude with confidence the possibility that the observed association results from random or systematic error, including confounding, measurement error and selection bias.
- Presence of a plausible biological gradient (dose-response) in the association. Such a gradient need not be linear or even in the same direction across the different levels of exposure, so long as this can be explained plausibly.
- Strong and plausible experimental evidence, either from human studies or relevant animal models, that typical human exposures can lead to relevant cancer outcomes.

Probable (strong evidence)

Evidence strong enough to support a judgement of a probable causal (or protective) relationship, which generally justifies recommendations designed to reduce the risk of cancer.

All of the following are generally required:

- Evidence from at least two independent cohort studies or at least five case-control studies.
- No substantial unexplained heterogeneity between or within study types in the presence or absence of an association, or direction of effect.
- Good-quality studies to exclude with confidence the possibility that the observed association results from random or systematic error, including confounding, measurement error and selection bias.
- Evidence for biological plausibility

Limited – suggestive

Evidence that is too limited to permit a probable or convincing causal judgement but is suggestive of a direction of effect. The evidence may be limited in amount or by methodological flaws, but shows a generally consistent direction of effect. This judgement is broad and includes associations where the evidence falls only slightly below that required to infer a probably causal association through to those where the evidence is only marginally strong enough to identify a direction of effect. This judgment is very rarely sufficient to justify recommendations designed to reduce the risk of cancer; any exceptions to this require special, explicit justification.

All of the following are generally required:

- Evidence from at least two independent cohort studies or at least five case-control studies.
- The direction of effect is generally consistent though some unexplained heterogeneity may be present.
- Evidence for biological plausibility.

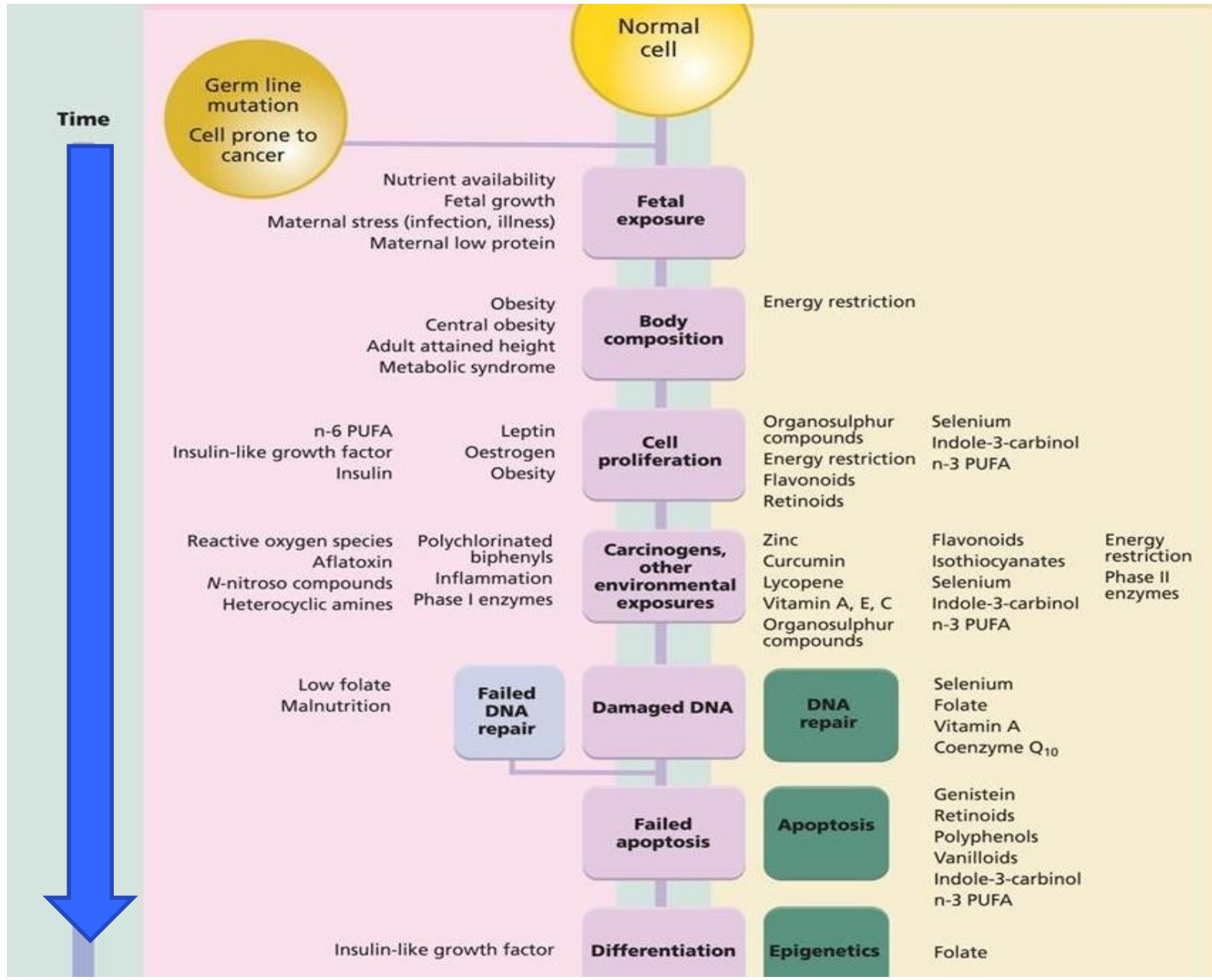
Limited – no conclusion

Evidence is so limited that no firm conclusion can be made. This judgement represents an entry level and is intended to allow any exposure for which there are sufficient data to warrant Panel consideration, but where insufficient evidence exists to permit a more definitive grading. This does not necessarily mean a limited quantity of evidence. A body of evidence for a particular exposure might be graded "limited – no conclusion" for number of reasons. The evidence may be limited by the amount of evidence in terms of the number of studies available, by inconsistency of direction of effect, by methodological flaws (for example, lack of adjustment for known confounders) or by any combination of these factors.

Criteria for the quality of evidence of effect

<i>Category of evidence:</i>	<i>Interpretation:</i>	<i>Inclusion criteria:</i>
A) Convincing	<p>Evidence strong enough to conclude on a causal relationship.</p> <p>They entitle to use in specific goals and recommendations for primary cancer prevention</p>	<ul style="list-style-type: none"> • Evidence from more than one type of study • Evidence from at least two independent cohort studies • No significant unexplained heterogeneity within or between studies • Elimination of the possibility that the association is caused by random or systematic errors, including selection bias
B) Probable	<p>Evidence strong enough to conclude on a probable causal relationship.</p> <p>Usually they entitle to use in the goals and recommendations for prevention.</p>	<ul style="list-style-type: none"> • Evidence from at least two cohort studies, or at least 5 case-control studies • No significant unexplained heterogeneity • Elimination of the possibility that the association is caused by random or systematic errors, including selection bias • Presence of <u>an</u> plausible biological explanation of the effect (mechanism)
C) Limited - suggestive	<p>Evidence too limited to draw a conclusion, but overall promising.</p> <p>Deficiencies may be methodological, limited number of studies, etc.</p> <p>They do not qualify for use in formulating recommendations!</p>	<ul style="list-style-type: none"> • Evidence from at least two cohort studies, or at least 5 case-control studies • The direction of the effect is generally consistent, although some heterogeneity may occur • Presence of <u>an</u> plausible biological explanation of the effect (mechanism)
D) Limited - no conclusions	<p>The evidence is so limited that it does not allow conclusions to be drawn</p>	<ul style="list-style-type: none"> • There is enough data to take the factor seriously into account in terms of possible effect, but there is insufficient evidence for a more precise classification
E) Effect unlikely	<p>The evidence is strong enough to conclude on this</p>	<ul style="list-style-type: none"> • Evidence from more than one type of study • Evidence from at least two independent cohort studies

The influence of nutritional factors on the process of carcinogenesis in various stages and on the risk of cancer



Effect of whole grains, vegetables and fruits on the risk of cancer

WHOLEGRAINS, VEGETABLES AND FRUIT					
Evidence (WCR/AICR grading)		Decreases risk		Increases risk	
		Exposure	Cancer site	Exposure	Cancer site
STRONG EVIDENCE	Convincing			Aflatoxins	• Liver
	Probable	Wholegrains	• Colorectum	Foods preserved by salting (including preserved non-starchy vegetables)	• Stomach
		Foods containing dietary fibre)	• Colorectum		
		Non-starchy vegetables and fruit (aggregated)	• Aerodigestive cancer and some other cancers (aggregated)		
LIMITED EVIDENCE	Limited – suggestive	Non-starchy vegetables	• Mouth, pharynx and larynx • Nasopharynx • Oesophagus • Lung (people who smoke) • Breast (oestrogen-receptors negative)	Non-starchy vegetables (low intake)	• Colorectum
		Fruit	• Oesophagus • Lung (people who smoke or used to smoke) • Breast (oestrogen-receptors negative)	Preserved non-starchy vegetables	• Nasopharynx
		Citrus fruit	• Stomach – cardia		
		Non-starchy vegetables and fruit	• Bladder	Fruit (low intake)	• Stomach • Colorectum
		Foods containing carotenoids	• Lung • Breast		
		Foods containing beta-carotene	• Lung		
		Foods containing vitamin C	• Lung (people who smoke tobacco) • Colorectum		
		Foods containing isoflavones	• Lung (people who have never smoked tobacco)		

Effect of meat, fish and dairy products

Diet, Nutrition, Physical Activity and Cancer: a Global Perspective – The Third Expert Report, 2018

MEAT, FISH AND DAIRY PRODUCTS					
Evidence (WCR/AICR grading)		Decreases risk		Increases risk	
		Exposure	Cancer site	Exposure	Cancer site
STRONG EVIDENCE	Convincing			Processed meat	• Colorectum
	Probable	Dairy products	• Colorectum	Red meat Cantonese-style salted fish	• Colorectum • Nasopharynx
LIMITED EVIDENCE	Limited – suggestive	Fish	• Liver • Colorectum	Red meat	• Nasopharynx • Lung • Pancreas
				Processed meat	• Nasopharynx • Oesophagus • Lung • Stomach • Pancreas
				Food containing haem iron	• Colorectum
				Grilled (broiled) or barbecued (charbroiled) meat or fish	• Stomach
		Dairy products	• Breast (pre-meno)		
Diets high in calcium	• Breast (pre-meno) • Breast (post-meno)	Dairy products	• Prostate		
				Diets high in calcium	• Prostate

PRESERVATION AND PROCESSING					
Evidence (WCR/AICR grading)		Decreases risk		Increases risk	
		Exposure	Cancer site	Exposure	Cancer site
STRONG EVIDENCE	Convincing			Processed meat	• Colorectum
	Probable			Cantonese-style salted fish	• Oesophagus
				Foods prepared by salting	• Stomach
LIMITED EVIDENCE	Limited – suggestive			Preserved non-starchy vegetables	• Nasopharynx
				Processed meat	• Nasopharynx • Oesophagus • Lung • Stomach • Pancreas

Diet, Nutrition, Physical Activity and Cancer: a Global Perspective – The Third Expert Report, 2018

ALCOHOLIC DRINKS					
Evidence (WCR/AICR grading)		Decreases risk		Increases risk	
		Exposure	Cancer site	Exposure	Cancer site
STRONG EVIDENCE	Convincing			Alcoholic drinks	<ul style="list-style-type: none"> • Mouth, pharynx and larynx • Liver • Colorectum • Breast (post-meno)
	Probable	Alcoholic drinks	• Kidney	Alcoholic drinks	<ul style="list-style-type: none"> • Stomach • Breast (pre-meno)
LIMITED EVIDENCE	Limited – suggestive			Alcoholic drinks	<ul style="list-style-type: none"> • Lung • Pancreas • Skin (basal cell ca and melanoma)

Other dietary exposures

Diet, Nutrition, Physical Activity and Cancer: a Global Perspective – The Third Expert Report, 2018

OTHER DIETARY EXPOSURES					
Evidence (WCR/AICR grading)		Decreases risk		Increases risk	
		Exposure	Cancer site	Exposure	Cancer site
STRONG EVIDENCE	Convincing			High-dose beta-carotene supplements	• Lung (in people who smoke or used to smoke tobacco)
	Probable	Calcium supplements	• Colorectum	Glycaemic load	• Endometrium
LIMITED EVIDENCE	Limited - suggestive	Healthy dietary patterns	• Mouth, pharynx and larynx	Foods and drinks containing fructose	• Pancreas
		Foods containing retinol	• Lung	Foods containing saturated fatty acids	• Pancreas
		Vitamin D	• Colorectum	Low plasma alpha-tocopherol concentrations	• Prostate
		Foods containing beta-carotene	• Mouth, pharynx	Low plasma selenium concentrations	• Prostate
		Multivitamin supplements	• Colorectum		

NON-ALCOHOLIC DRINKS					
Evidence (WCR/AICR grading)		Decreases risk		Increases risk	
		Exposure	Cancer site	Exposure	Cancer site
STRONG EVIDENCE	Convincing			Arsenic in drinking water	• Lung
	Probable	Coffee	<ul style="list-style-type: none"> • Liver • Endometrium¹ 	Arsenic in drinking water	<ul style="list-style-type: none"> • Bladder • Skin
				Mate ²	• Oesophagus
LIMITED EVIDENCE	Limited - suggestive	Coffee	<ul style="list-style-type: none"> • Mouth, pharynx and larynx • Skin 	Arsenic in drinking water	• Kidney
		Tea	• Bladder	Mate	• Mouth, pharynx, larynx

Effect of other dietary exposures on the risk of cancer

Diet, Nutrition, Physical Activity and Cancer: a Global Perspective – The Third Expert Report, 2018

OTHER DIETARY EXPOSURES

Evidence (WCR/AICR grading)		Decreases risk		Increases risk	
		Exposure	Cancer site	Exposure	Cancer site
STRONG EVIDENCE	Convincing			High-dose beta-carotene supplements	• Lung (in people who smoke or used to smoke tobacco)
	Probable	Calcium supplements	• Colorectum	Glycaemic load	• Endometrium
LIMITED EVIDENCE	Limited - suggestive	Healthy dietary patterns	• Mouth, pharynx and larynx	Foods and drinks containing fructose	• Pancreas
		Foods containing retinol	• Lung	Foods containing saturated fatty acids	• Pancreas
		Vitamin D	• Colorectum	Low plasma alpha-tocopherol concentrations	• Prostate
		Foods containing beta-carotene	• Mouth, pharynx	Low plasma selenium concentrations	• Prostate
		Multivitamin supplements	• Colorectum		

Effect of overweight and obesity

Diet, Nutrition, Physical Activity and Cancer: a Global Perspective – The Third Expert Report, 2018

OVERWEIGHT, OBESITY AND WEIGHT GAIN					
Evidence (WCR/AICR grading)		Increases risk		Decreases risk	
		Exposure	Cancer site	Exposure	Cancer site
STRONG EVIDENCE	Convincing			Adult body fatness	<ul style="list-style-type: none"> • Oesophagus • Pancreas • Liver • Colorectum • Breast post-meno • Endometrium • Kidney
				Adult weight gain	<ul style="list-style-type: none"> • Breast post-meno
	Probable	Adult body fatness	<ul style="list-style-type: none"> • Breast (pre-meno) 	Adult body fatness	<ul style="list-style-type: none"> • Mouth, pharynx and larynx • Stomach (cardia) • Gallbladder • Ovary • Prostate (advances)
Body fatness in young adulthood (18–30r.)		<ul style="list-style-type: none"> • Breast (pre-meno) • Breast (post-meno) 			
LIMITED EVIDENCE	Limited - suggestive			Adult body fatness	<ul style="list-style-type: none"> • Cervix (BMI ≥29)

World Cancer Research Fund International: *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective - The Third Expert Report*. London, UK: World Cancer Research Fund International; 2018 Available from: <https://www.wcrf.org/dietandcancer>

PHYSICAL ACTIVITY					
Evidence (WCR/AICR grading)		Decreases risk		Increases risk	
		Exposure	Cancer site	Exposure	Cancer site
STRONG EVIDENCE	Convincing	Physical activity	• Colorectum (colon)		
	Probable	Physical activity	• Breast (postmeno) • Endometrium		
		Vigorous intensity PA	• Colorectum		
LIMITED EVIDENCE	Limited - suggestive	Physical activity	• Oesophagus • Lung • Liver • Breast (premeno)	Sedentary behaviour	• Endometrium

Effect of lactation

LACTATION					
Evidence (WCR/AICR grading)		Decreases risk		Increases risk	
		Exposure	Cancer site	Exposure	Cancer site
STRONG EVIDENCE	Convincing				
	Probable	Lactation	• Breast		
LIMITED EVIDENCE	Limited - suggestive	Lactation	• Ovary		

World Cancer Research Fund International: *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective - The Third Expert Report*. London, UK: World Cancer Research Fund International; 2018 Available from: <https://www.wcrf.org/dietandcancer>

Strong effect – summary of evidence matrix	Mouth, pharynx, larynx	Nasopharynx	Oesophagus adeno	Oesophagus squamo	Lung	Stomach	Pancreas	Gallbladder	Liver	Colorectum	Breast premeno	Breast postmenopausal	Ovary	Endometrium	Prostate	Kidney	Bladder	Skin	Aerodigestive ca
Wholegrain										Green									
Foods containing dietary fibre										Green									
Aflatoxins									Red										
Food containing beta-caroten																			
Non-starchy vegetables or fruits																			Green
Red meat										Orange									
Processed meat										Red									
Cantonese style salted fish		Orange																	
Dairy products										Green									
Food preserved by salting						Orange													
Arsenic					Red												Orange	Orange	
Mate				Orange															
Coffee									Green					Green					
Sugar sweetened drinks																			
Alcoholic drinks	Red			Red		Orange			Red	Red	Orange	Red					Green		
Mediterranean																			
Western type diet																			
Fast food																			
Glycemic load																			
Hi-dose beta-carotene					Red														
Beta-carotene																			
Calcium supplements										Green									
Physical activity (moderate + vigorous)										Green		Green		Green					
Vigorous PA											Green	Green							
Walking																			
Screen time children																			
Screen time adults																			
Adult body fatness	Orange		Red			Orange	Red	Orange	Red	Red	Green	Red		Red			Red		
Body fatness in young adulthood											Green	Green							
Adult Weight gain												Red							

Summary of evidence matrix		Mouth, pharynx, larynx	Nasopharynx	Oesophagus adeno	Oesophagus squamo	Lung	Stomach	Pancreas	Gallbladder	Liver	Colorectum	Breast premenopausal	Breast postmenopausal	Ovary	Endometrium	Prostate	Kidney	Bladder	Skin	Aerodigestive ca	
Wholegrains, vegetables & fruit	Wholegrain																				
	Refined grains																				
	Foods containing dietary fibre																				
	Aflatoxins																				
	Non-starchy vegetables (greater intake)																				
	Non-starchy vegetables (low intake)																				
	Preserved non-starchy vegetables																				
	Fruit (greater intake)																				
	Fruit (low intake)																				
	Citrus fruit																				
	Non-starchy vegetables & fruit																				
	Foods containing carotenoids																				
	Food containing beta-carotene																				
	Foods containing vit C																				
	Foods containing isoflavones																				
Non-starchy vegetables or fruits (aggregated)																					
Meat, fish & dairy	Red meat																				
	Processed meat																				
	Foods containing haem iron																				
	Fish																				
	Cantonese style salted fish																				
	Grilled (broiled) or barbecued (charbroiled) meat and																				
	Dairy products																				
Soft drinks	Diets high in calcium																				
	Food preserved by salting																				
	Arsenic in drinking water																				
	Mate																				
Other dietary exposures	Coffee																				
	Tea																				
	Sugar sweetened drinks																				
	Alcoholic drinks																				
	Healthy dietary patterns																				
	Mediterranean type dietary pattern																				
	Western type diet																				
	Fast foods																				
	Glycemic load																				
	Foods & drinks containing fructose																				
Fitness	Foods containing saturated fatty acids																				
	Foods containing retinol																				
	Vitamin D (food containing, serum, supplements)																				
	Low plasma alpha-tocopherol																				
	Low plasma selenium concentrations																				
	Hi-dose beta-carotene supplements																				
	Beta-carotene																				
	Calcium supplements																				
	Multivitamin supplements																				
	Physical activity																				
Fitness	Vigorous physical activity																				
	Walking																				
	Sedentary behaviors																				
	Adult body fatness																				
Body fatness in young adulthood																					
Adult Weight gain																					

1) Be a healthy weight

Keep your weight within the healthy range¹ and avoid weight gain in adult life

Goals:

- Ensure that body weight during childhood and adolescence projects towards the lower end of the healthy adult BMI range
- Keep your weight as low as you can within the healthy range through life
- Avoid weight gain (measured as body weight or waist circumference)² throughout adulthood

¹The healthy (or, as defined by WHO, “normal”) range of BMI for adults is 18.5/24.9 m². Different reference ranges have been proposed for Asian populations. Where these ranges differ from the WHO definition, they are to be used as the guide. Further research is required to establish appropriate thresholds in other ethnic groups. The health range for BMI during childhood varies with age.

²WHO recommends keeping waist circumference below 94 cm in men and 80 cm in women (based on data from European people). These values are roughly equivalent to a BMI of around 25 kg/m². For Asian populations, cut-offs for waist circumferences of 90 cm for men and 80 cm for women have been proposed. Further research is required to establish appropriate waist circumference values for other ethnic groups.

2) Be physically active

Be physically active as part of everyday life – walk more and sit less

Goals:

- Be at least moderately physically active¹, and follow or exceed national guidelines
- Limit sedentary habits

¹Moderate physical activity increases heart rate to about 60 to 75 per cent of its maximum.

WHO advises adults to be active daily, taking part through each week in at least 150 min of moderate-intensity, aerobic physical activity or at least 75 min of vigorous, aerobic physical activity (or a combination). This represents a minimum amount of PA for cardiometabolic health. For cancer prevention, it is likely that the greater amount of PA, the greater the benefit. To have significant impact on weight control, higher levels are required (45-60 min of moderate-intensity PA per day).

3) Eat a diet rich in wholegrains

Make wholegrains, vegetables, fruit, and pulses (legumes) such as beans and lentils a major part of your usual diet

Goals:

- Consume diet that provides at least 30 grams per day of fibre¹ from food sources
- Include in most meals foods containing wholegrains, non-starchy vegetables, fruit and pulses (legumes) such as beans and lentils
- Eat a diet high in all types of plant foods including at least five portions of servings (at least 400 grams in total) of a variety of non-starchy vegetables and fruit every day
- If you eat starchy roots and tubers as staple foods, eat non-starchy vegetables, fruit and pulses (legumes) regularly too if possible

¹Measured by the AOAC method.

4) Limit consumption of “fast foods” and other processed foods high in fat, starches or sugars

Limiting these foods helps control calorie intake and maintain a healthy weight

Goals:

- Limit consumption of processed foods high in fat, starches or sugars – including “fast foods”¹, many pre-prepared dishes, snacks, bakery foods and desserts; and confectionery (candy)

¹ “Fast foods” are readily available convenience foods that tend to be energy dense and are often consumed frequently and in large portions

5) Limit consumption of red and processed meat

Eat no more than moderate amounts of red meat¹, such as beef, pork and lamb. Eat little, if any, processed meat²

Goals:

- If you eat red meat, limit consumption to no more than about three portions per week. Three portions is equivalent to about 350 to 500 grams cooked weight of red meat.³ Consume very little, if any, processed meat.

¹ The term “red meat” refers to all types of mammalian muscle meat, such as beef, veal, pork, lamb, mutton, horse and goat.

² The Term “processed meat” refers to meat that has been transformed through salting

³ 500 grams of cooked red meat is roughly equivalent to 700-750 grams of raw meat, but the exact conversion depends on the cut of meat, the proportions of lean meat and fat, and the method and degree of cooking.

6) Limit consumption of sugar sweetened drinks

Drink mostly water and unsweetened drinks

Goals:

- Do not consume sugar sweetened drinks¹

¹ Sugar sweetened drinks are defined here as liquids that are sweetened by adding the sugars, such as sucrose, high fructose corn syrup and sugars naturally present in honey, syrups, fruit juices and fruit juice concentrate. This includes, among others, sodas, sports drinks, energy drinks, sweetened waters, cordials, barley water, and coffee- and tea-based beverages with sugars or syrups added. This does not include versions of these drinks which are “sugar free” or sweetened only with artificial sweeteners.

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7) Limit alcohol consumption

For cancer prevention, it's best not to drink alcohol

Goal:

- For cancer prevention it's best not to drink alcohol

- Drinking alcohol is a cause of many cancers
- Drinking alcohol helps protect against kidney cancer (at least up to 30 grams or two drinks per day), but this is far outweighed by the increased risk for other cancers

8) Do not use supplements for cancer prevention

Aim to meet nutritional needs through diet alone

Goal:

- High-dose dietary supplements¹ are not recommended for cancer prevention – aim to meet nutritional needs through diet alone

¹ A dietary supplement is a product intended for ingestion that contains a 'dietary ingredient' intended to achieve levels of consumption of micronutrients or other food components what are usually achievable through diet alone

9) For mothers: breastfeed your baby, if you can

Breastfeeding is good for both mother and baby

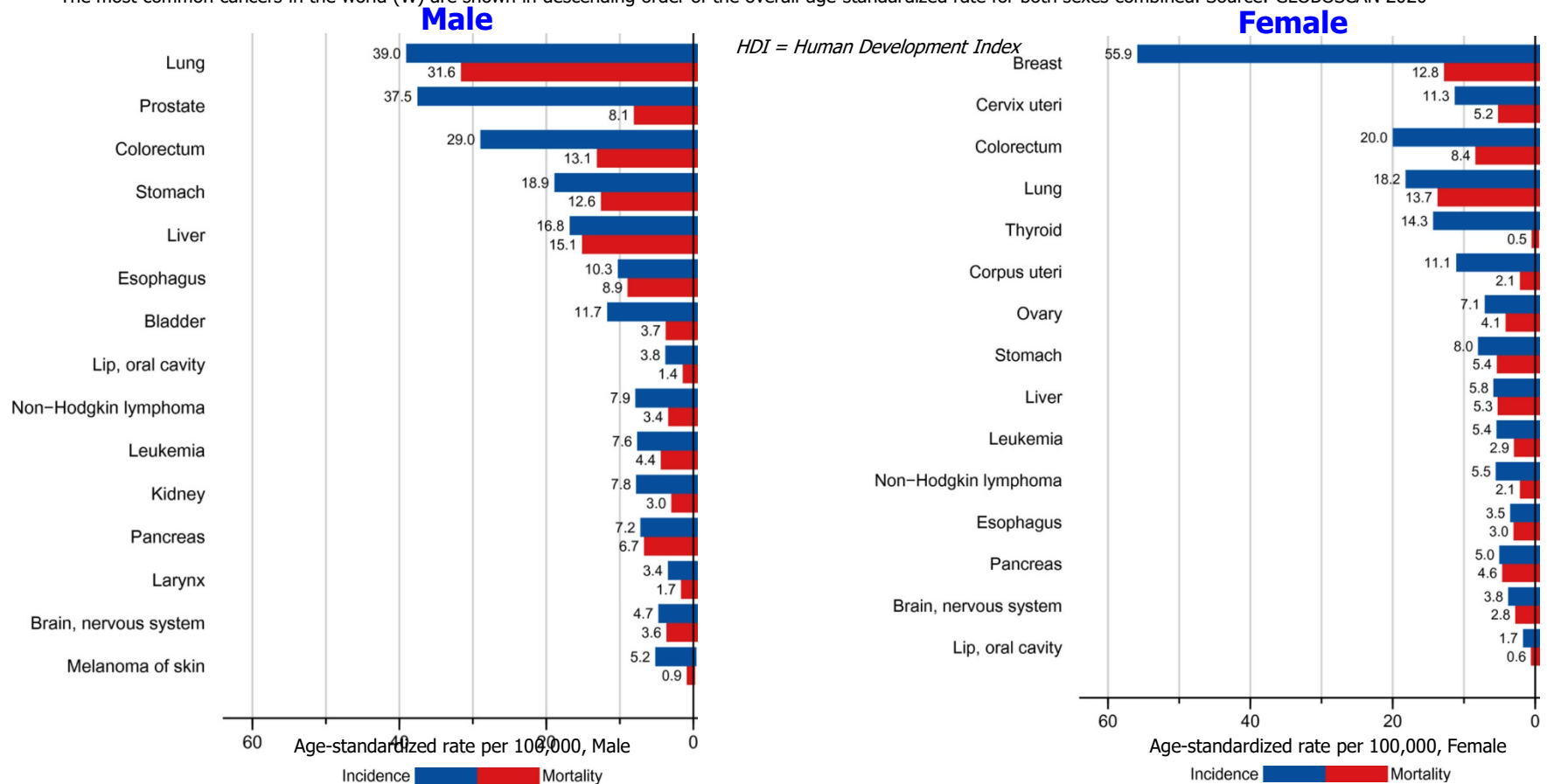
Goal:

- This recommendation aligns with the advice of the WHO, which recommends infants are exclusively breastfed¹ for 6 months, and then up to 2 years of age or beyond alongside appropriate complementary foods

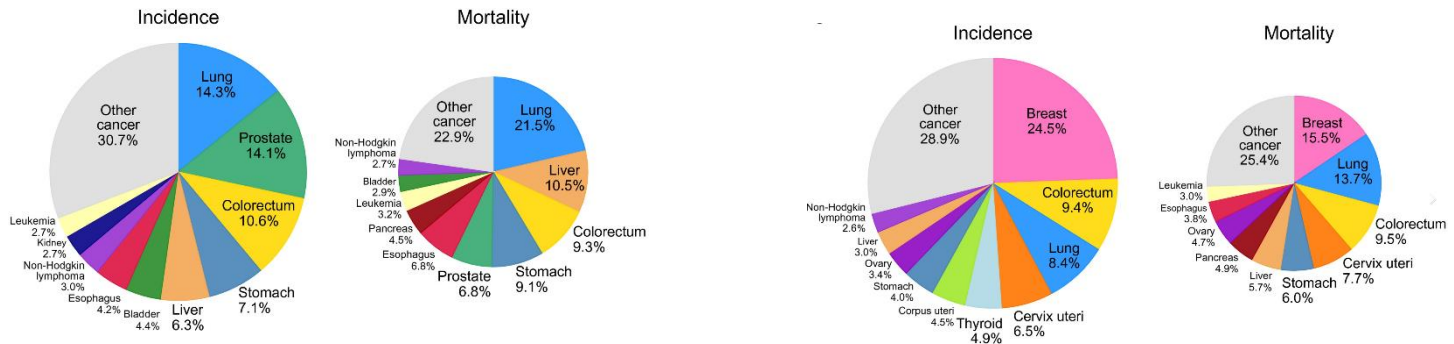
¹ Exclusive breastfeeding is defined as giving a baby only breastmilk (including breastmilk that has been expressed or is from a wet nurse) and nothing else – no other liquids or solid foods, not even water. It does, however, allow to infant to receive oral rehydration solution, drops or syrups consisting of vitamins, minerals, supplements or medicine.

Epidemiology - Cancer incidence and mortality in high HDI countries (Age-Standardized Rates)

The most common cancers in the world (W) are shown in descending order of the overall age-standardized rate for both sexes combined. Source: GLOBSCAN 2020



The World-wide most frequent cancers:



Cancer prevention recommendations as an overarching package

WCR/AICR: Diet, Nutrition, Physical Activity and Cancer: a Global Perspective – The Third Expert Report, 2018



Colorectal Cancer Factors

		DECREASES RISK	INCREASES RISK
STRONG EVIDENCE	Convincing	Physical activity ^{1,2}	Processed meat ³ Alcoholic drinks ⁴ Body fatness ⁵ Adult attained height ⁶
	Probable	Wholegrains Foods containing dietary fibre ⁷ Dairy products ⁸ Calcium supplements ⁹	Red meat ¹⁰

	Limited – suggestive	Foods containing vitamin C ¹¹ Fish Vitamin D ¹² Multivitamin supplements ¹³	Low intakes of non-starchy vegetables ¹⁴ Low intakes of fruits ¹⁴ Foods containing haem iron ¹⁵
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World Cancer Research Fund International: *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective - The Third Expert Report*. London, UK: World Cancer Research Fund International; 2018 Available from: <https://www.wcrf.org/dietandcancer>

Pre-menopausal Breast Cancer factors

		DECREASES RISK	INCREASES RISK
STRONG EVIDENCE	Convincing		Adult attained height ¹
	Probable	Vigorous physical activity Body fatness ² Lactation ³	Alcoholic drinks ⁴ Greater birthweight ⁵

Post-menopausal Breast Cancer factors

		DECREASES RISK	INCREASES RISK
STRONG EVIDENCE	Convincing		Alcoholic drinks ¹ Body fatness ² Adult weight gain Adult attained height ³
	Probable	Physical activity ⁴ Body fatness in young adulthood ⁵ Lactation ⁶	

World Cancer Research Fund International: *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective - The Third Expert Report*. London, UK: World Cancer Research Fund International; 2018
 Available from: <https://www.wcrf.org/dietandcancer>

Prostate Cancer Factors

		DECREASES RISK	INCREASES RISK
STRONG EVIDENCE	Convincing		
	Probable		Body fatness (advanced prostate cancer)^{1,2} Adult attained height³
STRONG EVIDENCE	Substantial effect on risk unlikely	Beta-carotene^{4,5}	
	Limited – suggestive		Dairy products Diets high in calcium Low plasma alpha-tocopherol concentrations Low plasma selenium concentrations

World Cancer Research Fund International: *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective - The Third Expert Report*. London, UK: World Cancer Research Fund International; 2018 Available from: <https://www.wcrf.org/dietandcancer>

Kidney cancer factors

		DECREASES RISK	INCREASES RISK
STRONG EVIDENCE	Convincing		Body fatness ¹
	Probable	Alcoholic drinks ²	Adult attained height ³

World Cancer Research Fund International: *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective - The Third Expert Report*. London, UK: World Cancer Research Fund International; 2018 Available from: <https://www.wcrf.org/dietandcancer>

List of Classifications by cancer sites with *sufficient* or *limited evidence* in humans, Volumes 1 to 114*

Cancer site	Carcinogenic agents with <i>sufficient evidence</i> in humans	Agents with <i>limited evidence</i> in humans
Lip, oral Cavity, and pharynx		
Lip		Hydrochlorothiazide Solar radiation
Oral cavity	Alcoholic beverages Betel quid with tobacco Betel quid without tobacco Human papillomavirus type 16 Tobacco, smokeless Tobacco smoking	Human papillomavirus type 18
Salivary gland	X-radiation, gamma-radiation	Radioiodines, including Iodine-131
Tonsil	Human papillomavirus type 16	
Pharynx	Alcoholic beverages Betel quid with tobacco Human papillomavirus type 16 Tobacco smoking	Asbestos (all forms) Mate drinking, hot Printing processes Tobacco smoke, secondhand
Nasopharynx	Epstein-Barr virus Formaldehyde Salted fish, Chinese-style Tobacco smoking Wood dust	
Digestive tract, upper	Acetaldehyde associated with consumption of alcoholic beverages	

Cancer site	Carcinogenic agents with <i>sufficient evidence</i> in humans	Agents with <i>limited evidence</i> in humans
Lung	<p>Acheson process, occupational exposures associated with</p> <p>Aluminum production</p> <p>Arsenic and inorganic arsenic compounds</p> <p>Asbestos (all forms)</p> <p>Beryllium and beryllium compounds</p> <p>Bis(chloromethyl)ether; chloromethyl methyl ether (technical grade)</p> <p>Cadmium and cadmium compounds</p> <p>Chromium(VI) compounds</p> <p>Coal, indoor emissions from household combustion</p> <p>Coal gasification</p> <p>Coal-tar pitch</p> <p>Coke production</p> <p>Engine exhaust, diesel</p> <p>Hematite mining (underground)</p> <p>Iron and steel founding</p> <p>MOPP (vincristine-prednisone-nitrogen mustard-procarbazine mixture)</p> <p>Nickel compounds</p> <p>Outdoor air pollution</p> <p>Painting</p> <p>Particulate matter in outdoor air pollution</p> <p>Plutonium</p> <p>Radon-222 and its decay products</p> <p>Rubber production industry</p> <p>Silica dust, crystalline</p> <p>Soot</p> <p>Sulfur mustard</p> <p>Tobacco smoke, secondhand</p> <p>Tobacco smoking</p> <p>X-radiation, gamma-radiation</p>	<p>Acid mists, strong inorganic</p> <p>Art glass, glass containers and pressed ware (manufacture of)</p> <p>Biomass fuel (primarily wood), indoor emissions from household combustion of</p> <p>Bitumens, occupational exposure to oxidized bitumens and their emissions during roofing</p> <p>Bitumens, occupational exposure to hard bitumens and their emissions during mastic asphalt work</p> <p>Carbon electrode manufacture</p> <p><i>alpha</i>-Chlorinated toluenes and benzoyl chloride (combined exposures)</p> <p>Cobalt metal with tungsten carbide</p> <p>Creosotes</p> <p>Diazinon</p> <p>Fibrous silicon carbide</p> <p>Frying, emissions from high-temperature</p> <p>Insecticides, non-arsenical, occupational exposures in spraying and application</p> <p>Printing processes</p> <p>2,3,7,8-Tetrachlorodibenzo-<i>para</i>-dioxin</p> <p>Welding fumes</p>

List of Classifications by cancer sites with *sufficient* or *limited evidence* in humans, Volumes 1 to 114*

Cancer site	Carcinogenic agents with <i>sufficient evidence</i> in humans	Agents with <i>limited evidence</i> in humans
Stomach	<i>Helicobacter pylori</i> Rubber production industry Tobacco smoking X-radiation, gamma-radiation	Asbestos (all forms) Epstein-Barr virus Lead compounds, inorganic Nitrate or nitrite (ingested) under conditions that result in endogenous nitrosation Pickled vegetables (traditional Asian) Salted fish, Chinese-style Processed meat (consumption of)
Colon and rectum	Alcoholic beverages Tobacco smoking X-radiation, gamma-radiation Processed meat (consumption of)	Asbestos (all forms) <i>Schistosoma japonicum</i> Red meat (consumption of)
Anus	Human immunodeficiency virus type 1 Human papillomavirus type 16	Human papillomavirus types 18, 33

Digestive 2

Liver and bile duct	<p>Aflatoxins</p> <p>Alcoholic beverages</p> <p><i>Clonorchis sinensis</i></p> <p>1,2-Dichloropropane</p> <p>Estrogen-progestogen contraceptives</p> <p>Hepatitis B virus</p> <p>Hepatitis C virus</p> <p><i>Opisthorchis viverrini</i></p> <p>Plutonium</p> <p>Thorium-232 and its decay products</p> <p>Tobacco smoking (in smokers and in smokers' children)</p> <p>Vinyl chloride</p>	<p>Androgenic (anabolic) steroids</p> <p>Arsenic and inorganic arsenic compounds</p> <p>Betel quid without tobacco</p> <p>DDT</p> <p>Dichloromethane (Methylene chloride)</p> <p>Human immunodeficiency virus type 1</p> <p><i>Schistosoma japonicum</i></p> <p>Trichloroethylene</p> <p>X-radiation, gamma-radiation</p>
Gall bladder	Thorium-232 and its decay products	
Pancreas	<p>Tobacco, smokeless</p> <p>Tobacco smoking</p>	<p>Alcoholic beverages</p> <p>Thorium-232 and its decay products</p> <p>X-radiation, gamma-radiation</p> <p>Red meat (consumption of)</p>

List of Classifications by cancer sites with *sufficient* or *limited evidence* in humans, Volumes 1 to 114*

Cancer site	Carcinogenic agents with <i>sufficient evidence</i> in humans	Agents with <i>limited evidence</i> in humans
Breast and female genital organs		
Breast	Alcoholic beverages Diethylstilbestrol Estrogen-progestogen contraceptives Estrogen-progestogen menopausal therapy X-radiation, gamma-radiation	Digoxin Estrogen menopausal therapy Ethylene oxide Polychlorinated biphenyls Shiftwork that involves circadian disruption Tobacco smoking
Vulva	Human papillomavirus type 16	Human immunodeficiency virus type 1 Human papillomavirus types 18, 33
Vagina	Diethylstilbestrol (exposure in utero) Human papillomavirus type 16	Human immunodeficiency virus type 1
Uterine cervix	Diethylstilbestrol (exposure in utero) Estrogen-progestogen contraceptives Human immunodeficiency virus type 1 Human papillomavirus types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 Tobacco smoking	Human papillomavirus types 26, 53, 66, 67, 68, 70, 73, 82
Endometrium	Estrogen menopausal therapy Estrogen-progestogen menopausal therapy Tamoxifen	Diethylstilbestrol
Ovary	Asbestos (all forms) Estrogen menopausal therapy Tobacco smoking	Talc-based body powder (perineal use) X-radiation, gamma-radiation

List of Classifications by cancer sites with *sufficient or limited evidence* in humans, Volumes 1 to 114*

Cancer site	Carcinogenic agents with <i>sufficient evidence</i> in humans	Agents with <i>limited evidence</i> in humans
Male genital organs		
Penis	Human papillomavirus type 16	Human immunodeficiency virus type 1 Human papillomavirus type 18
Prostate		Androgenic (anabolic) steroids Arsenic and inorganic arsenic compounds Cadmium and cadmium compounds Malathion Rubber production industry Thorium-232 and its decay products X-radiation, gamma-radiation Red meat (consumption of)
Testis		DDT Diethylstilbestrol (exposure in utero) Perfluorooctanoic acid

List of Classifications by cancer sites with *sufficient* or *limited evidence* in humans, Volumes 1 to 114*

Cancer site	Carcinogenic agents with <i>sufficient evidence</i> in humans	Agents with <i>limited evidence</i> in humans
Urinary tract		
Kidney	Tobacco smoking X-radiation, gamma-radiation Trichloroethylene	Arsenic and inorganic arsenic compounds Cadmium and cadmium compounds Perfluorooctanoic acid Printing processes
Renal pelvis and ureter	Aristolochic acid, plants containing Phenacetin Phenacetin, analgesic mixtures containing Tobacco smoking	Aristolochic acid
Urinary bladder	Aluminum production 4-Aminobiphenyl Arsenic and inorganic arsenic compounds Auramine production Benzidine Chlornaphazine Cyclophosphamide Magenta production 2-Naphthylamine Painting Rubber production industry <i>Schistosoma haematobium</i> Tobacco smoking <i>ortho</i> -Toluidine X-radiation, gamma-radiation	4-Chloro- <i>ortho</i> -toluidine Coal-tar pitch Coffee Dry cleaning Engine exhaust, diesel Hairdressers and barbers, occupational exposure Pioglitazone Printing processes Soot Textile manufacturing Tetrachloroethylene

Cancer site	Carcinogenic agents with <i>sufficient evidence</i> in humans	Agents with <i>limited evidence</i> in humans
Leukaemia and/or lymphoma	Azathioprine Benzene Busulfan 1,3-Butadiene Chlorambucil Cyclophosphamide Cyclosporine Epstein-Barr virus Etoposide with cisplatin and bleomycin Fission products, including Strontium-90 Formaldehyde <i>Helicobacter pylori</i> Hepatitis C virus Human immunodeficiency virus type 1 Human T-cell lymphotropic virus type 1 Kaposi sarcoma herpes virus Lindane Melphalan MOPP (vincristine-prednisone-nitrogen mustard-procarbazine mixture) Phosphorus-32 Rubber production industry Semustine (methyl-CCNU) Thiotepa Thorium-232 and its decay products Tobacco smoking Treosulfan X-radiation, gamma-radiation	Bischloroethyl nitrosourea (BCNU) Chloramphenicol DDT Diazinon Dichloromethane (Methylene chloride) Ethylene oxide Etoposide Glyphosate Hepatitis B virus Magnetic fields, extremely low frequency (childhood leukaemia) Malathion Mitoxantrone Nitrogen mustard Painting (childhood leukaemia from maternal exposure) Petroleum refining, occupational exposures Polychlorinated biphenyls Polychlorophenols or their sodium salts (combined exposures) Radioiodines, including Iodine-131 Radon-222 and its decay products Styrene Teniposide Trichloroethylene 2,3,7,8-Tetrachlorodibenzo- <i>para</i> -dioxin Tobacco smoking (childhood leukaemia in smokers' children) Malaria (caused by infection)