KONTROVERSE GI CANCER 2018
Ernährung und Magen - Darm - Krebs

Krebs durch Ernährung: Mögliche Bedrohungen und wahre Risiken

David Fäh

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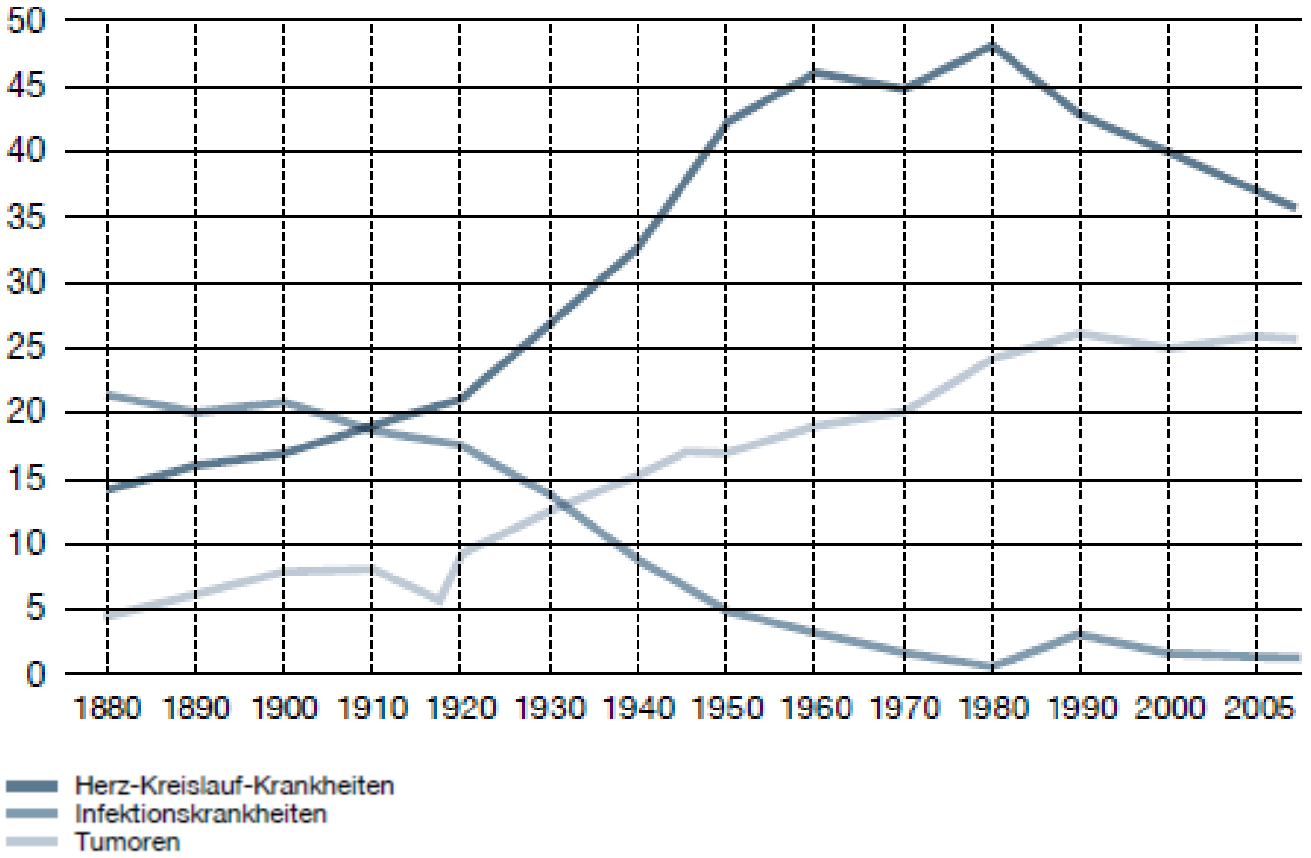
Inhalt

- Krebs-Epidemiologie
- Ernährung: neue Bedrohungen (?)
- Was ins Gewicht fällt
- Generelle Limitationen der Krebsforschung

Anteil (%) der Todesfälle nach Haupt-Todesursachen-Gruppe

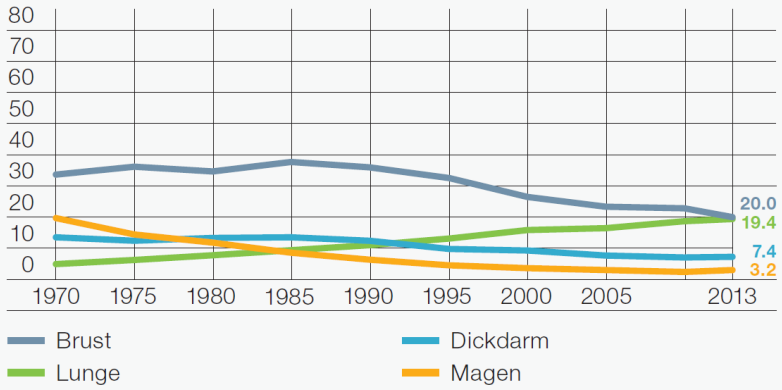


Raymond Kohli, Sterblichkeit nach Todesursachen in der Schweiz, 1998/2003

Krebsmortalität Schweiz, nach Geschlecht

Krebssterblichkeit nach Organ bei Frauen

Todesfälle pro 100 000 weibliche Einwohnerinnen

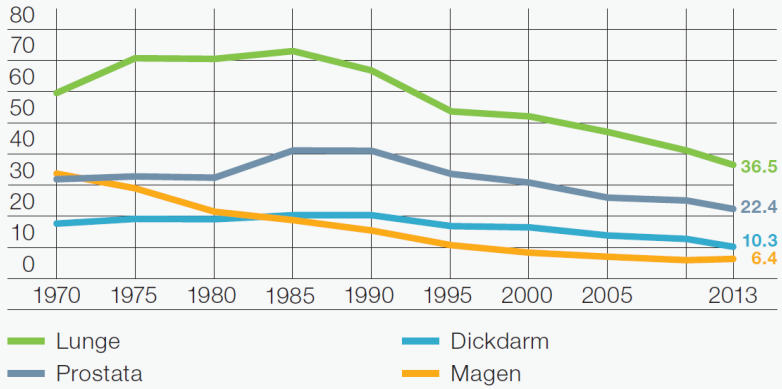


Quelle: Todesursachenstatistik, Bundesamt für Statistik, diverse Jahrgänge.

Berechnung: direkte Methode, europäische Standardbevölkerung.

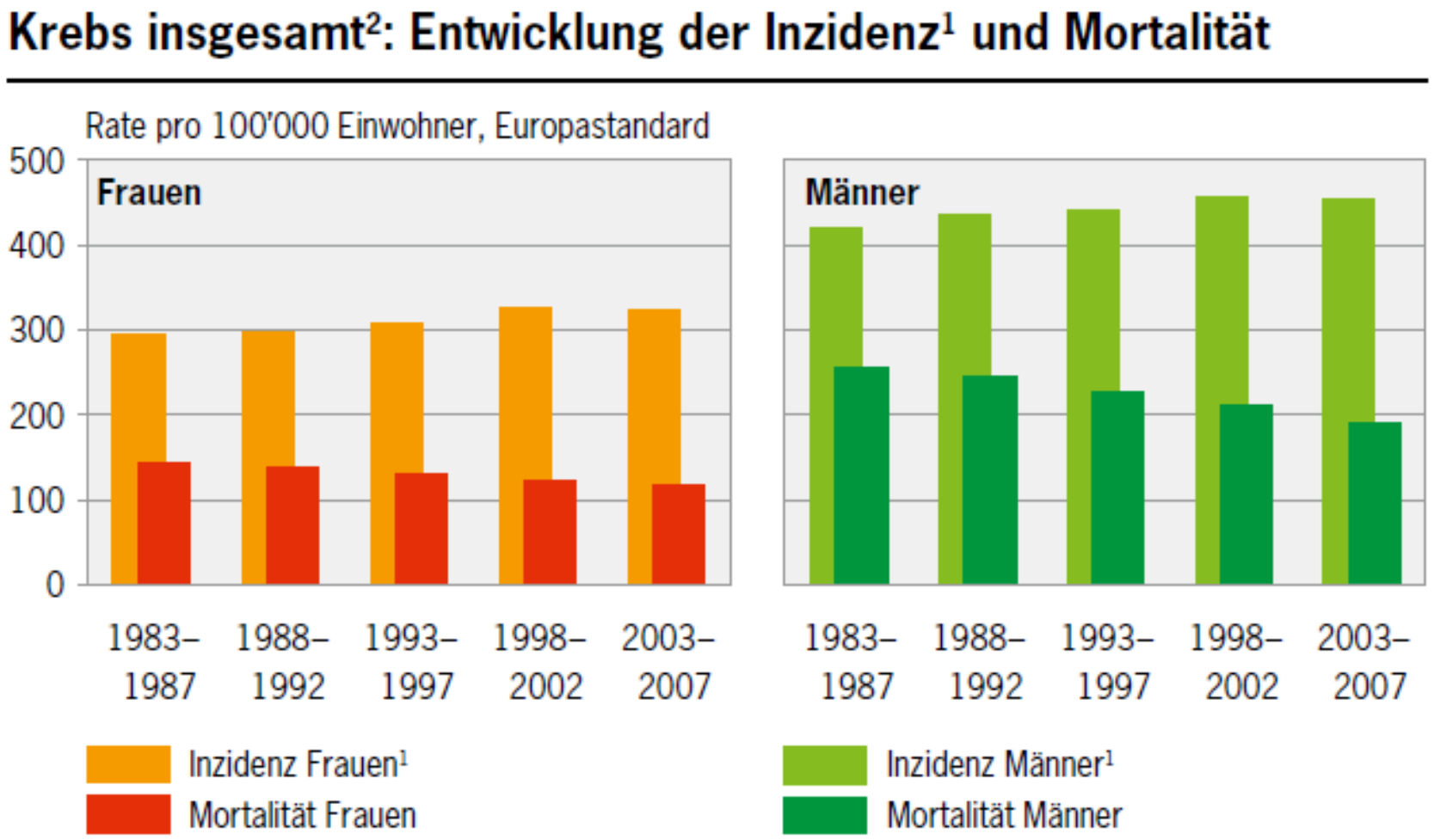
Krebssterblichkeit nach Organ bei Männern

Todesfälle pro 100 000 männliche Einwohner

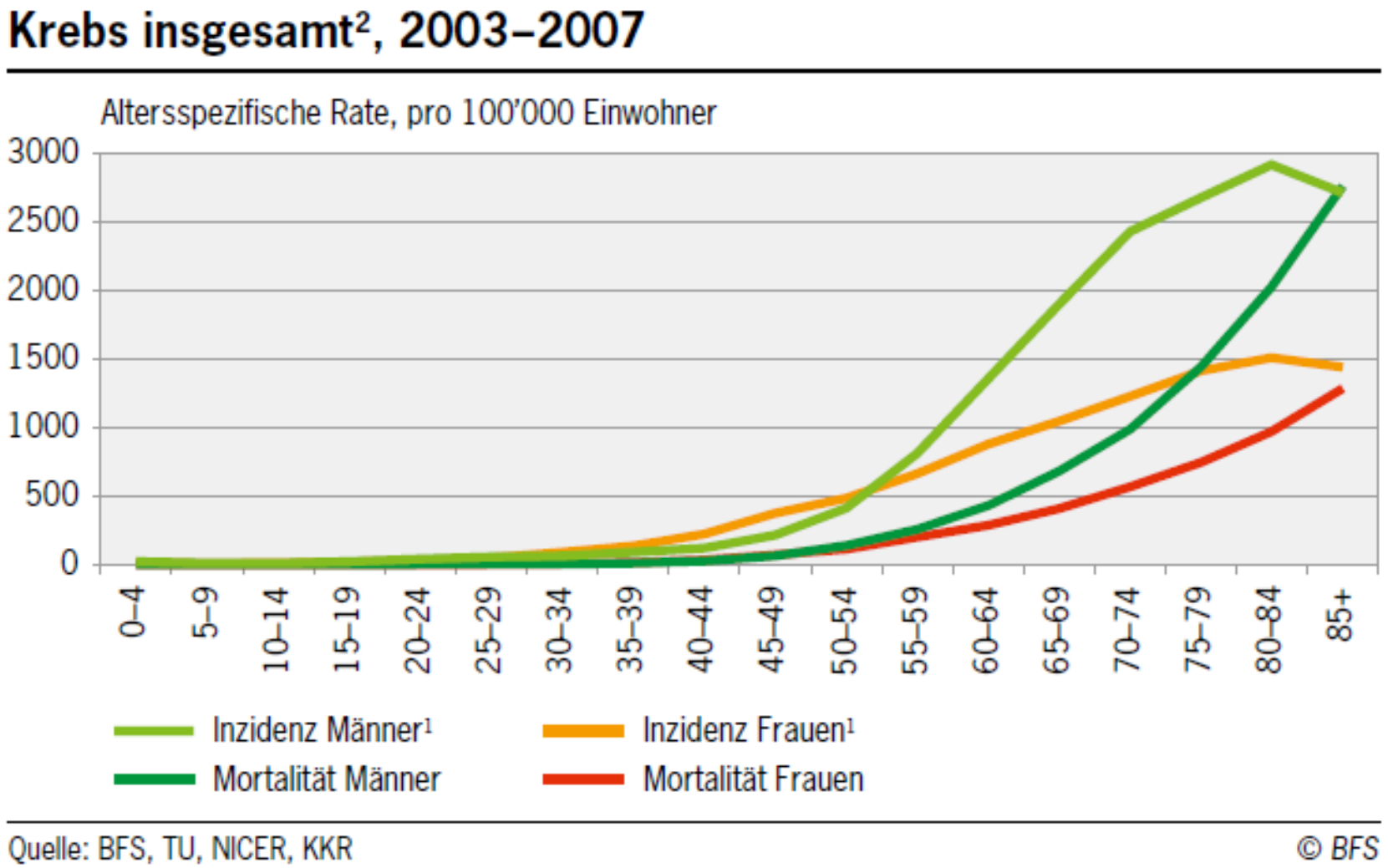


Quelle: Todesursachenstatistik, Bundesamt für Statistik, diverse Jahrgänge.

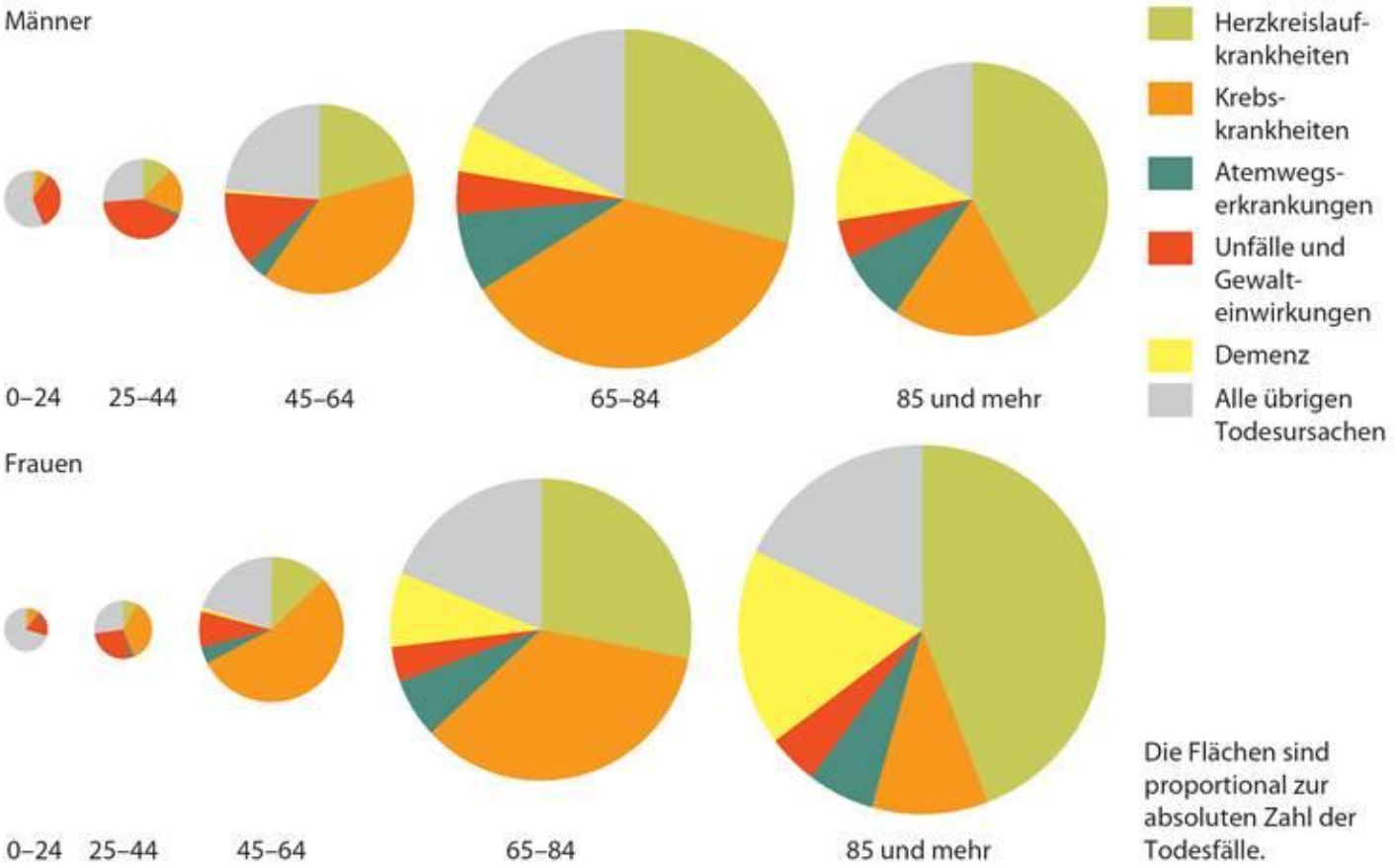
Krebs-Trends nach Geschlecht



Krebs nach Alter & Geschlecht



Todesursachen-Gruppen, nach Altersgruppe und Geschlecht, Schweiz, 2014



Quelle: BFS – Todesursachenstatistik

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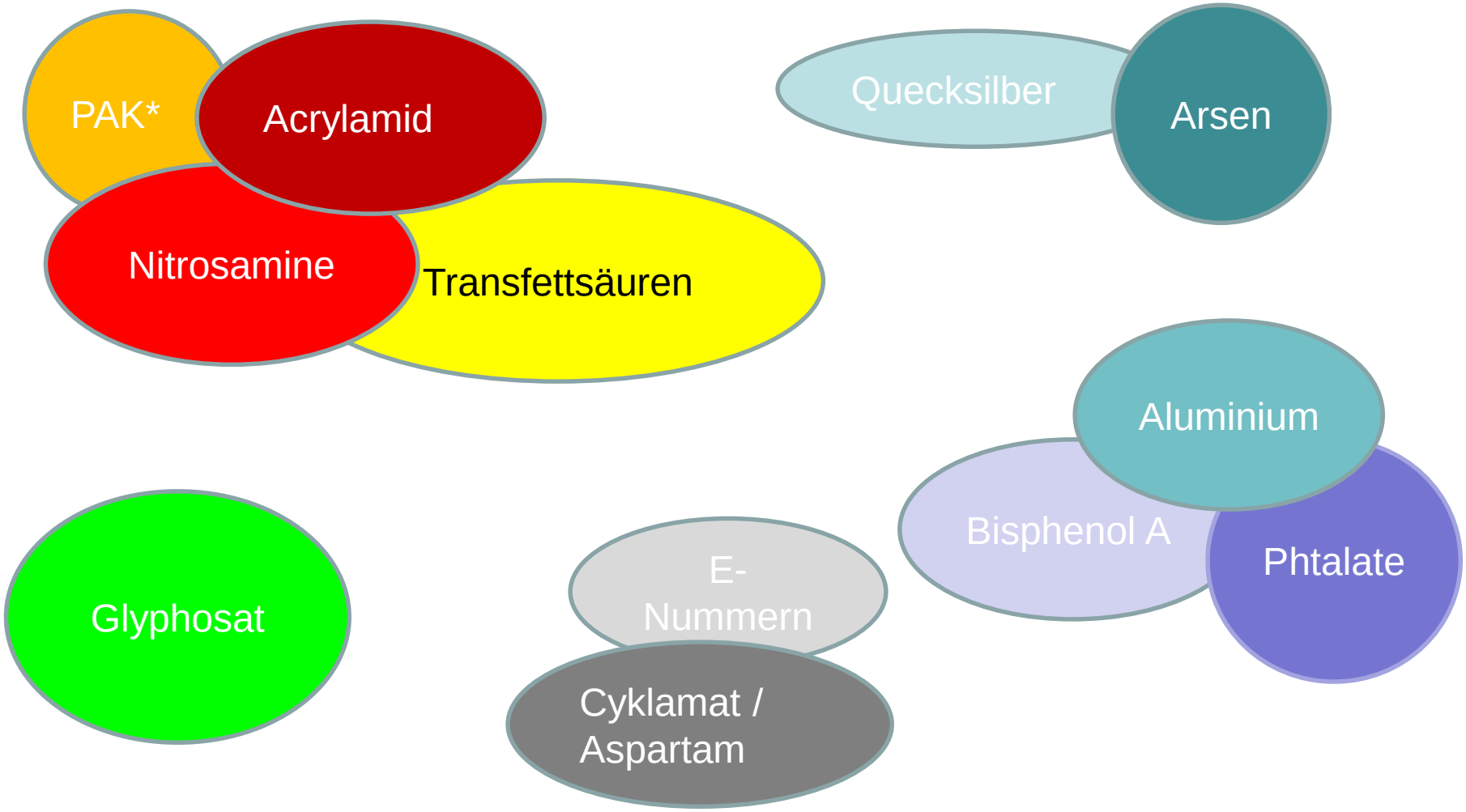
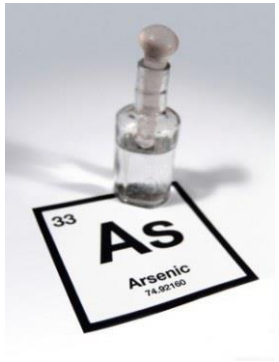
Ernährung: neue Bedrohungen (?)



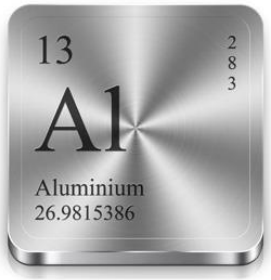
*Polyzyklische aromatische Kohlenwasserstoffe (PAK)

Ernährung: neue Bedrohungen (?)

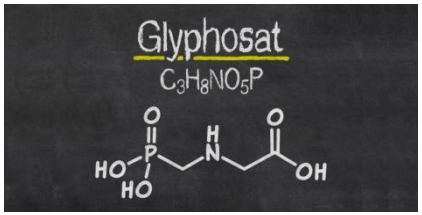


Arsen

Aluminium



Glyphosat



*Polyzyklische aromatische Kohlenwasserstoffe (PAK)

Wie gelangt Arsen in den Körper?

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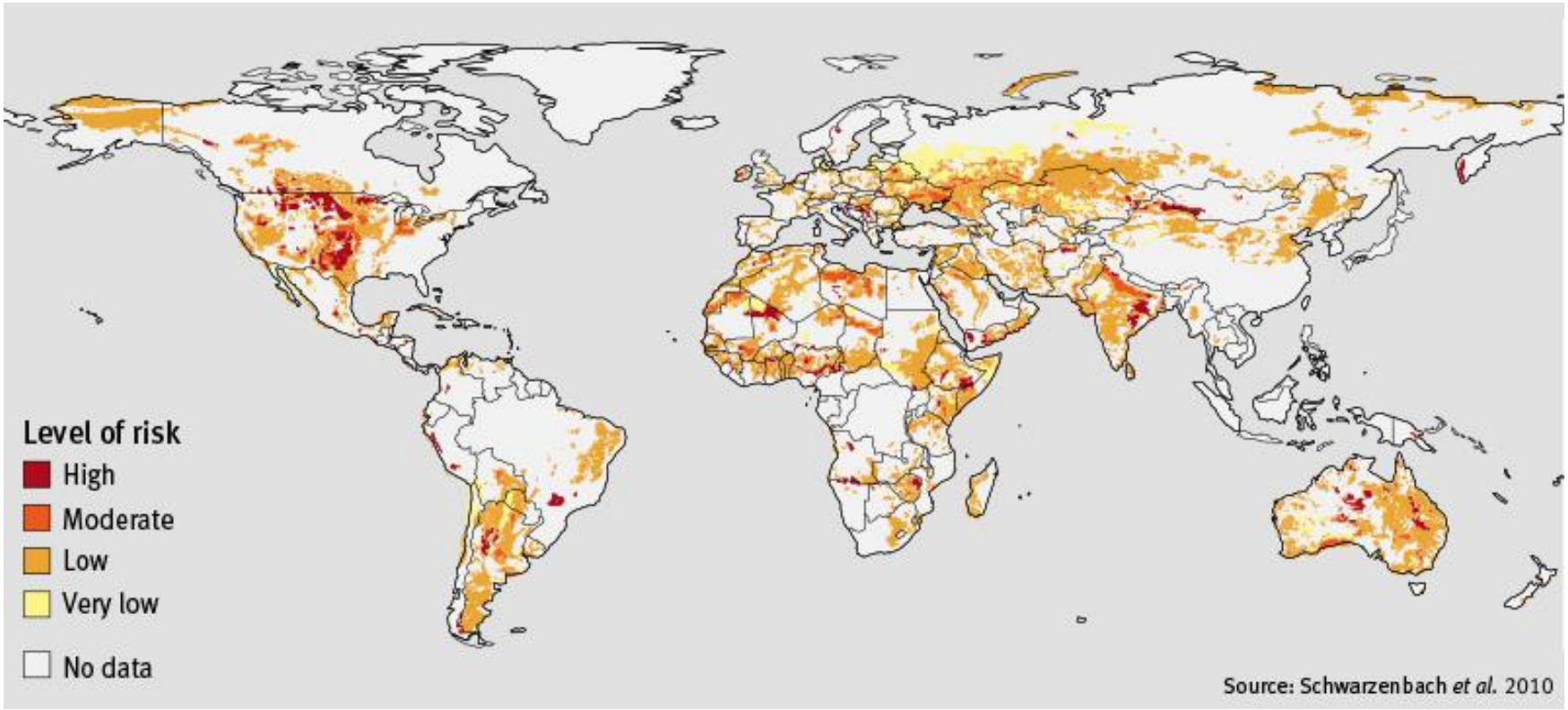
Arsen im Trinkwasser, global



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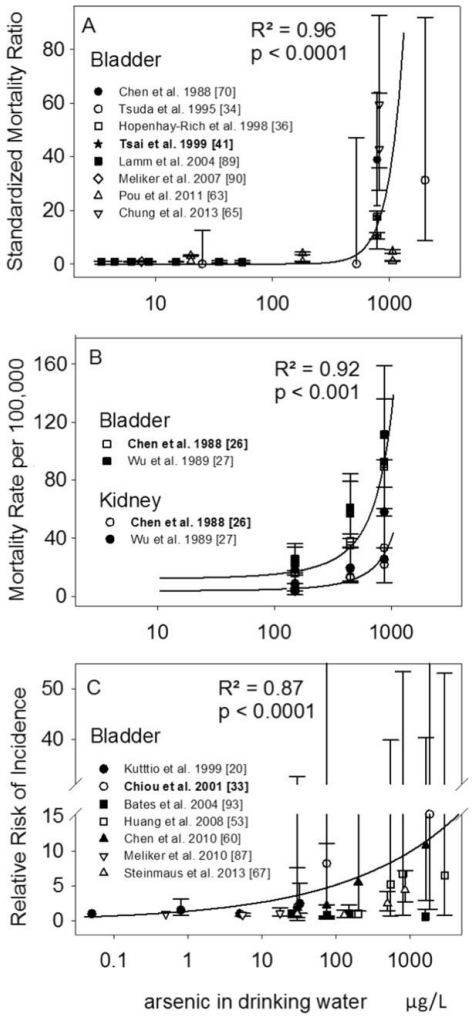
Arsen im Trinkwasser, assoziiertes Risiko

- Erhöhtes Risiko für Blasen- und Nierenkrebs



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4088919/
Krebs durch Ernährung, David Fäh, 8.3.2018

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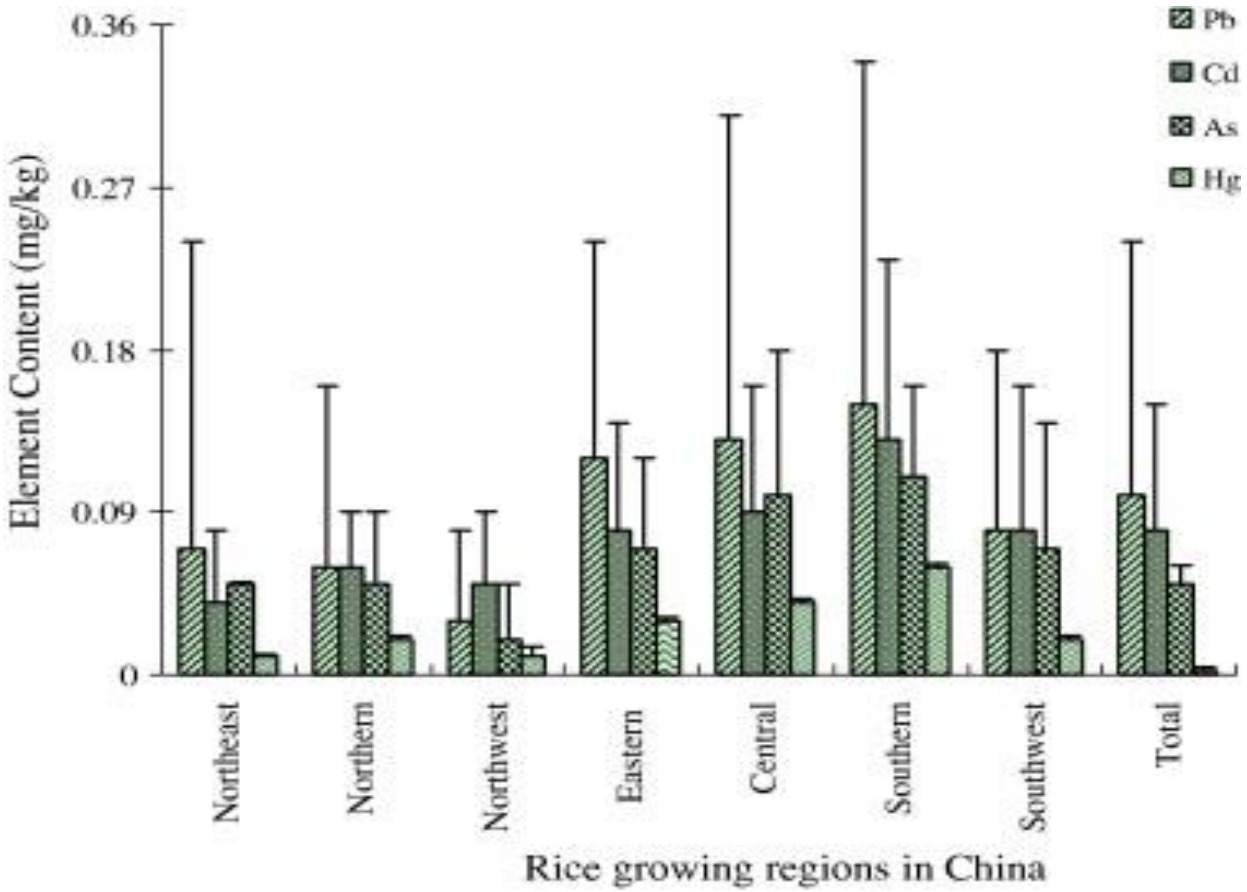
Arsen-Belastung von Reis, China



http://www.tandfonline.com/doi/abs/10.1080/19440041003636661?journalCode=tfac20

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Arsen im Reis: Senkung des Risikos

- Problematisch ist v.a. die Verwendung von Arsen-belastetem Reis für Baby-Nahrung
- Deutlich ärmer an Arsen als Reis aus China ist Reis aus der Himalaya-Region, Nordindien, Nordpakistan, Nepal
- Brauner Reis enthält in der Regel deutlich mehr Arsen als weisser, Basmati- und Jasmin-Reis hingegen deutlich weniger
- Spülen und Kochen mit überschüssigem Wasser verringert die Arsenkonzentration im Reis um ca. 75%

http://www.bfr.bund.de/cm/343/arsen-in-reis-und-reisprodukten.pdf
http://www.sciencemag.org/cgi/pmidlookup?view=long&pmid=18621644

Konzentrationen im Urin und Blut nach Glutenfreie-Diät-Status, NHANES 2009-14

Metal	Gluten-free Diet[a] N = 73 Geometric Mean (SE)[b]	Non-gluten-free Diet N = 7,398 Geometric Mean (SE)[b]	Geometric Mean Ratio (95% CI)[b]
Urinary concentrations			
Total arsenic (µg/L)	12.1 (1.5)	7.8 (0.23)	1.5 (1.2, 2.0)
Estimated total arsenic 1 (µg/L)[c]	6.1 (1.0)	3.2 (0.14)	1.9 (1.3, 2.6)
Estimated total arsenic 2 (µg/L)[d]	8.2 (0.5)	6.4 (0.07)	1.3 (1.1, 1.4)
Dimethylarsonic acid (µg/L)	5.3 (0.5)	3.7 (0.06)	1.4 (1.2, 1.7)
Cadmium (µg/L)	0.18 (0.01)	0.16 (0.00)	1.1 (1.0, 1.3)
Lead (µg/L)	0.40 (0.04)	0.37 (0.01)	1.1 (0.9, 1.3)
Blood concentrations			
Cadmium (µg/L)	0.29 (0.03)	0.29 (0.00)	1.0 (0.8, 1.2)
Lead (µg/dl)	1.1 (0.10)	0.96 (0.01)	1.1 (0.9, 1.3)
Inorganic mercury (µg/L)	0.30 (0.02)	0.28 (0.00)	1.1 (1.0, 1.2)
Total mercury (µg/L)	1.3 (0.25)	0.80 (0.02)	1.7 (1.1, 2.4)

[a]For NHANES 2009–2010 and 2011–2012, a gluten-free diet was defined as a "yes" response to "Are you on a gluten-free diet?" (MCQ086) in the medical questionnaire or "Gluten-free/Celiac diet" (DRQSDT11) to "What kind of diet are you on?" in the dietary interview day 1; for NHANES 2013–2014, a gluten-free diet was defined as a "yes" response to "Are you on a gluten-free diet?" (MCQ086) in the medical questionnaire.

[b]Calculated using survey-weighted linear regression, adjusting for age (continuous), sex (male/female), race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican, Hispanic, or other), and survey cycle (2009–2010, 2011–2012, or 2013–2014) with additional adjustment for urinary creatinine (continuous) in urinary concentration models.

[c]Estimated as [total arsenic in µg/L − (arsenocholine in µg/L + arsenobetaine in µg/L)] with negative values set to 0.01 µg/L.

[d]Estimated as [arsenite in µg/L + arsenate in µg/L + monomethylacrsonic acid in µg/L + dimethylarsonic acid in µg/L].

CI indicates confidence interval, SE standard error.

https://insights.ovid.com/crossref?an=00001648-201705000-00027

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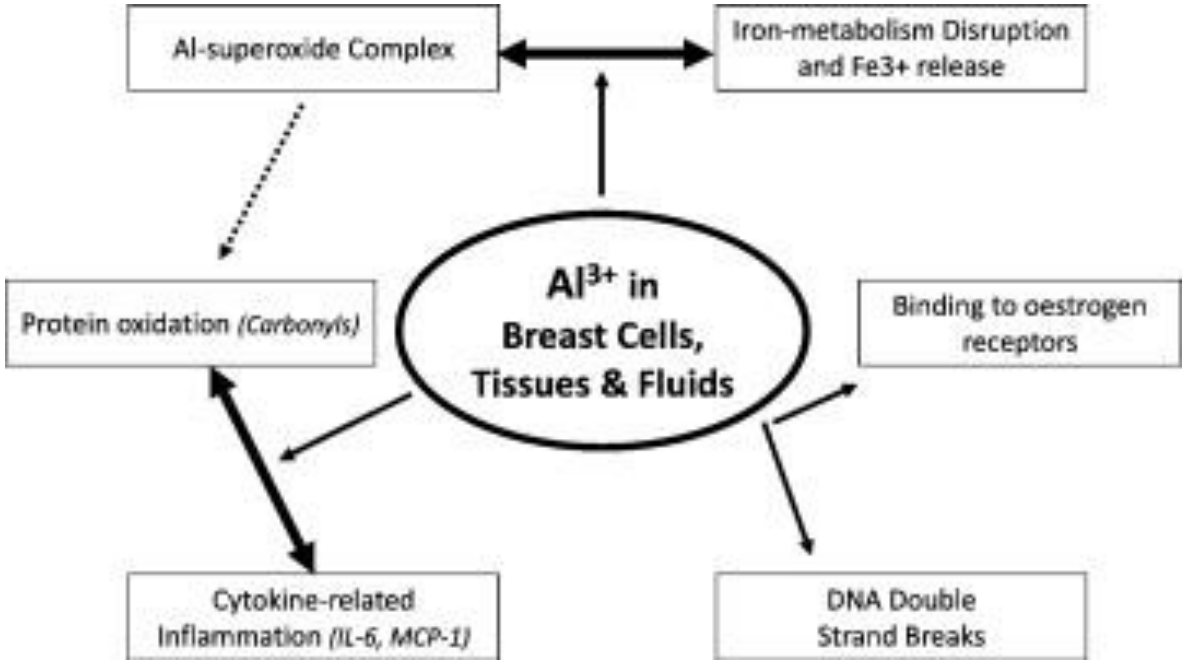
Aluminium und Brustkrebsrisiko



http://onlinelibrary.wiley.com/doi/10.1002/ijc.30393/full
https://www.sciencedirect.com/science/article/pii/S0162013413001608

Aluminium: Gehalt in Lebensmitteln

Table 3 Aluminium in foodstuffs (milligrammes per kilogramme or milligrammes per litre)

Product	Number	Minimum	Maximum	Mean value[a]	Median value
Flour	65	1	19	4	3
Baking premix	37	1	737	51	6
Bread	107	1	14	3	2
Loaf-shaped yeast fruit cakes	60	3	22	10	9
Fine bakery wares in aluminium trays	38	1	537	19	3
Salt pretzels and similar savoury biscuits	185	2	218	13	4
Pasta	24	1	76	10	4
Herb-teas	12	14	67	40	45
Cocoa powder	37	80	312	165	160
Chocolate	84	6	150	48	39
Confectionery	115	1	184	17	8
Malt	50	1	12	7	7
Beer and mixed drinks containing beer, draught beer	237	0.4	4.2	0.5	0.4
Fruit juice and fruit juice drinks	59	0.4	47	3	1
Wine and fruit wine	65	0.4	15	2	1
Mineral water, spring water and table water	171	0.1	0.07	0.01	0.006
Ready-cooked meals in aluminium trays	31	1	13	3	1
Soups	16	1	15	5	3
Diverse products	38	1	138	16	7
Total	1,431	n.n.	737	19	2

[a]Arithmetic mean

https://link.springer.com/article/10.1186/2190-4715-23-37

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Aluminium: Aufnahme & Ausscheidung

- Bei Gesunden wird lediglich 0.3% von oral aufgenommenen Aluminium über den Gastrointestinaltrakt aufgenommen

- > 95% davon wird an Transferrin gebunden und renal ausgeschieden

- Akkumulation von Aluminium im Körper nur bei parenteraler Aufnahme oder Niereninsuffizienz

https://emedicine.medscape.com/article/165315-overview

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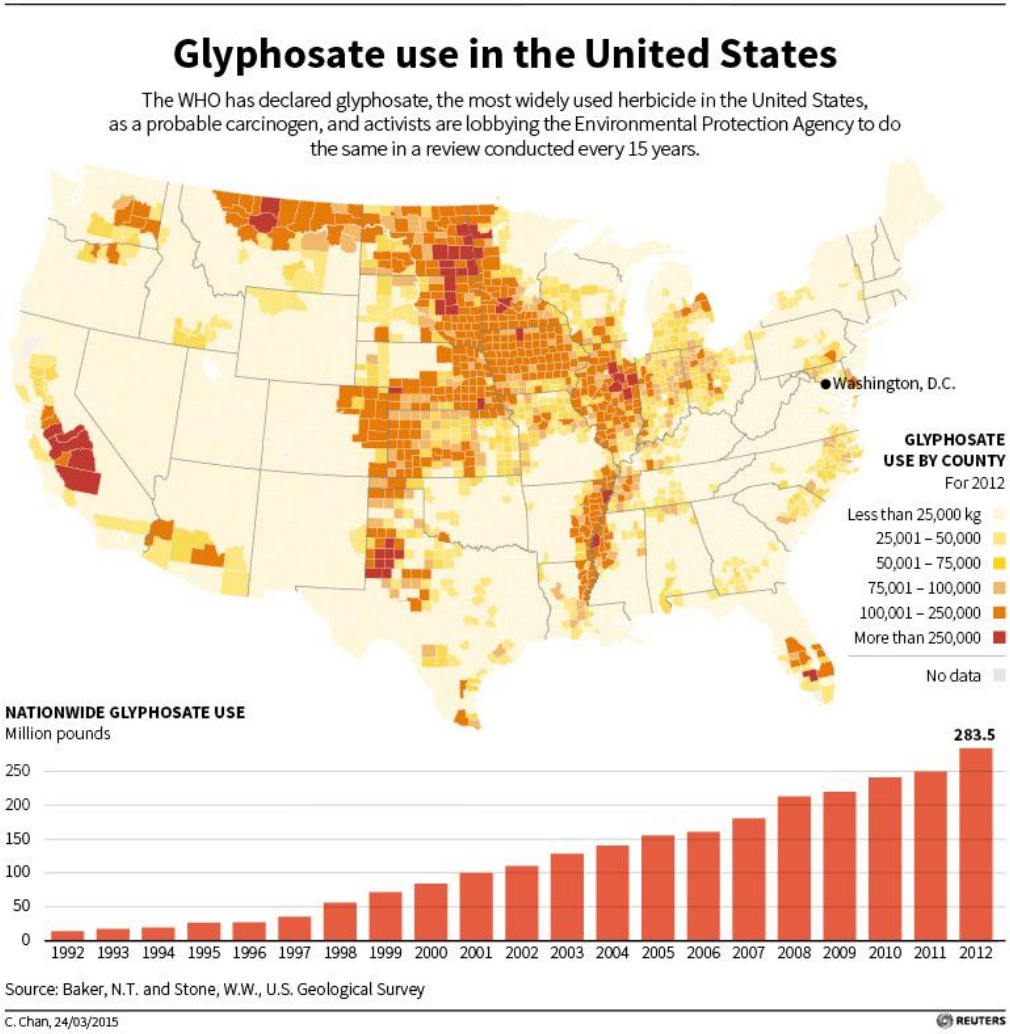
Glyphosat: Verwendung USA



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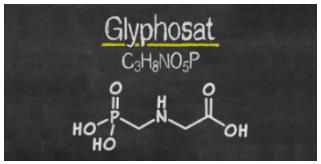
Glyphosat: Verbot Europa



Debate has been rife for years about the **potential health and safety risks involved with widespread glyphosate** use on crops and in public places. With **contrasting scientific evidence** from a number of bodies including The World Health Organisation, the **EU has been divided on the issue**.

On May 19th, the **European Commission failed to come to a decision** on whether to relicense it's use altogether. Instead of waiting for a final decision to be made, many **European countries have already taken steps to ban glyphosate** either partially or completely, regardless of the vote. The graphic below illustrates the current EU landscape on glyphosate, highlighting countries who have either:

Widespread ban
Banned extensively across the country

Limited ban
Banned glyphosate in isolated areas

Impending or potential ban
Expressed plans to ban or has called for a ban

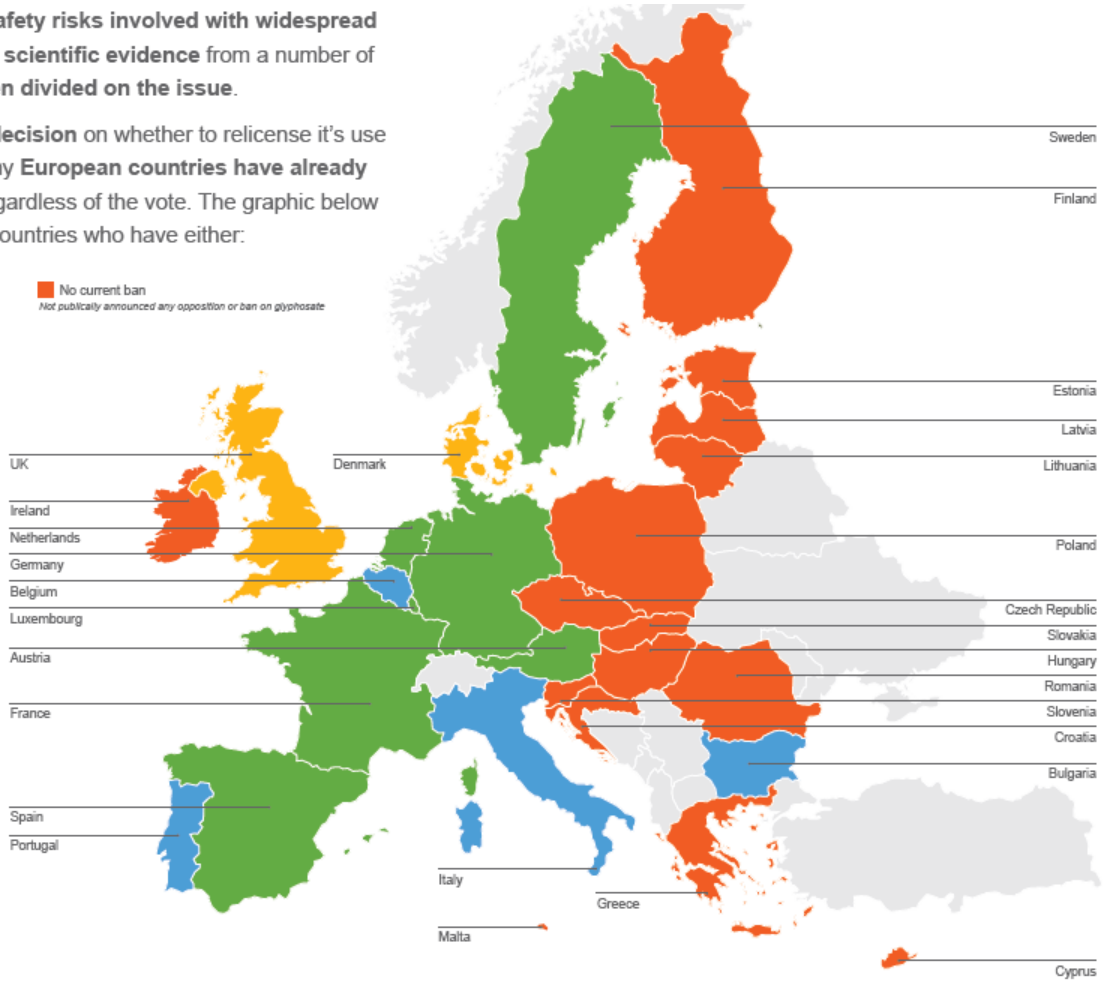
No current ban
Not publically announced any opposition or ban on glyphosate

7 countries have widespread bans in place

2 countries have a limited ban in place

4 countries have impending or potential bans

15 countries have no bans in place



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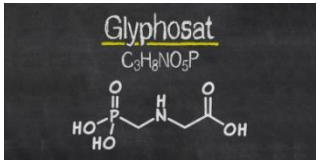
Glyphosat: Einschätzung Gesundheitsrisiko

- Die internationale Agentur für Krebsforschung (IARC) der WHO: Glyphosat = „wahrscheinlich krebserregend“ (2015)

- Europäische Behörde für Lebensmittelsicherheit (EFSA): Glyphosat: „weder erbgutschädigend noch krebserzeugend“ (2015)

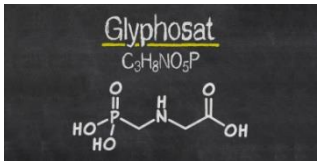


- Experten-Meeting des JMPR* (2016): “unwahrscheinlich, dass Glyphosat über die Ernährung ein Krebsrisiko für den Menschen darstellt“

*Joint FAO/WHO Meeting on Pesticide Residues

https://www.blv.admin.ch/blv/de/home/lebensmittel-und-ernaehrung/lebensmittelsicherheit/stoffe-im-fokus/glyphosat.html

Glyphosat: Lebensmittel Schweiz



- Max. akzeptable Tagesdosis: 30 mg für eine erwachsene Person
- > 230 Lebensmittelproben aus 19 Kategorien untersucht: Ca. 40 % der Lebensmittel enthalten messbare Spuren von Glyphosat

Gemessene Glyphosatwerte in Lebensmitteln, Mai 2017

	N Proben	Median (1) [µg/kg]	Konzentrations-bereich (2) [µg/kg]
Hartweizen und Teigwaren	18	139	<1 - 421
Frühstückscerealien	10	3.6	<1 - 145
Hülsenfrüchte	41	1.2	<1 - 2948

(1) Der Median ist der mittlere Wert, bei dem die eine Hälfte der Werte darunter und die andere Hälfte darüber liegt
(2) Niedrigster und höchster gemessener Wert

https://www.blv.admin.ch/blv/de/home/lebensmittel-und-ernaehrung/lebensmittelsicherheit/stoffe-im-fokus/glyphosat.html

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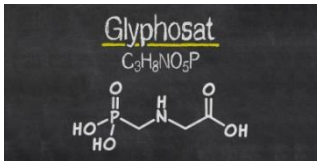
Glyphosat: Risiko Konsumäquivalent



Erst bei einem Konsum von

- 72 kg Teigwaren
- 655 kg Brot
- 10 kg Kichererbsen
- 1600 Liter Wein

der jeweils am stärksten glyphosatbelasteten Probe müsste ein Erwachsener mit gesundheitsschädigenden Folgen rechnen

https://www.blv.admin.ch/blv/de/home/lebensmittel-und-ernaehrung/lebensmittelsicherheit/stoffe-im-fokus/glyphosat.html

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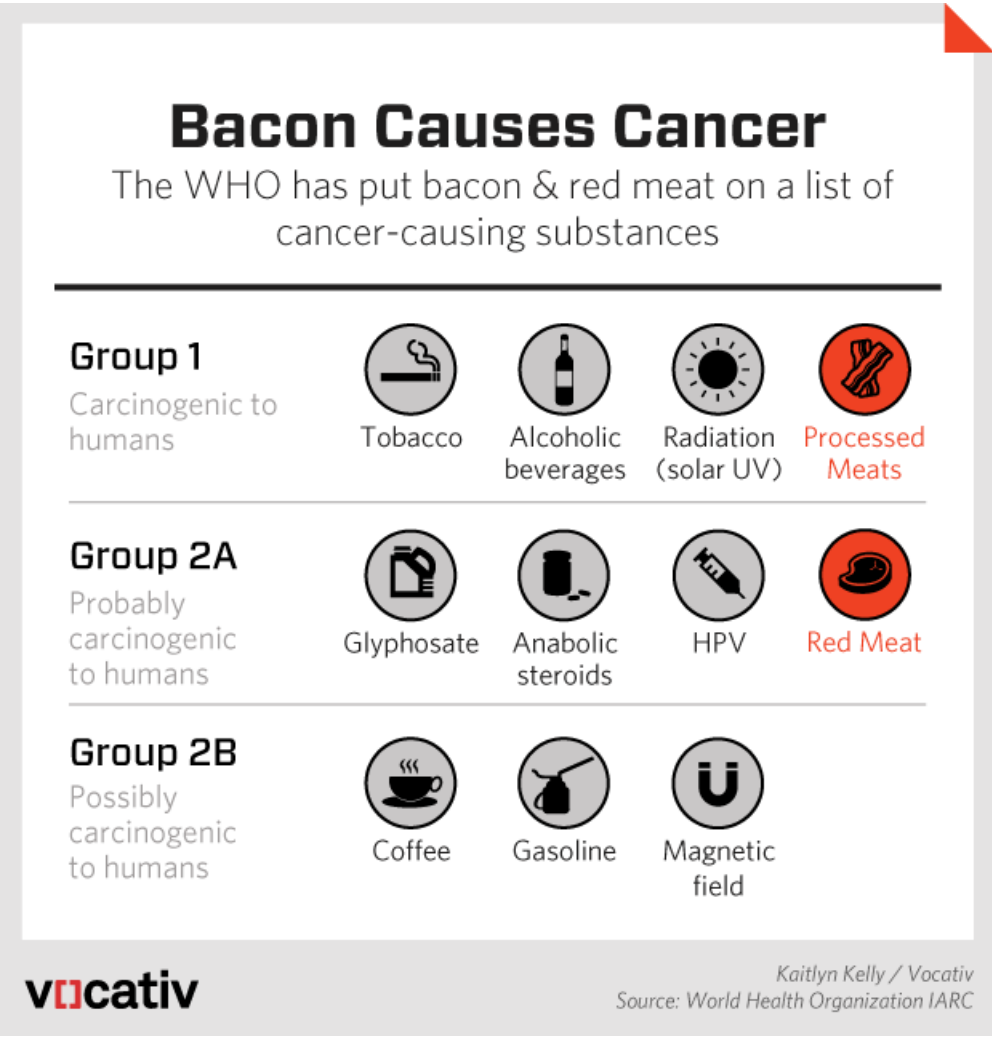
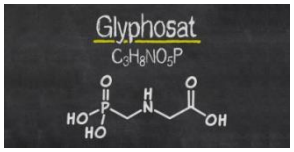
Glyphosat: Risiko-Einschätzung im Vergleich





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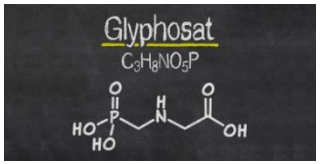
Agricultural Health Study (AHS), 2017



- In North Carolina und Iowa lebende Bauern
- Prospektive Kohorte: 54’251 Personen, wovon 82.8% Glyphosat verwendeten, 5’779 inzidente Krebsfälle
- Glyphosat-Exposition (Intensität und Dauer: 1993-2005) mit Fragebogen ermittelt
- Resultat: Kein Zusammenhang zwischen Glyphosat und Krebs (auch nicht non-Hodgkin Lymphom) aber gewisse Evidenz für ein erhöhtes Risiko für akute myeloische Leukämie in der Gruppe mit der höchsten Exposition

https://academic.oup.com/jnci/advance-article/doi/10.1093/jnci/djx233/4590280

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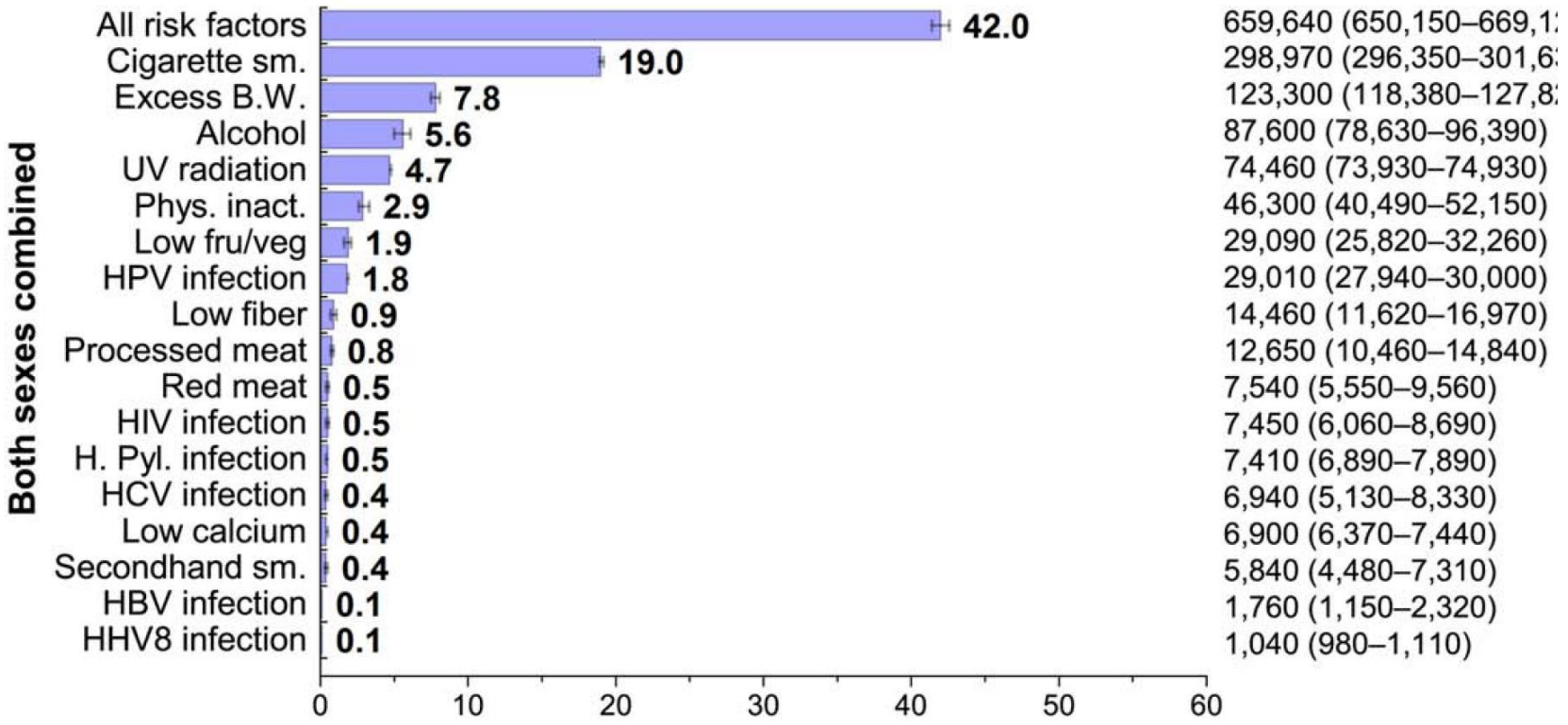
Anteil (%*) vermeidbarer Krebsfälle nach Risikofaktor, USA 2014



*Population Attributable Fraction (PAF), Inzidenz

http://onlinelibrary.wiley.com/doi/10.3322/caac.21440/full

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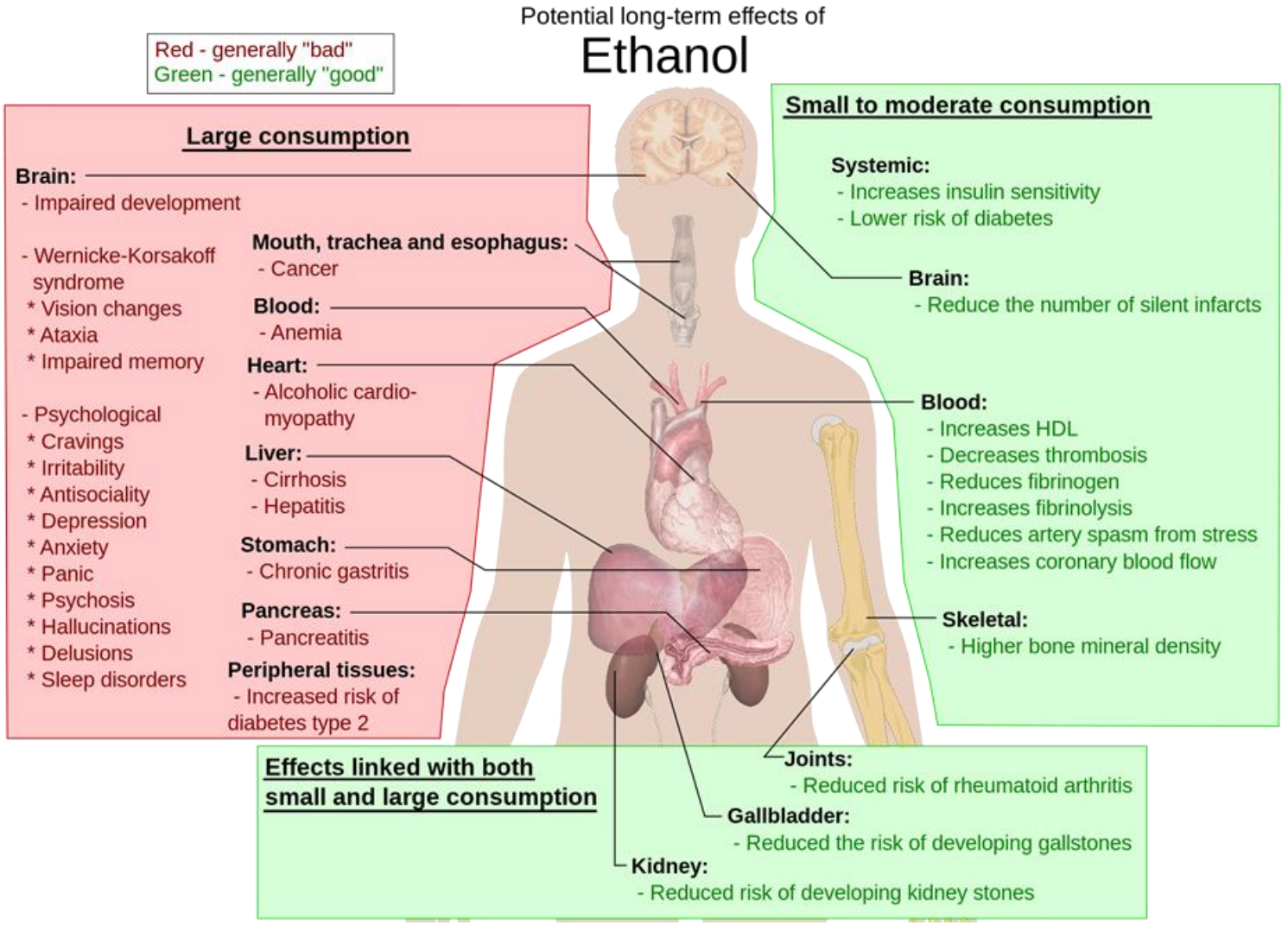
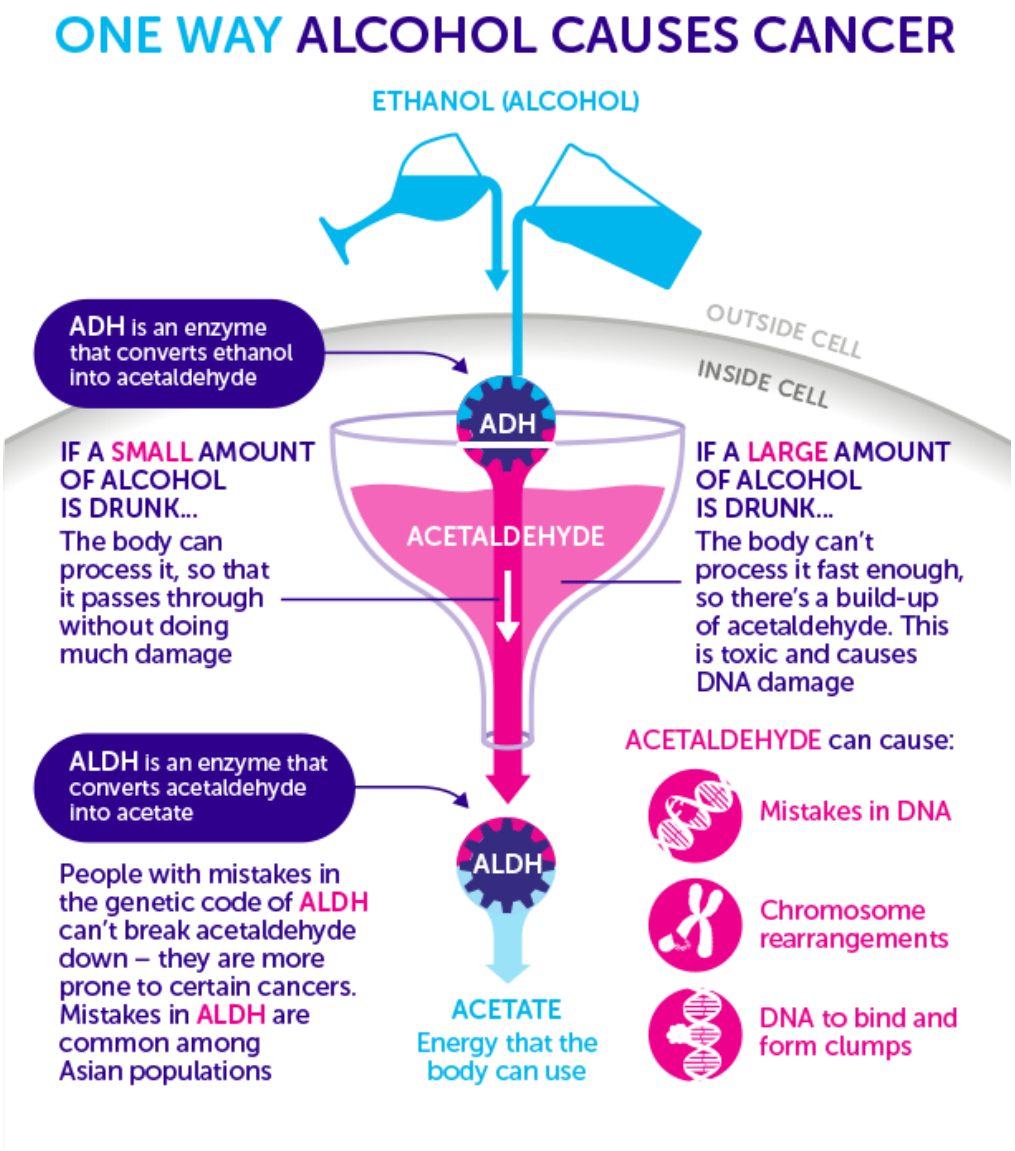
Alkohol





http://cancerprogressreport.org/2016/Documents/CPR2016.pdf

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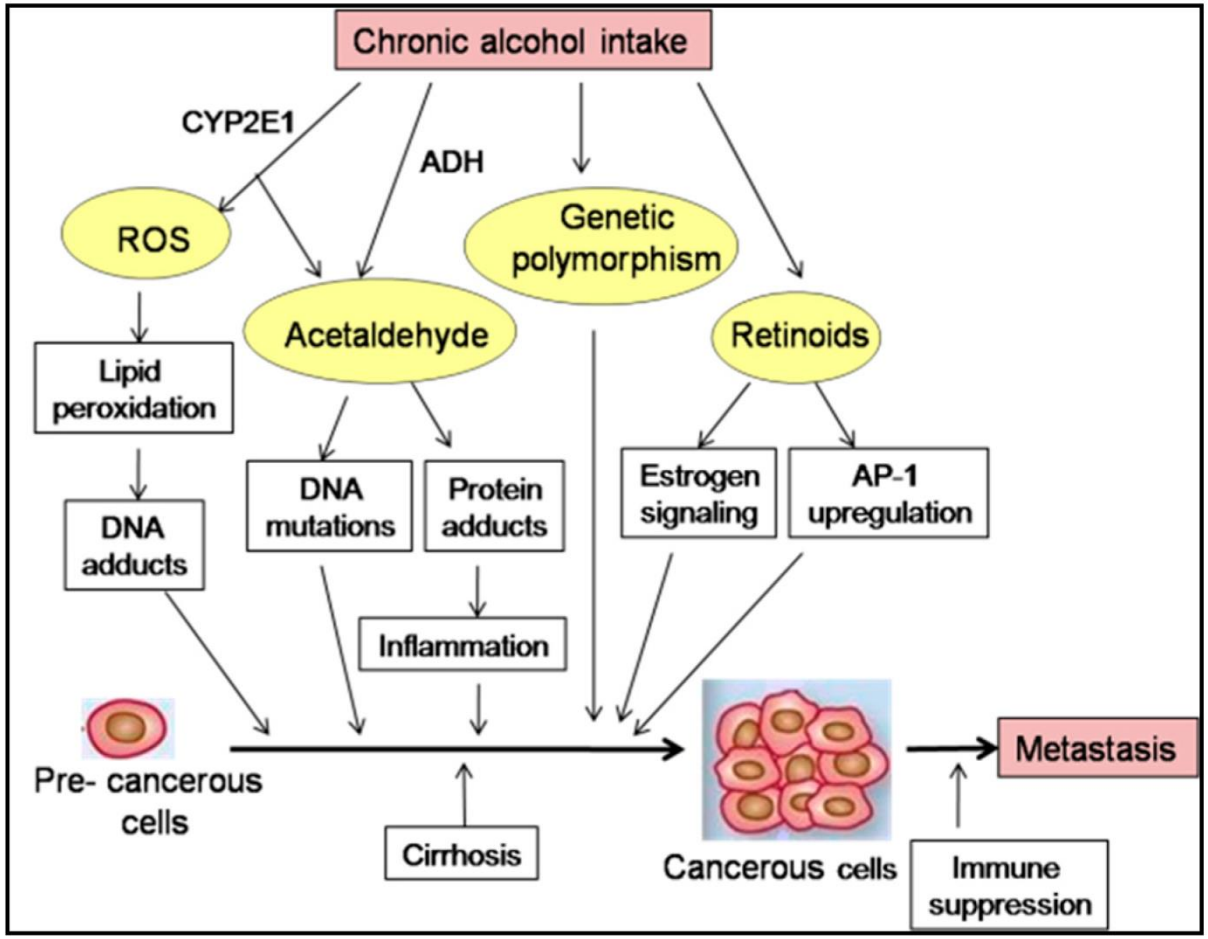
Alkohol und Krebs: mögliche Mechanismen



http://www.mdpi.com/2218-273X/7/3/61
https://www.nature.com/articles/nrc2191

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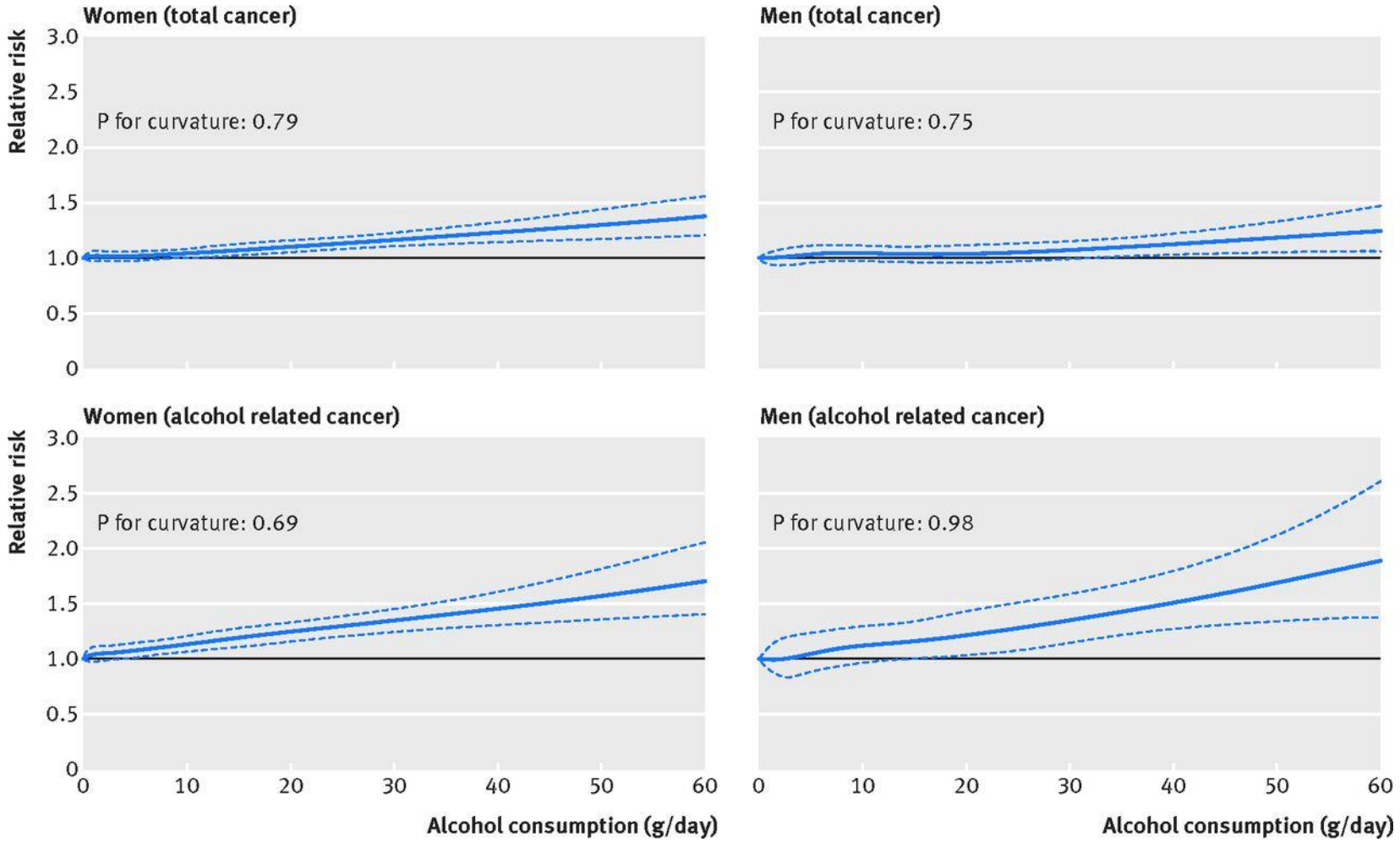
Zusammenhang zw. Alkoholkonsum und Krebs (gesamt und alkohol-assoziiiert)



http://www.bmj.com/content/351/bmj.h4238

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Alkoholabhängige Krebsarten

Table 2.3.1. Cancers where alcohol consumption may be a component cause

Disease	ICD-10 code	Effect[a]	Epidemiological evidence[a]
Malignant neoplasms			
Cancers of the upper aerodigestive tract			
Cancer of the oral cavity and pharynx	C00–C13	Detrimental	Causally related
Cancer of the larynx	C32	Detrimental	Causally related
Cancer of the oesophagus	C15	Detrimental	Causally related
Cancer of the colorectum	C18–C21	Detrimental	Causally related
Cancer of the liver and hepatobiliary tract	C22	Detrimental	Causally related
Cancer of the stomach	C16	Detrimental	Insufficient causal evidence
Cancer of the pancreas	C25	Detrimental	Causality may need to be re-evaluated
Cancer of the lung	C33–C34	Detrimental	Insufficient causal evidence
Cancer of the female breast	C50	Detrimental	Causally related
Cancer of the prostate	C61	Detrimental	Insufficient causal evidence
Cancer of the kidney and cancer of the urinary bladder	C64–C66, C68 (except C68.9)	Beneficial[b]/no association[a] (renal cell carcinoma only)	Insufficient causal evidence
Cancers of the lymphatic and haematopoietic system			
Hodgkin lymphoma	C81	Beneficial[c]/no association[a]	Insufficient causal evidence
Non-Hodgkin lymphoma	C82–C85, C96	Beneficial[d]/no association[a]	Insufficient causal evidence

WHO: World Cancer Report: http://publications.iarc.fr/Non-Series-Publications/World-Cancer-Reports/World-Cancer-Report-2014

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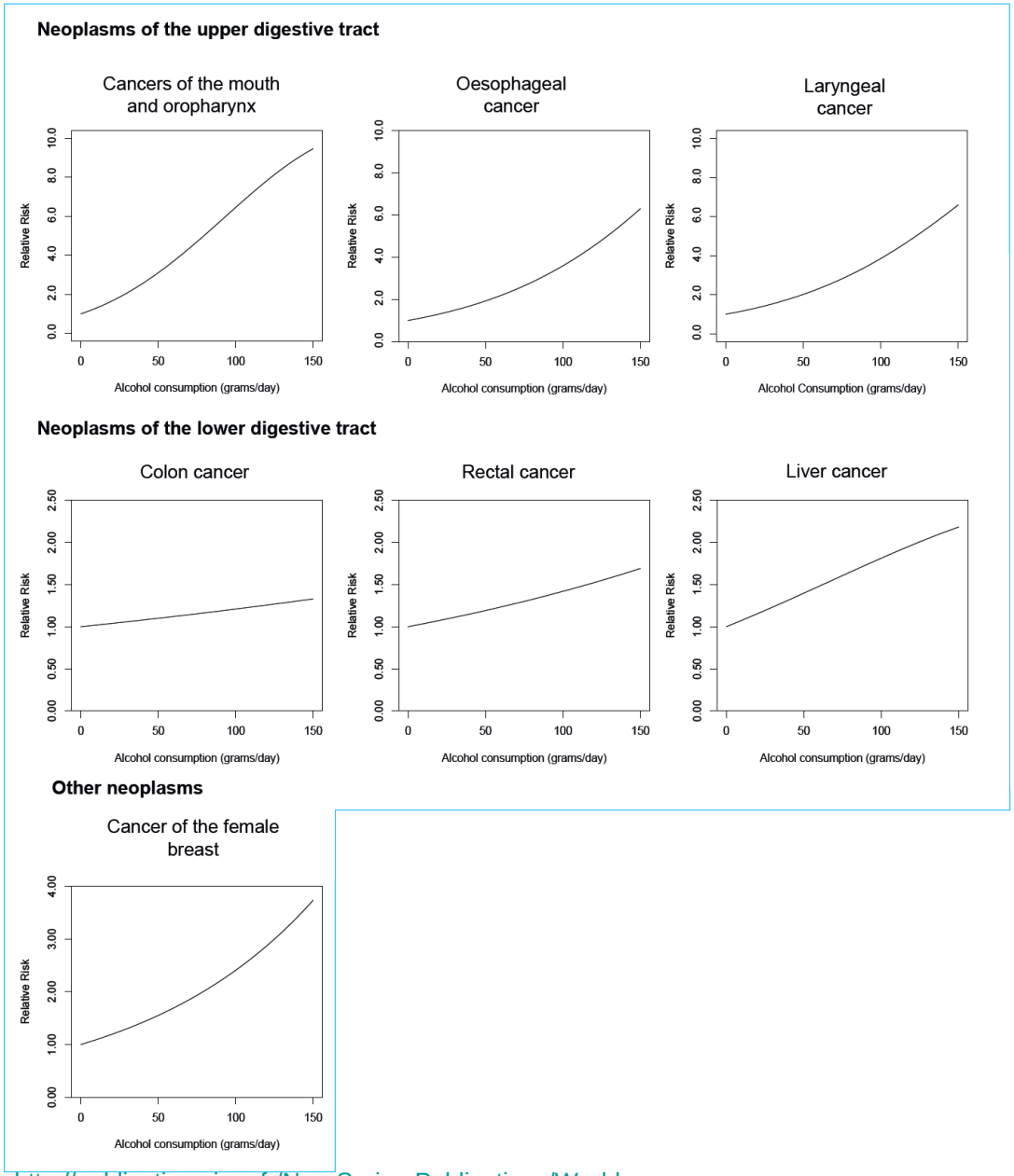
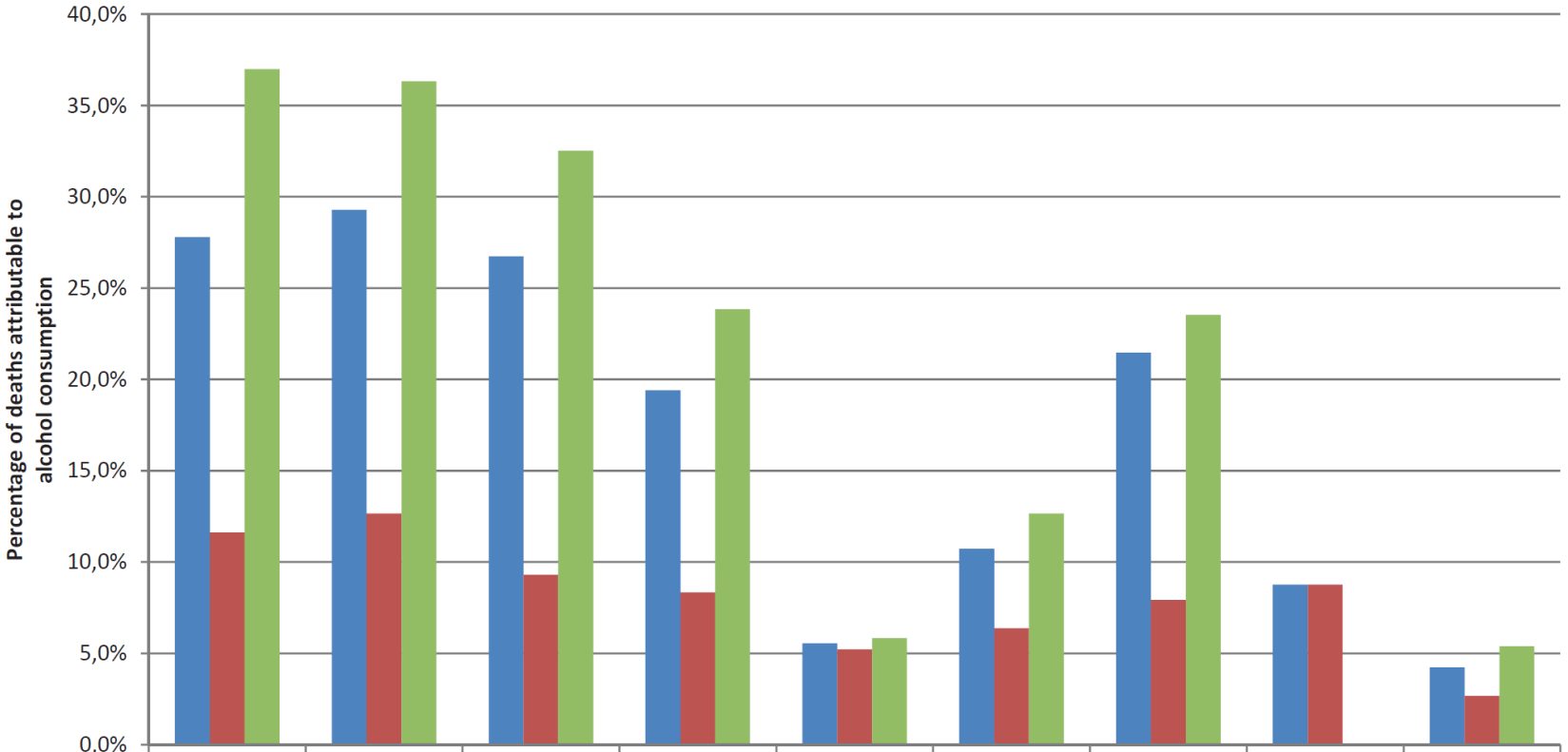
Box 2.3.1. The relationship between average daily alcohol consumption and relative risk of cancer.



WHO: World Cancer Report: http://publications.iarc.fr/Non-Series-Publications/World-Cancer-Reports/World-Cancer-Report-2014

Fig. 2.3.1. Percentage of deaths from various forms of cancer attributable to alcohol consumption, in 2010.

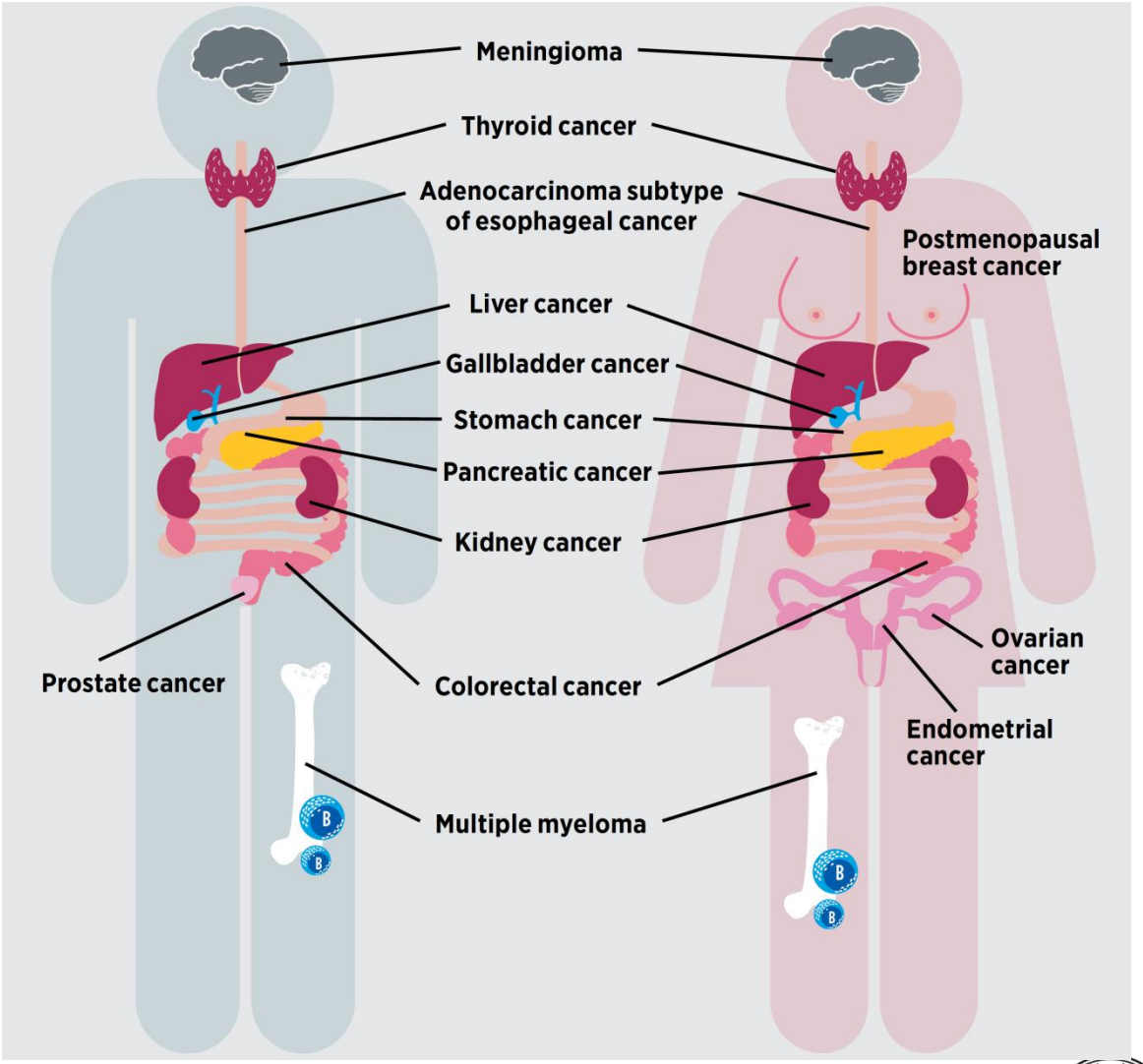


	Mouth cancer	Cancer of the nasopharynx	Cancer of other part of pharynx and oropharynx	Oesophageal cancer	Cancers of the colon and rectum	Liver cancer	Laryngeal cancer	Cancer of the female breast	All cancer deaths
Total	27,8%	29,3%	26,7%	19,4%	5,5%	10,7%	21,5%	8,8%	4,2%
Women	11,6%	12,6%	9,3%	8,3%	5,2%	6,4%	7,9%	8,8%	2,7%
Men	37,0%	36,3%	32,5%	23,8%	5,8%	12,7%	23,5%		5,4%

WHO: World Cancer Report: http://publications.iarc.fr/Non-Series-Publications/World-Cancer-Reports/World-Cancer-Report-2014


Societal factors
Drinking culture
Alcohol policy
Drinking environment
Health care system
Alcohol consumption
Volume | Patterns | Quality
Incidence & disability:
Chronic diseases and conditions
Health outcomes
Mortality by cause
Population group
Gender
Age
Poverty marginalization

Adipositas und Krebs



http://cancerprogressreport.org/2016/Documents/CPR2016.pdf

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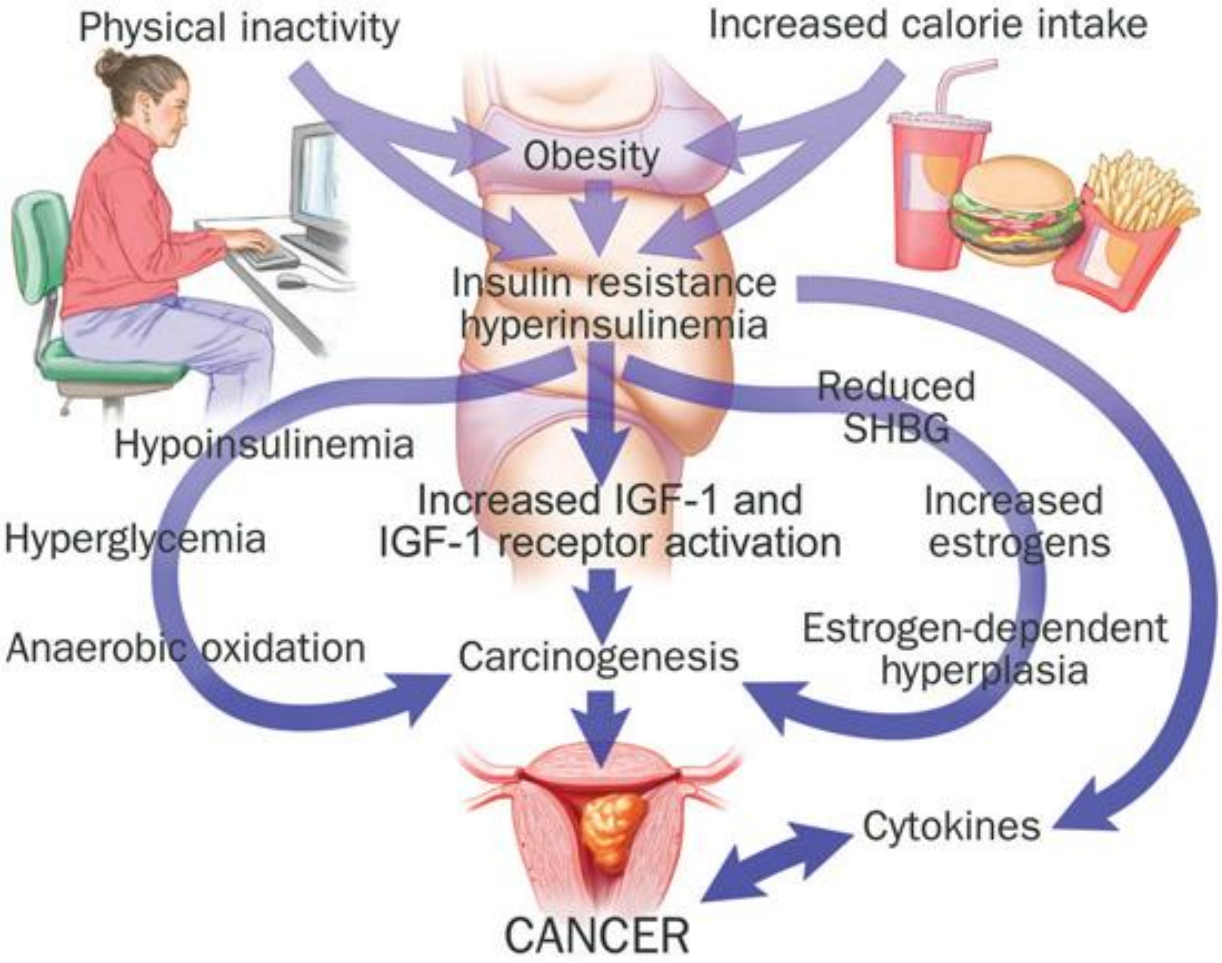
BMI: Welche Krebsarten betroffen?

Table 2. Strength of the Evidence for a Cancer-Preventive Effect of the Absence of Excess Body Fatness, According to Cancer Site or Type.*

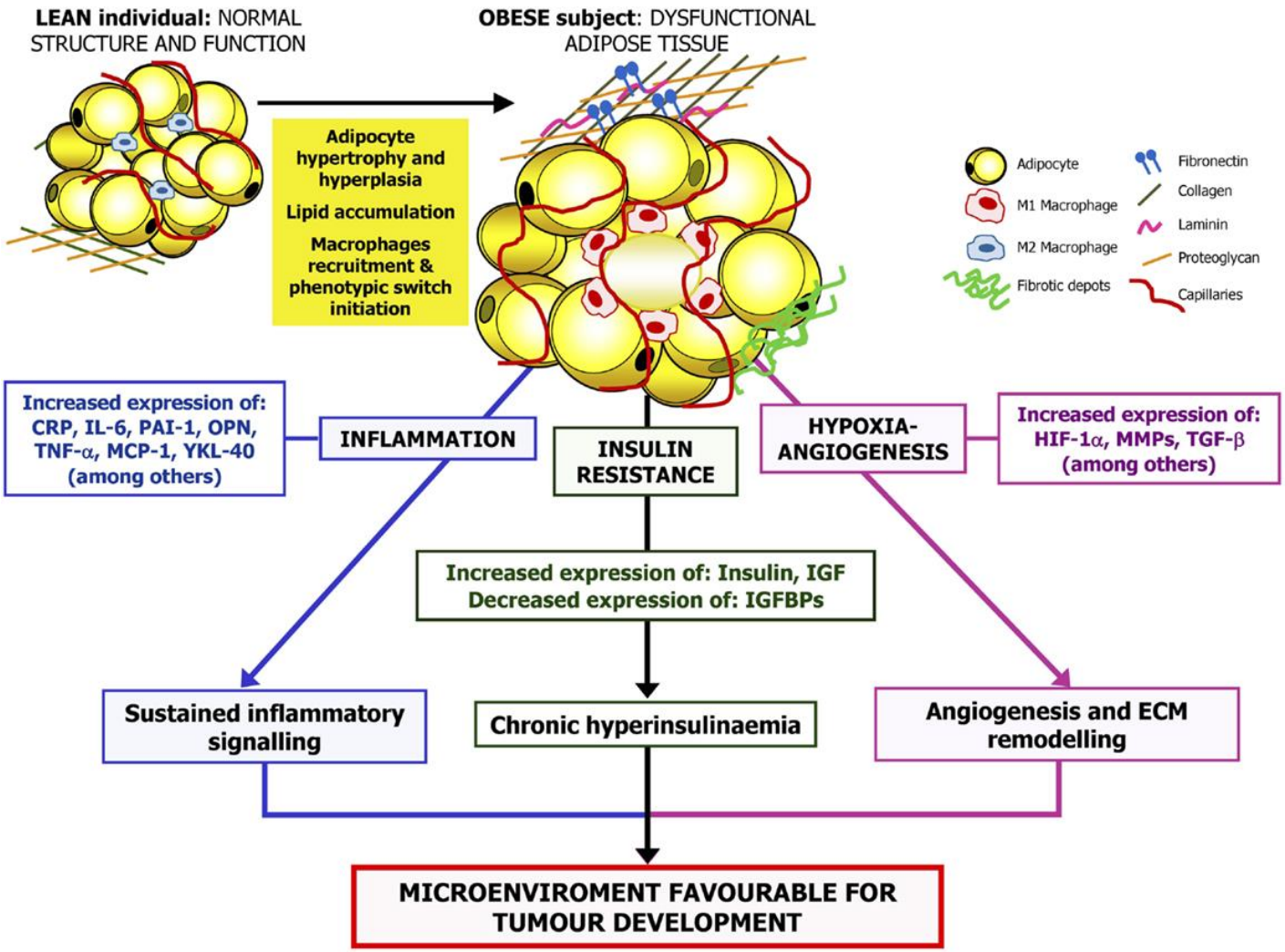
Cancer Site or Type	Strength of the Evidence in Humans†	Relative Risk of the Highest BMI Category Evaluated versus Normal BMI (95% CI)‡
Esophagus: adenocarcinoma	Sufficient	4.8 (3.0–7.7)
Gastric cardia	Sufficient	1.8 (1.3–2.5)
Colon and rectum	Sufficient	1.3 (1.3–1.4)
Liver	Sufficient	1.8 (1.6–2.1)
Gallbladder	Sufficient	1.3 (1.2–1.4)
Pancreas	Sufficient	1.5 (1.2–1.8)
Breast: postmenopausal	Sufficient	1.1 (1.1–1.2)§
Corpus uteri	Sufficient	7.1 (6.3–8.1)
Ovary	Sufficient	1.1 (1.1–1.2)
Kidney: renal-cell	Sufficient	1.8 (1.7–1.9)
Meningioma	Sufficient	1.5 (1.3–1.8)
Thyroid	Sufficient	1.1 (1.0–1.1)§
Multiple myeloma	Sufficient	1.5 (1.2–2.0)
Male breast cancer	Limited	NA
Fatal prostate cancer	Limited	NA
Diffuse large B-cell lymphoma	Limited	NA
Esophagus: squamous-cell carcinoma	Inadequate	NA
Gastric noncardia	Inadequate	NA
Extrahepatic biliary tract	Inadequate	NA
Lung	Inadequate	NA
Skin: cutaneous melanoma	Inadequate	NA
Testis	Inadequate	NA
Urinary bladder	Inadequate	NA
Brain or spinal cord: glioma	Inadequate	NA

http://www.nejm.org/doi/full/10.1056/NEJMsr1606602

Adipositas: Mögliche Gründe für erhöhtes Krebsrisiko



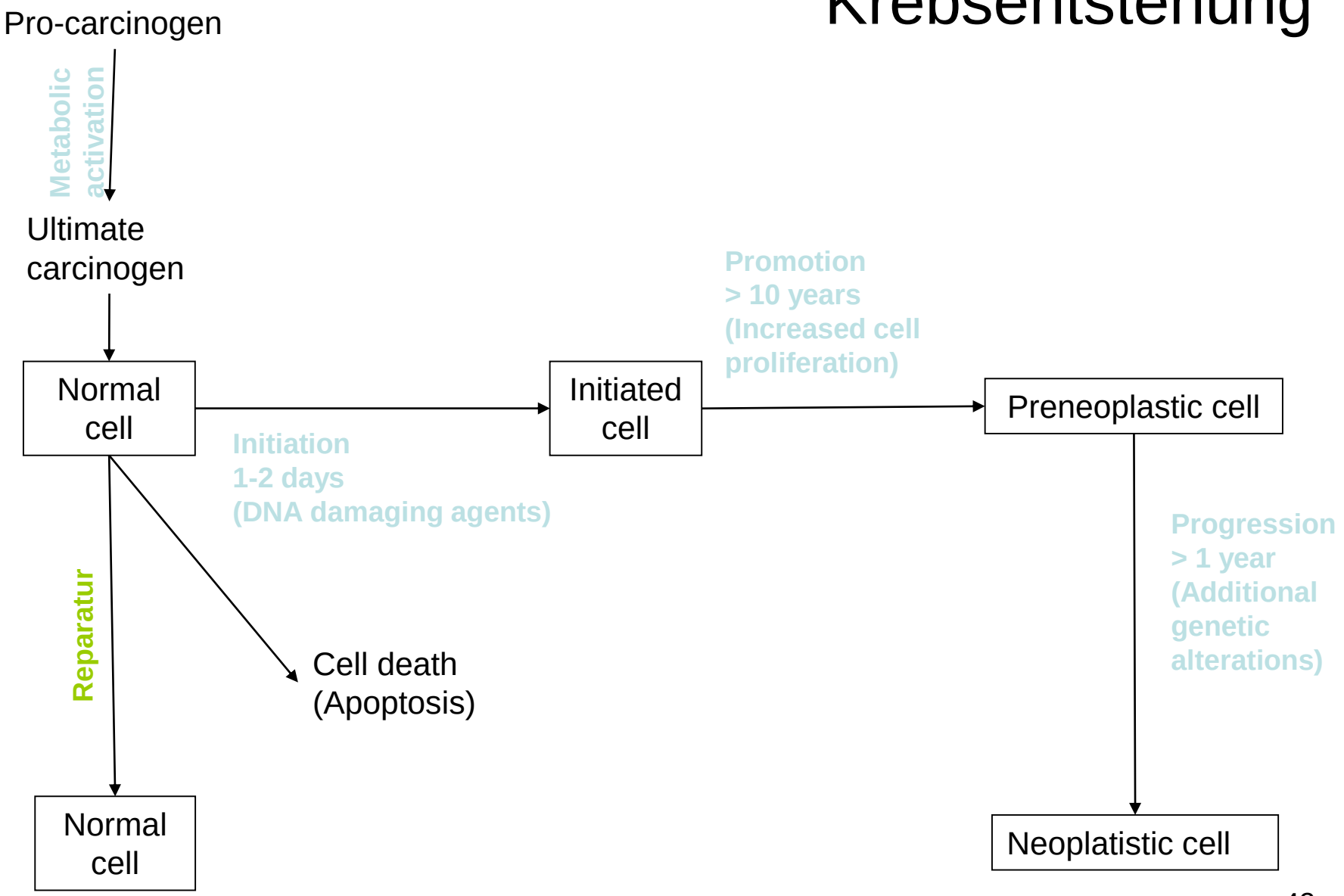
Adipositas & Krebs: mögliche Mechanismen



Inhalt

- Krebs-Epidemiologie
- Ernährung: neue Bedrohungen (?)
- Was ins Gewicht fällt
- Generelle Limitationen der Krebsforschung

Krebsentstehung



Mit freundlicher Genehmigung von Prof. Sabine Rohrmann

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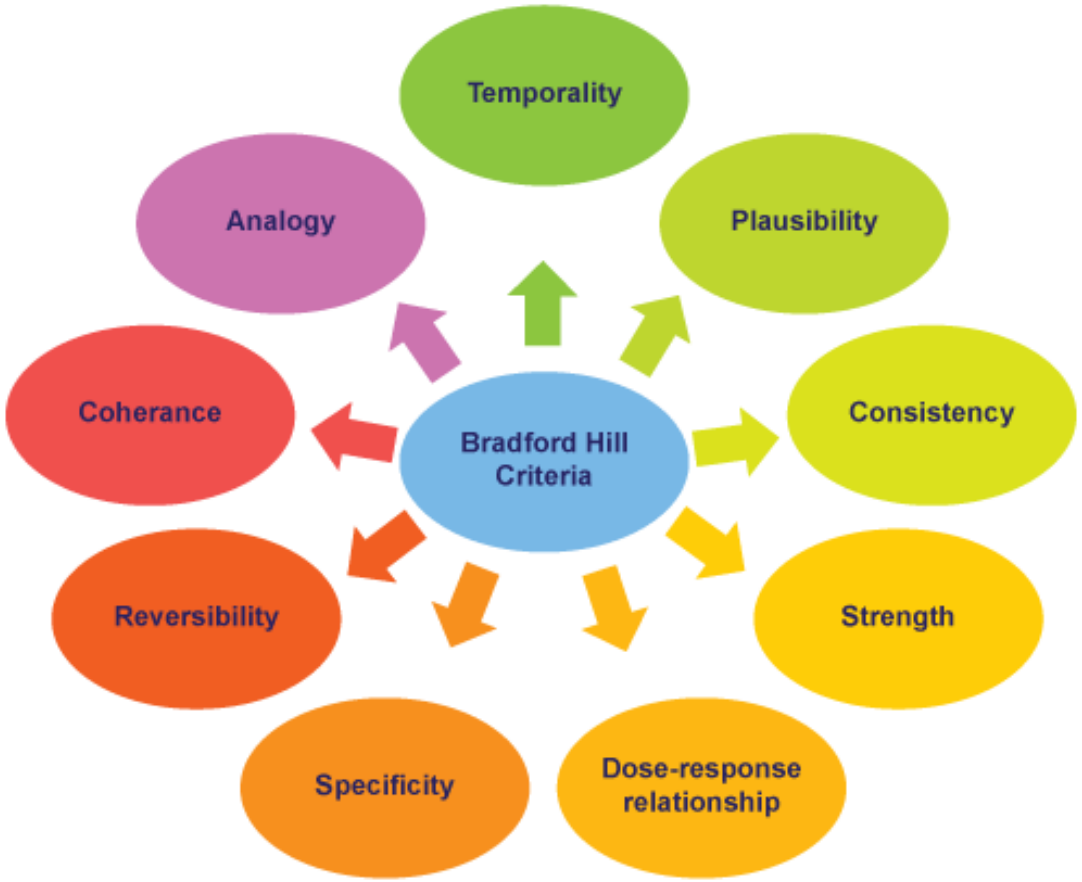
Wann ist ein Zusammenhang ursächlich?

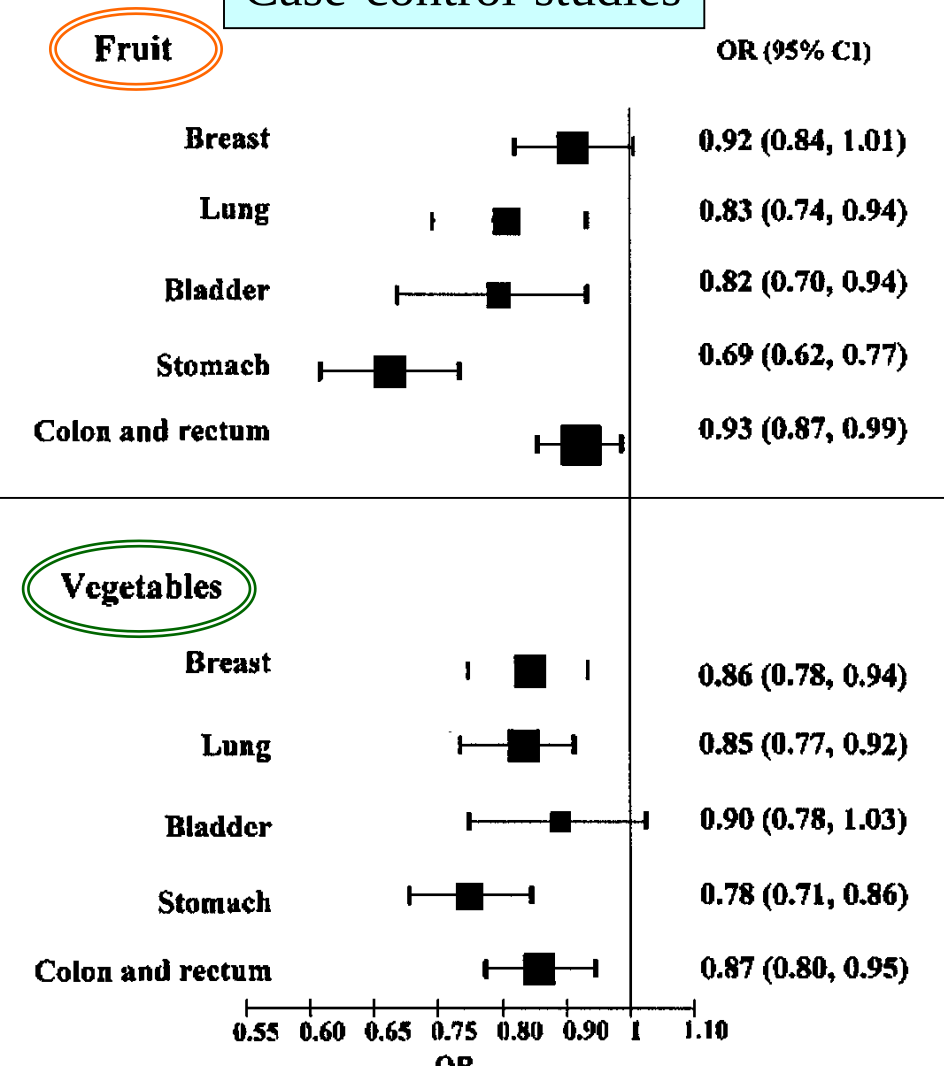


https://www.edwardtufte.com/tufte/hill

Level of Evidence	Type of Study
1a	Systematic reviews of randomized controlled trials (RCTs)
1b	Individual RCTs with narrow confidence interval
2a	Systematic reviews of cohort studies
2b	Individual cohort studies and low-quality RCTs
3a	Systematic reviews of case-control studies
3b	Case-controlled studies
4	Case series and poor-quality cohort and case-control studies
5	Expert opinion

Früchte- und Gemüsekonsum und Krebsrisiko (pro 100 Gramm Konsum)

Case-control-studies

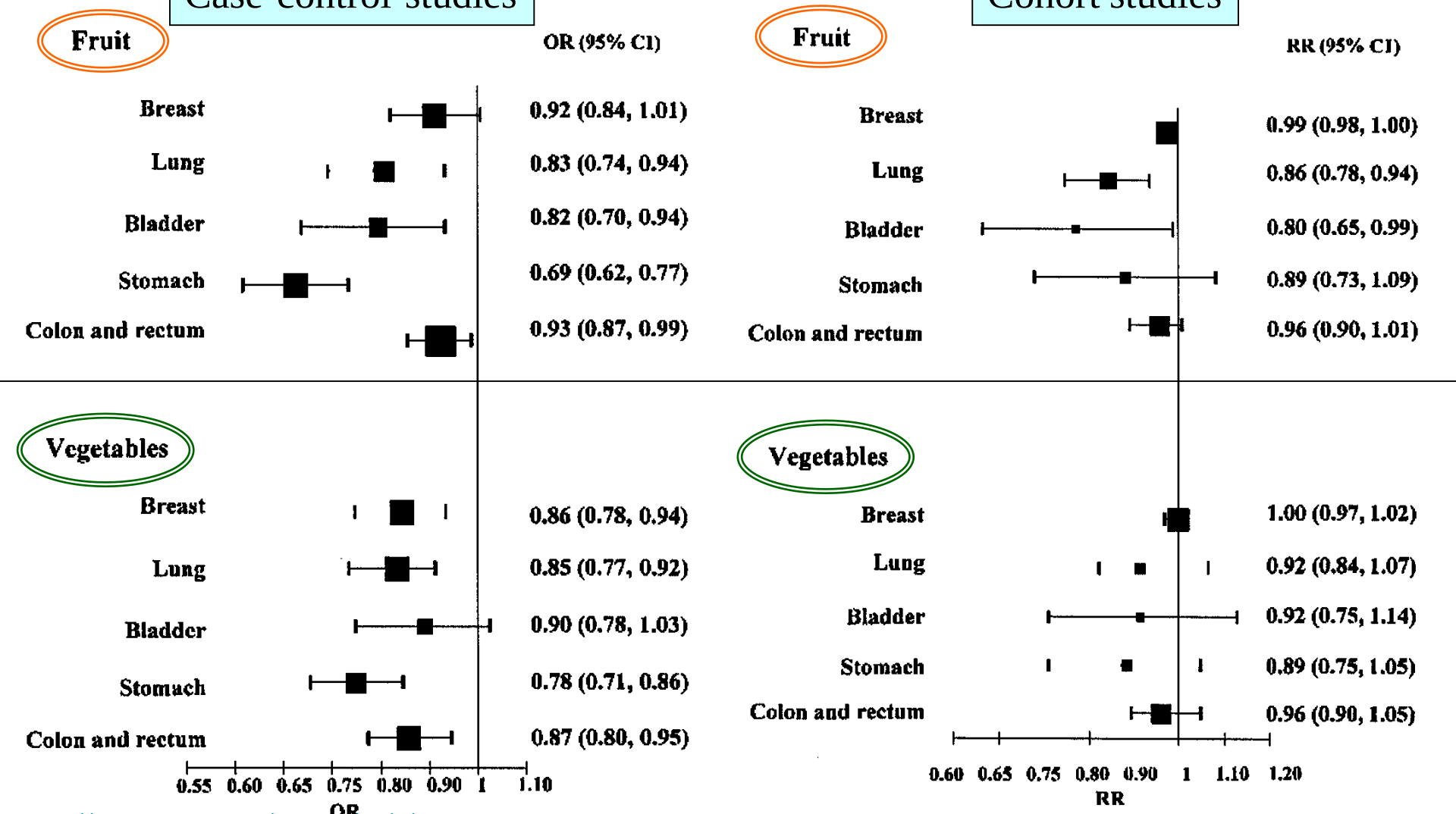


http://ajcn.nutrition.org/content/78/3/559S.long

Früchte- und Gemüsekonsum und Krebsrisiko (pro 100 Gramm Konsum)

Case-control-studies

Cohort studies

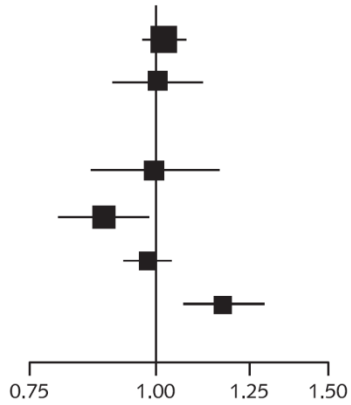


http://ajcn.nutrition.org/content/78/3/559S.long

Omega-3 Fettsäuren: Kohortenstudien

Figure 1. **RRs for coronary outcomes in prospective cohort studies of dietary fatty acid intake.**

Fatty Acid Intake	Studies, *n*	Participants, *n*	Events, *n*	RR (95% CI)*
Total saturated fatty acids	20	276 763	10 155	1.03 (0.98–1.07)
Total monounsaturated fatty acids	9	144 219	6031	1.00 (0.91–1.10)
Total ω-3 fatty acids				
α-Linolenic	7	157 258	7431	0.99 (0.86–1.14)
Total long-chain ω-3	16	422 786	9089	0.87 (0.78–0.97)
Total ω-6 fatty acids	8	206 376	8155	0.98 (0.90–1.06)
Total trans fatty acids	5	155 270	4662	1.16 (1.06–1.27)



RR (95% CI) Comparing Top vs. Bottom Thirds of Baseline Dietary Fatty Acid Intake

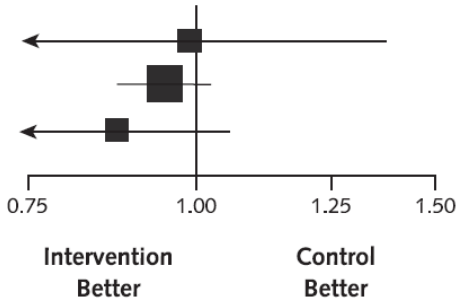
Size of the data marker is proportional to the inverse of the variance of the RR. RR = relative risk.
* Pooled estimate based on random-effects meta-analysis. Corresponding forest plots, I^2 estimates, and pooled RRs based on fixed-effects meta-analysis are provided in **Supplement 1**, available at www.annals.org.

Ann Intern Med. 2014;160:398-406.

Omega-3 Fettsäuren: RCTs

Figure 3. Effect of fatty acid supplementation on risk for coronary event, derived from available randomized, controlled trials.

Fatty Acid Supplement	Studies, *n*	Events/Participants, *n/N*		RR (95% CI)*
		Intervention Group	Control Group	
α-Linolenic acid	4	199/9444	220/9422	0.97 (0.69–1.36)
Long-chain ω-3 fatty acid	17	2426/38 303	2548/38 277	0.94 (0.86–1.03)
ω-6 fatty acid†	8	459/7245	515/7231	0.86 (0.69–1.07)



Conclusion: Current evidence does not clearly support cardiovascular guidelines that encourage high consumption of polyunsaturated fatty acids and low consumption of total saturated fats

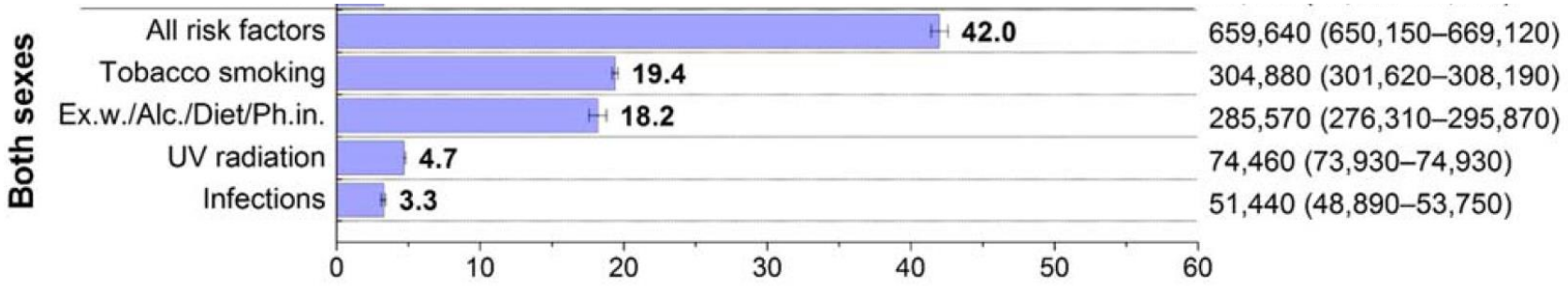
Ann Intern Med. 2014;160:398-406.

Bradford-Hill Criteria

1. **Strength** (effect size): A small association does not mean that there is not a causal effect, though the larger the association, the more likely that it is causal.
2. **Consistency** (reproducibility): Consistent findings observed by different persons in different places with different samples strengthens the likelihood of an effect.
3. **Specificity**: Causation is likely if there is a very specific population at a specific site and disease with no other likely explanation. The more specific an association between a factor and an effect is, the bigger the probability of a causal relationship.
4. **Temporality**: The effect has to occur after the cause (and if there is an expected delay between the cause and expected effect, then the effect must occur after that delay).
5. **Biological gradient**: Greater exposure should generally lead to greater incidence of the effect. However, in some cases, the mere presence of the factor can trigger the effect. In other cases, an inverse proportion is observed: greater exposure leads to lower incidence.
6. **Plausibility**: A plausible mechanism between cause and effect is helpful (but Hill noted that knowledge of the mechanism is limited by current knowledge).
7. **Coherence**: Coherence between epidemiological and laboratory findings increases the likelihood of an effect. However, Hill noted that "... lack of such [laboratory] evidence cannot nullify the epidemiological effect on associations".
8. **Experiment**: "Occasionally it is possible to appeal to experimental evidence".
9. **Analogy**: The effect of similar factors may be considered.

https://www.edwardtufte.com/tufte/hill

Anteil (%*) vermeidbarer Krebsfälle nach Risikofaktor-Gruppe, USA 2014



*Population Attributable Fraction (PAF), Inzidenz

http://onlinelibrary.wiley.com/doi/10.3322/caac.21440/full

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