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Prostate Cancer in Switzerland – large differences in a small country

Sabine Rohrmann

EBPI

University of Zurich

Overview

Introduction

- Some information about cancer registration in CH
- Some facts about prostate cancer epidemiology
- The Swiss National Cohort SNC

Results

- Prostate cancer mortality and its relationship with nationality, place of birth and place of residence

Discussion

- How can we explain these findings?

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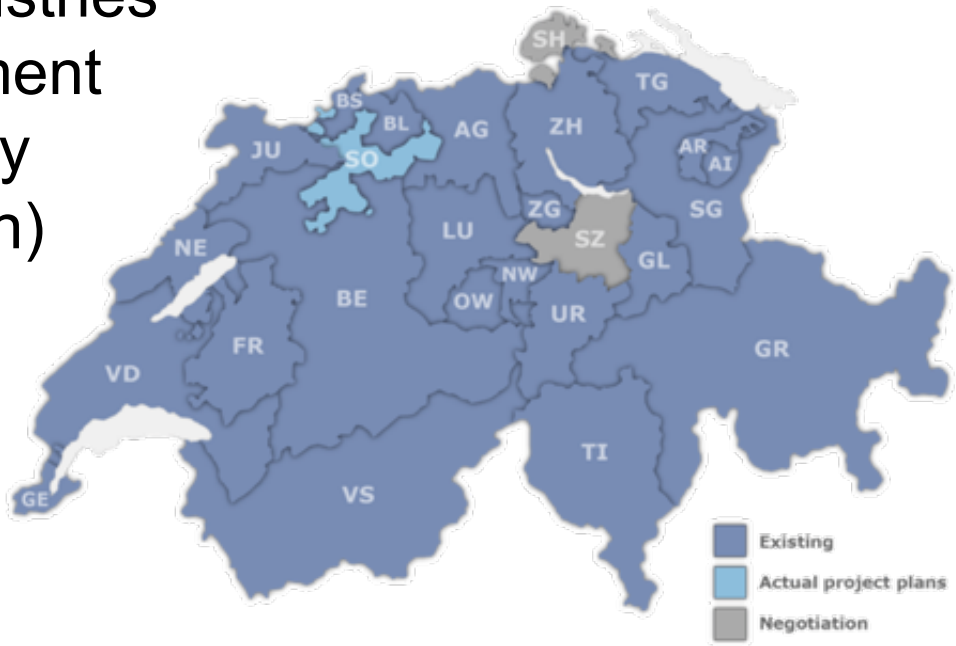
Cancer registration in Switzerland

- 26 cantons, each with its own legislation on cancer registration until Dec. 2020
- Not all cantons were covered by a cancer registry, but completeness is very good in those cantons with a registry
- Jan. 2020: enactment of the national law on cancer registration for the registries (with an earlier enactment for the National Agency for Cancer Registration)



Progression of cancer registration in Switzerland

1969 Basel

1970 Geneva

1974 Waadt and Neuchâtel

1980 Zurich, St. Gallen-Appenzell

1989 Wallis, Graubünden

1992 Glarus

1996 Tessin

2005 Jura

2010/11 cantons of Central Switzerland, Zug

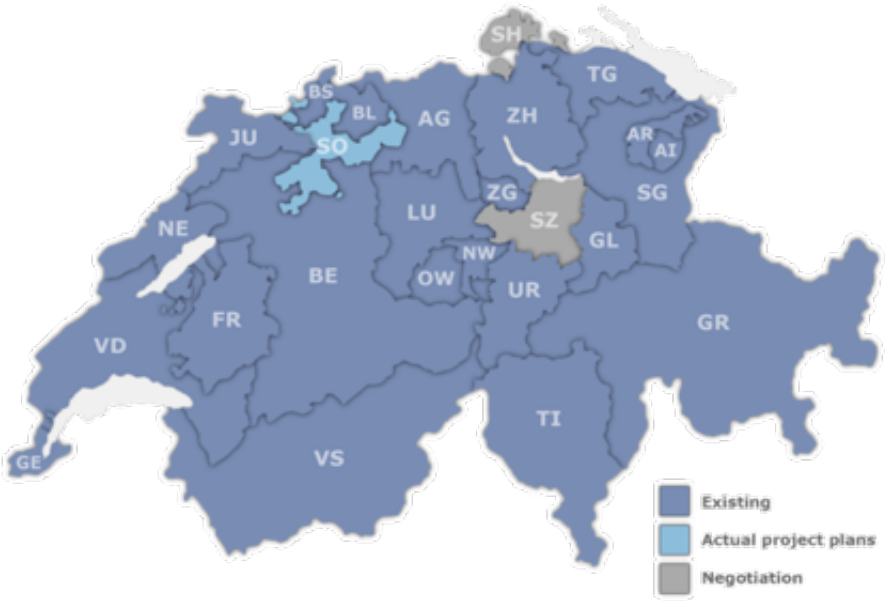
2012 Thurgau (2012),

2013 Aargau (2013)

2014 Bern (2014) and

2019 Solothurn (2019).

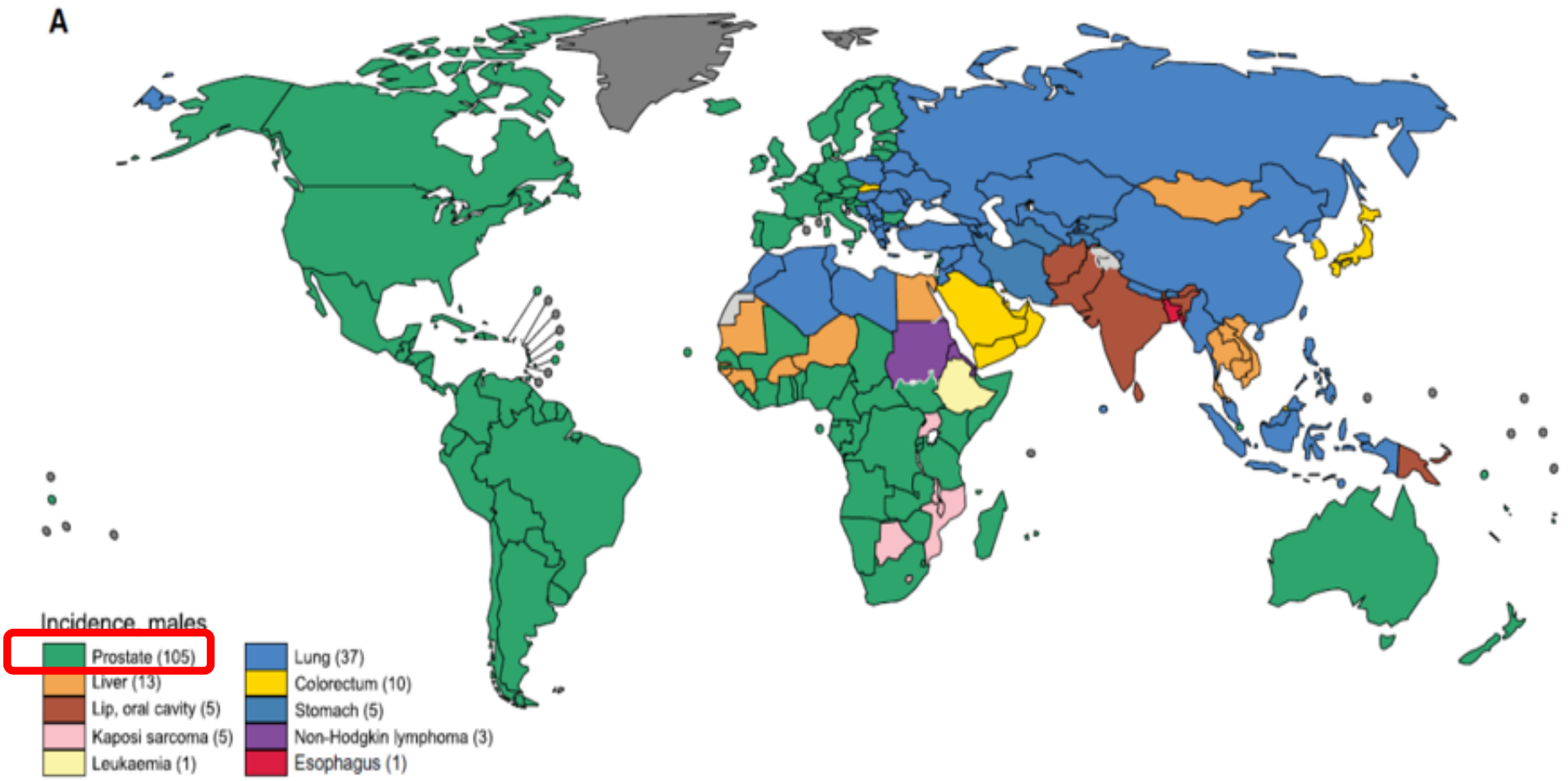
2020 Schwyz, Schaffhausen



nicer

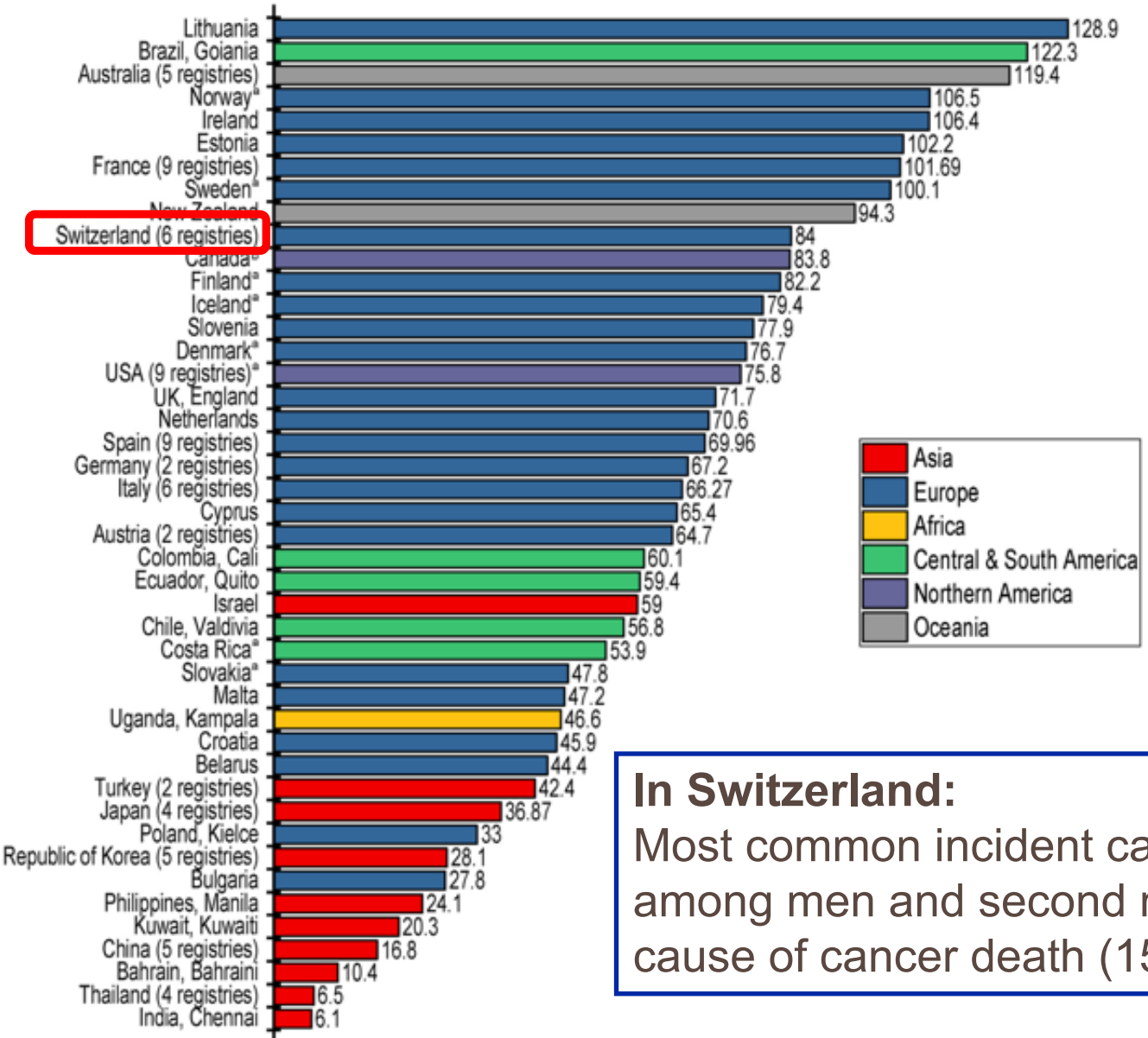
National Institute for Cancer Epidemiology and Registration
Nationales Institut für Krebsepidemiologie und Registrierung
Institut National pour l'Epidémiologie et l'Enregistrement du Cancer
Istituto Nazionale per l'Epidemiologia et la Registrazione del Cancro

Most Common Type of Cancer Incidence in 2018 in Each Country Among Men



GLOBOCAN 2018

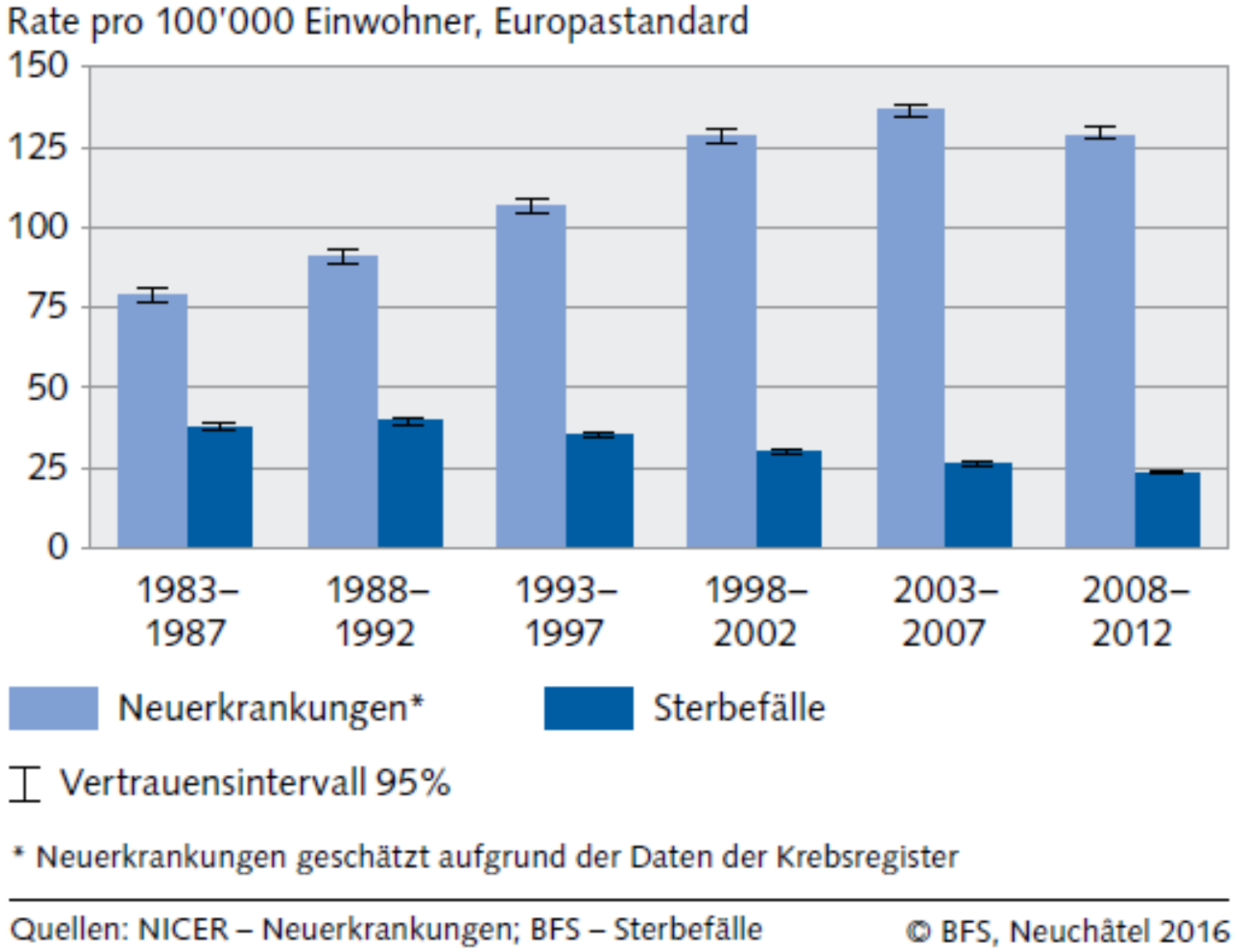
Prostate cancer incidence rates, 2008–2012



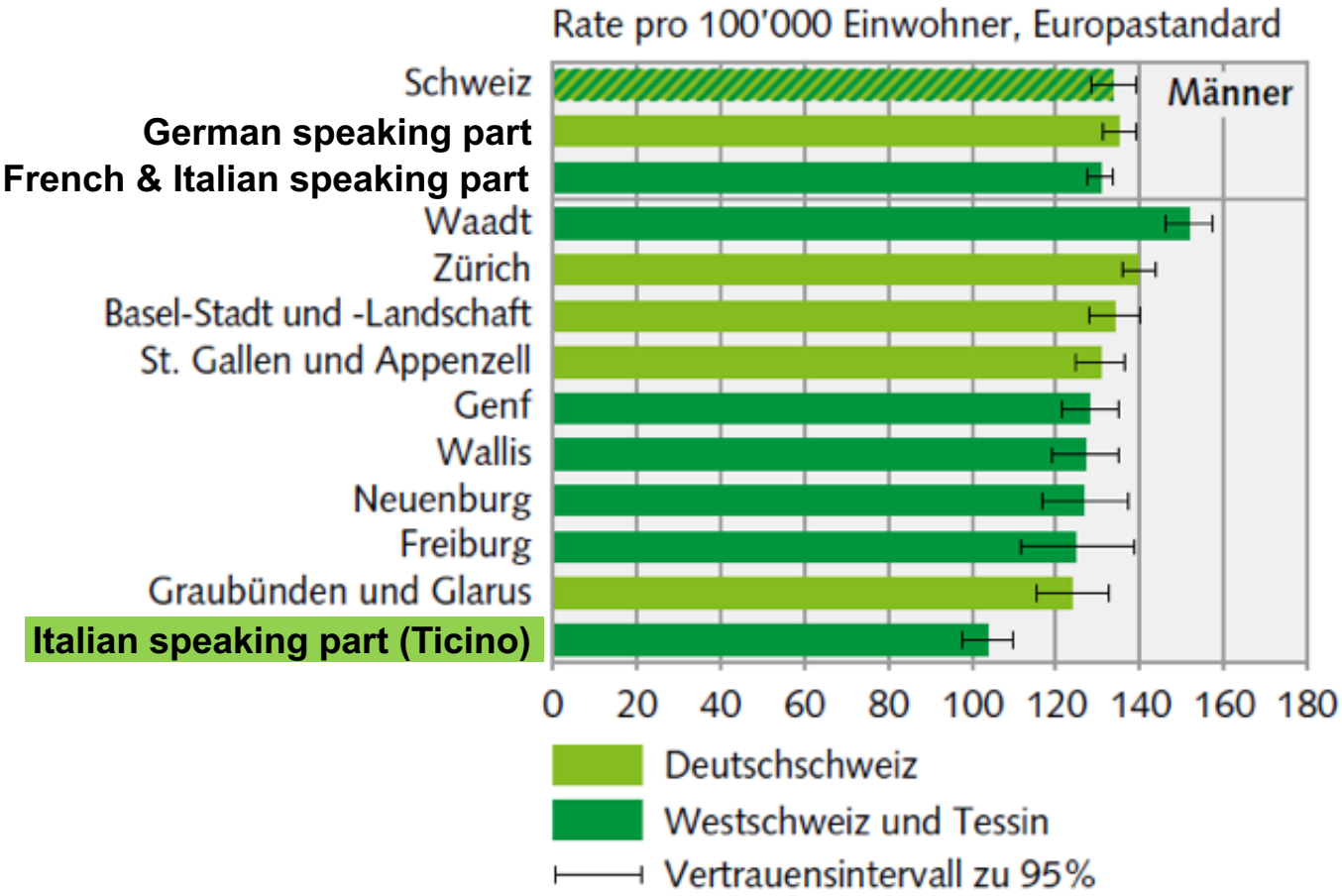
In Switzerland:
Most common incident cancer (25%) among men and second most common cause of cancer death (15%).

Culp et al. 2020

Increase in prostate cancer incidence until about 2007



This is how our research started: Differences in incidence rates by region (2003-2007)

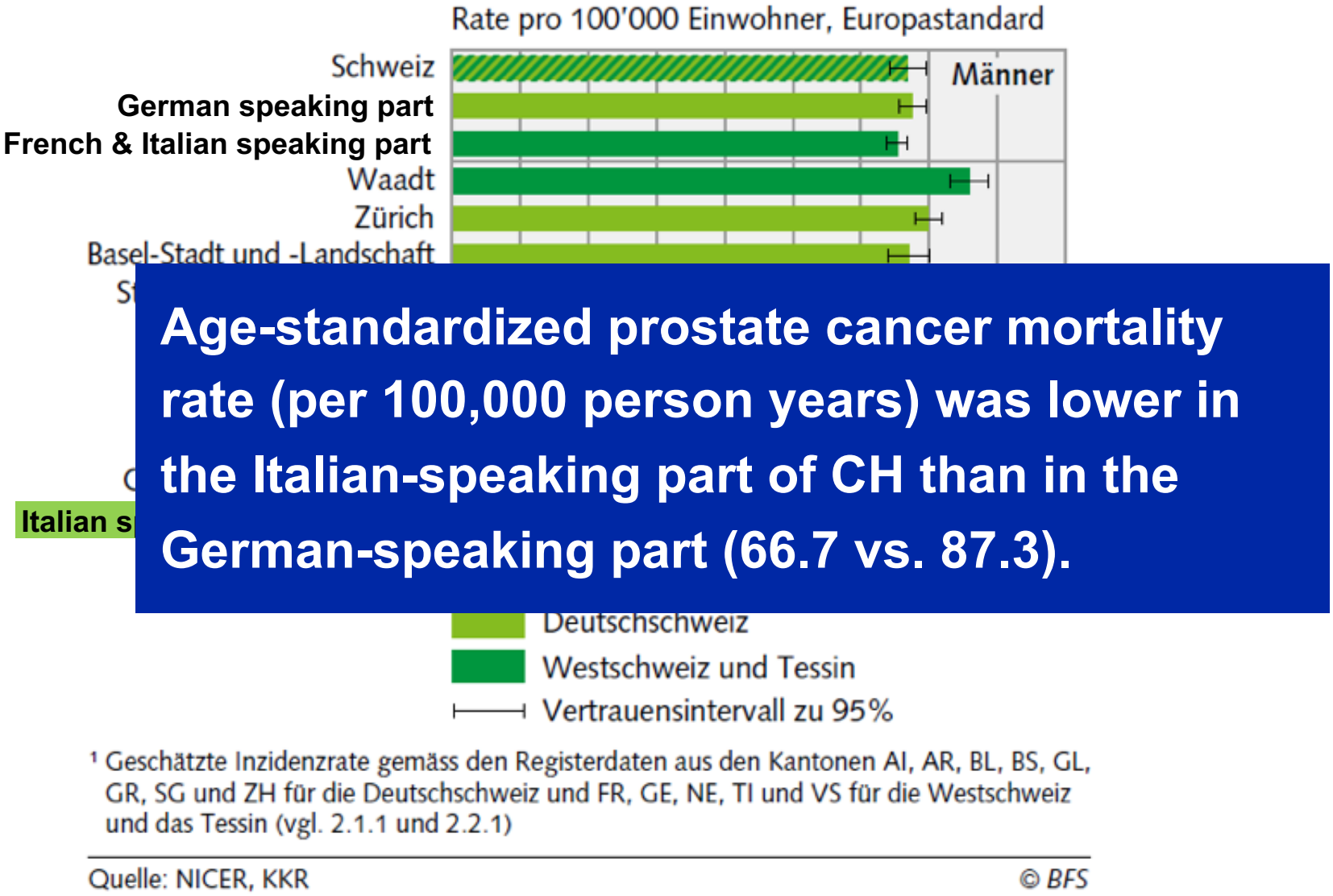


[1] Geschätzte Inzidenzrate gemäss den Registerdaten aus den Kantonen AI, AR, BL, BS, GL, GR, SG und ZH für die Deutschschweiz und FR, GE, NE, TI und VS für die Westschweiz und das Tessin (vgl. 2.1.1 und 2.2.1)

Quelle: NICER, KKR

© BFS

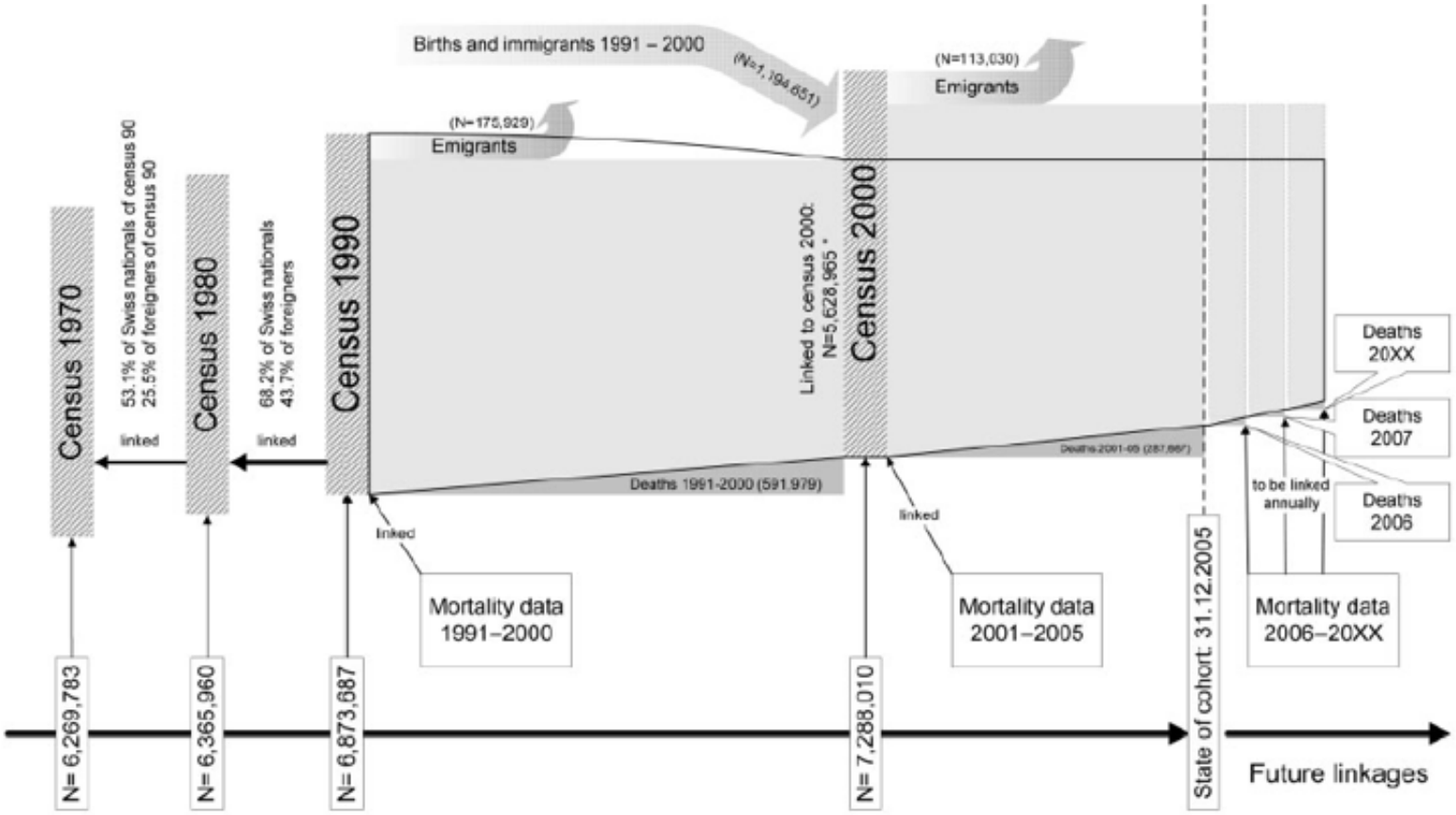
This is how our research started: Differences in incidence rates by region (2003-2007)



Age-standardized prostate cancer mortality rate (per 100,000 person years) was lower in the Italian-speaking part of CH than in the German-speaking part (66.7 vs. 87.3).

Swiss National Cohort

Articifial cohort by anonymous record linkage of Swiss Census data with mortality information



* 476,814 individuals could not be linked to the census 2000, a mortality or emigration record (see table 2).

Examples of previous studies

Linking Swiss Census data with mortality information

- Lower mortality from coronary heart disease and stroke at higher altitudes in Switzerland
- Aircraft noise, air pollution, and mortality from myocardial infarction
- Educational inequalities in mortality and associated risk factors: German- versus French-speaking Switzerland
- Healthy migrants but unhealthy offspring? A retrospective cohort study among Italians in Switzerland
- Religion and assisted and non-assisted suicide in Switzerland: National Cohort Study

➢ **Information on place of residence, place of birth and nationality**

Age-standardized prostate cancer mortality rates in CH, 1990-2008

Age-standardized prostate mortality rates (MR) per 100,000 person-years, 1990-2008, men aged 40+ years at baseline[a]

	German Switzerland		French Switzerland		Italian Switzerland	
Men[b]	MR	95% CI	MR	95% CI	MR	95% CI
CH, CH	88.1	(86.7-89.5)	83.5	(81.0-86.1)	69.5	(63.9-75.0)
CH, IT / IT, CH	59.2	(46.5-72.0)	78.1	(59.0-97.1)	63.6	(47.9-79.3)
IT, IT	66.8	(51.1-82.6)	53.1	(41.4-64.9)	55.0	(42.0-68.1)
Total	**87.3**	**(85.9-88.7)**	**82.1**	**(79.6-84.5)**	**66.7**	**(62.0-71.4)**

[a] Baseline at December 4, 1990

[b] Nationality is set before comma, and place of birth after comma

Richard A., Cancer Causes Control 2014

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Richard A., Cancer Causes Control 2014

Risk of dying from prostate cancer by nationality, place of birth and language region, CH 1990-2008

Nationality and place of birth[a]	Language region	HR[b]	95% CI
CH, CH	**German**	**1.00**	**ref.**
CH, IT or IT, CH	German	0.67	[0.58,0.77]
IT, IT	**German**	**0.68**	**[0.49,0.95]**
CH, CH	**French**	**0.95**	**[0.92,0.99]**
CH, IT or IT, CH	French	0.64	[0.54,0.77]
IT, IT	French	0.74	[0.51,1.08]
CH, CH	**Italian**	**0.79**	**[0.73,0.85]**
CH, IT or IT, CH	**Italian**	**0.64**	**[0.52,0.79]**
IT, IT	Italian	0.92	[0.59,1.42]

[b] adjusted for age, squared age, education level, observation period

[a] nationality is set before comma, and place of birth after comma

Richard A., Cancer Causes Control 2014

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CH, CH			**[0.92,0.99]**
CH, IT or IT, C			[0.54,0.77]
IT, IT			[0.51,1.08]
CH, CH	**Italian**	**0.79**	**[0.73,0.85]**
CH, IT or IT, CH	**Italian**	**0.64**	**[0.52,0.79]**
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WHY?

[b] adjusted for age, squared age, education level, observation period

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Richard A., Cancer Causes Control 2014

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WHY?

- **Lower incidence (i.e., less cases to start with)?**
- Different stage distribution (more cases diagnosed at an earlier stage)?
- Differences in lifestyle?

[b] adjusted for age, squared age, education level, observation period

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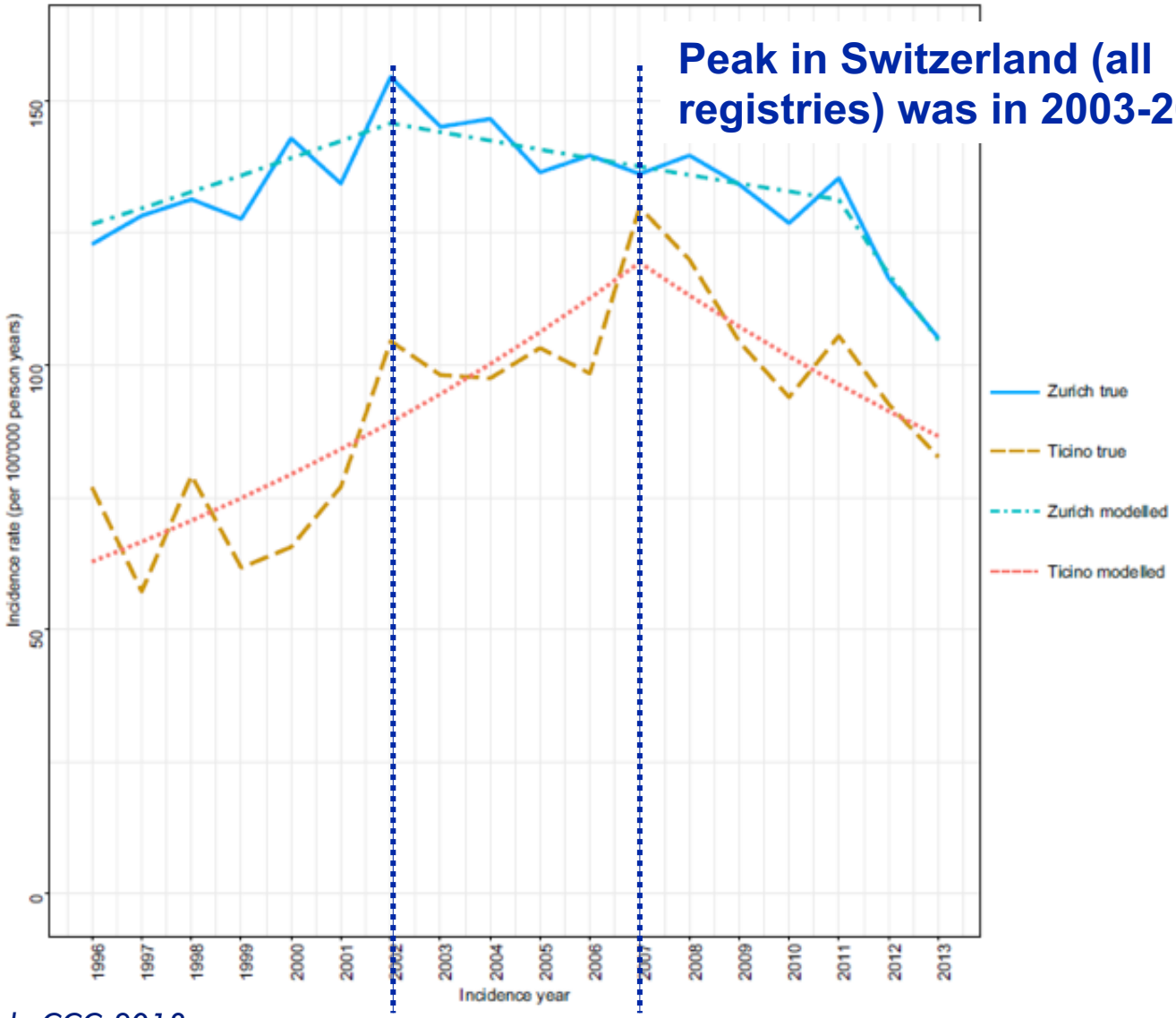
Richard A., Cancer Causes Control 2014

Age-standardized prostate cancer incidence rate in the canton of Zurich and in Ticino 1996-2013



Wanner M et al., CCC 2018

Due to differences in prostate cancer screening?

Percentage of men, 50+ years old, who have had a prostate examination in the last two years
(Swiss Health Surveys 1992-2012)

	1992 N = 1371	1997 N = 1353	2002 N = 2846	2007 N = 2764	2012 N = 3700
Linguistic area					
German	34.4	36.1	36.0	41.1	40.7
French	27.9	32.0	36.3	45.9	46.9
Italian	26.6	27.5	34.4	46.6	48.5

Guessous I, Prev Med 2016

Risk of dying from prostate cancer by nationality, place of birth and language region, CH 1990-2008

Nationality and place of birth[a]	Language region	HR[b]	95% CI
CH, CH	German	1.00	ref.
[illegible]	[illegible]	[illegible]	[illegible]
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Richard A., Cancer Causes Control 2014

Age-standardized prostate cancer incidence rate in the canton of Zurich and in Ticino 1996-2013 by T stage

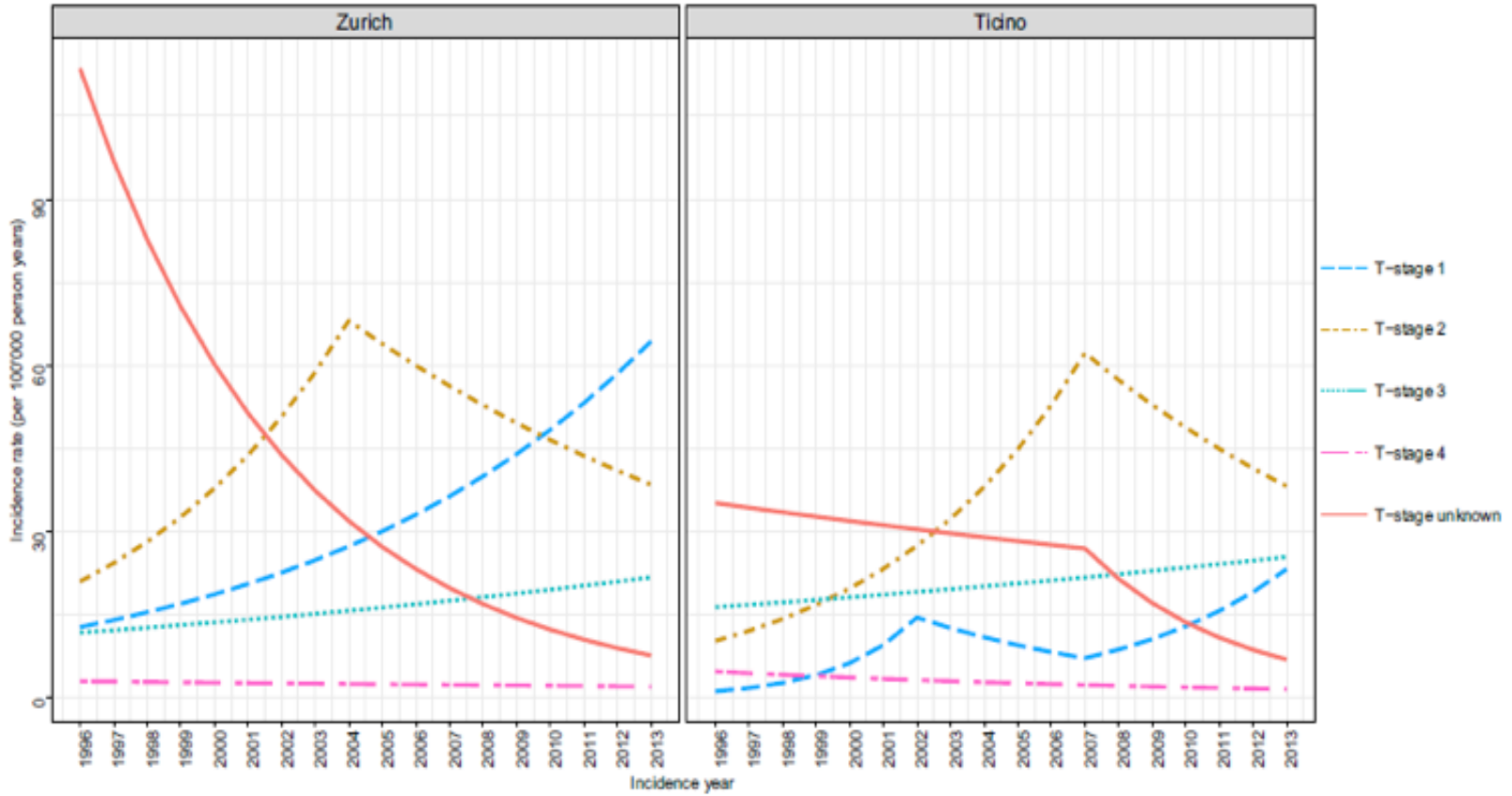

Fig. 4 Age-standardized incidence rates of prostate cancer (per 100,000) modeled by joinpoint regression analysis according to T-stage, 1996–2013, Zurich and Ticino (Switzerland)

Wanner M et al., CCC 2018

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WHY?

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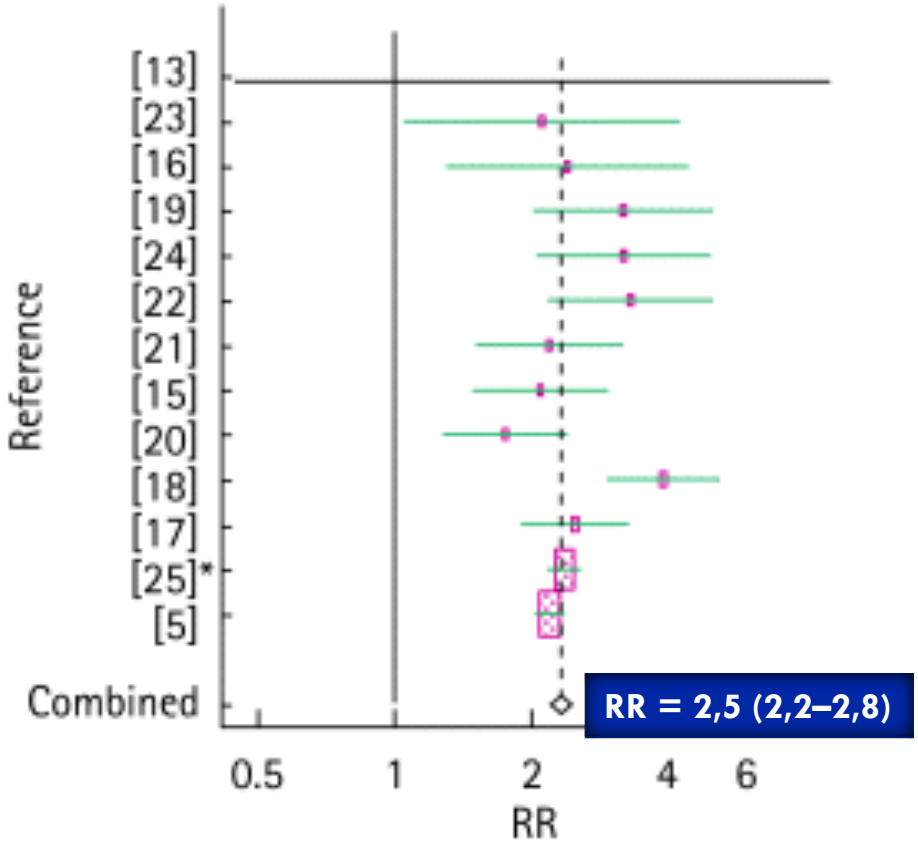
- Different stage distribution (more cases diagnosed at an earlier stage)?
- **Differences in lifestyle?**

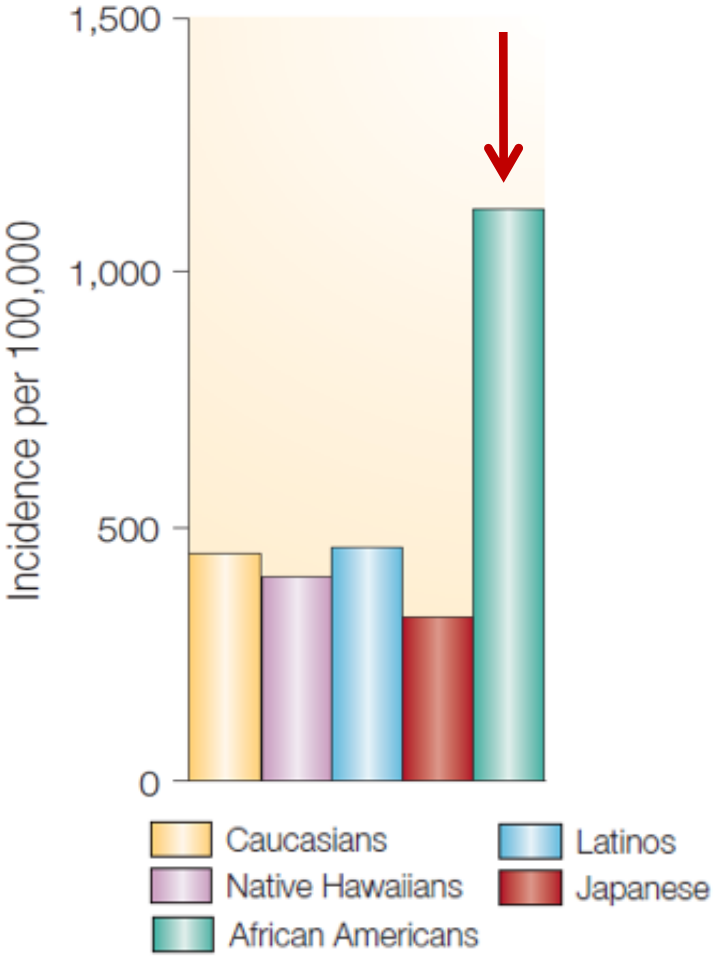
Richard A., Cancer Causes Control 2014

Established prostate cancer risk factors

Risk of prostate cancer associated with having one or more first-degree relatives affected with the disease

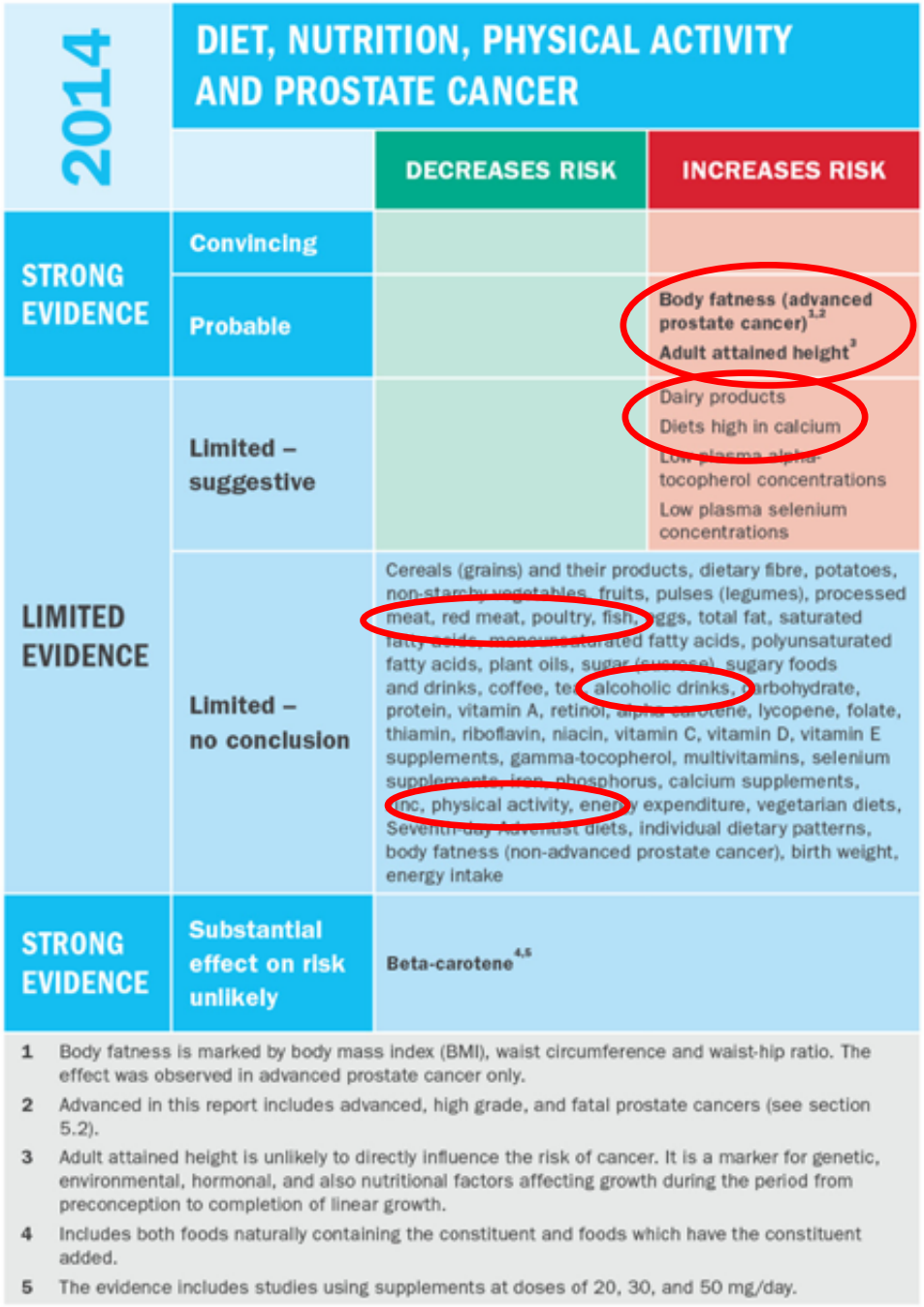


(Johns & Houlston, BJU Int. 2003)



(Kolonel et al. 2004)

Lifestyle and prostate cancer – what do we actually know? 2014 (most recent update)



2014

DIET, NUTRITION, PHYSICAL ACTIVITY AND PROSTATE CANCER

		DECREASES RISK	INCREASES RISK
STRONG EVIDENCE	Convincing		
	Probable		Body fatness (advanced prostate cancer)[1,2] Adult attained height[3]
LIMITED EVIDENCE	Limited – suggestive		Dairy products Diets high in calcium Low plasma alpha-tocopherol concentrations Low plasma selenium concentrations
	Limited – no conclusion	Cereals (grains) and their products, dietary fibre, potatoes, non-starchy vegetables, fruits, pulses (legumes), processed meat, red meat, poultry, fish, eggs, total fat, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, plant oils, sugar (sucrose), sugary foods and drinks, coffee, tea, alcoholic drinks, carbohydrate, protein, vitamin A, retinol, alpha-carotene, lycopene, folate, thiamin, riboflavin, niacin, vitamin C, vitamin D, vitamin E supplements, gamma-tocopherol, multivitamins, selenium supplements, iron, phosphorus, calcium supplements, zinc, physical activity, energy expenditure, vegetarian diets, Seventh-day Adventist diets, individual dietary patterns, body fatness (non-advanced prostate cancer), birth weight, energy intake	
STRONG EVIDENCE	Substantial effect on risk unlikely	Beta-carotene[4,5]	

1 Body fatness is marked by body mass index (BMI), waist circumference and waist-hip ratio. The effect was observed in advanced prostate cancer only.

2 Advanced in this report includes advanced, high grade, and fatal prostate cancers (see section 5.2).

3 Adult attained height is unlikely to directly influence the risk of cancer. It is a marker for genetic, environmental, hormonal, and also nutritional factors affecting growth during the period from preconception to completion of linear growth.

4 Includes both foods naturally containing the constituent and foods which have the constituent added.

5 The evidence includes studies using supplements at doses of 20, 30, and 50 mg/day.

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Examples of previous studies

Linking Swiss Census data with mortality information

- Lower mortality from coronary heart disease and stroke at higher altitudes in Switzerland
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- Educational inequalities in mortality and associated risk factors: German- versus French-speaking Switzerland
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- Religion and assisted and non-assisted suicide in Switzerland: National Cohort Study

➢ **Limited information on lifestyle, e.g. nutrition, physical activity; hardly any biological specimens (blood, genetic information)**

Linking SNC data with older Swiss cross-sectional studies

Study	Follow-up (years)	Eligible Participants (n)	Linked to SNC (n)	Deaths (all)	Deaths (cancer)
NRP 1A	31	8539	8008	2427	937
MONICA I	25	3442	3324	734	296
MONICA II	21	3466	3404	502	200
MONICA III	16	3252	3125	290	140
SOMIPOPS	26	4254	4104	1240	354
SHS 1992/93	16	15288	13370	2219	657
Total		**38026**	**35335**	**7412**	**2584**

Person years: For survivals we counted the whole follow-up period. For those expected to be deceased during follow-up-time we counted half of the follow-up time.

Association between the WCRF lifestyle score and mortality by cancer type

	Lifestyle score				
	Categorical				
Mortality	1[2]	2	3	Missing	*P*-trend[3]
Specific cancer types					
Lung	1	0.93 (0.68, 1.28)	0.72 (0.51, 0.99)		0.001
Cases, *n*	71	61	55	72	
UADT	1	0 0.82 (0.47, 1.45)	0.49 (0.26, 0.92)		0.002
Cases, *n*	23	19	15	18	
Stomach	1	0.60 (0.25, 1.39)	0.34 (0.14, 0.83)		0.021
Cases, *n*	11	4	6	18	
Colorectal	1	1.15 (0.68, 1.96)	0.84 (0.50, 1.42)		0.912
Cases, *n*	18	26	35	34	
Liver	1	0.56 (0.25, 1.26)	1.07 (0.54, 2.11)		0.909
Cases, *n*	12	8	20	11	
Pancreatic	1	0.83 (0.43, 1.60)	0.65 (0.35, 1.20)		0.754
Cases, *n*	15	16	24	17	
Urinary tract	1	0.38 (0.15, 0.97)	0.63 (0.31, 1.28)		0.835
Cases, *n*	13	7	19	11	
Blood	1	1.24 (0.76, 2.02)	1.04 (0.65, 1.67)		0.124
Cases, *n*	21	36	58	30	
Prostate	1	0.67 (0.39, 1.18)	0.48 (0.28, 0.82)		0.053
Cases, *n*	32	18	21	27	

Lohse T, Am J Clin Nutr 2016

Association between the WCRF lifestyle score and mortality by cancer type

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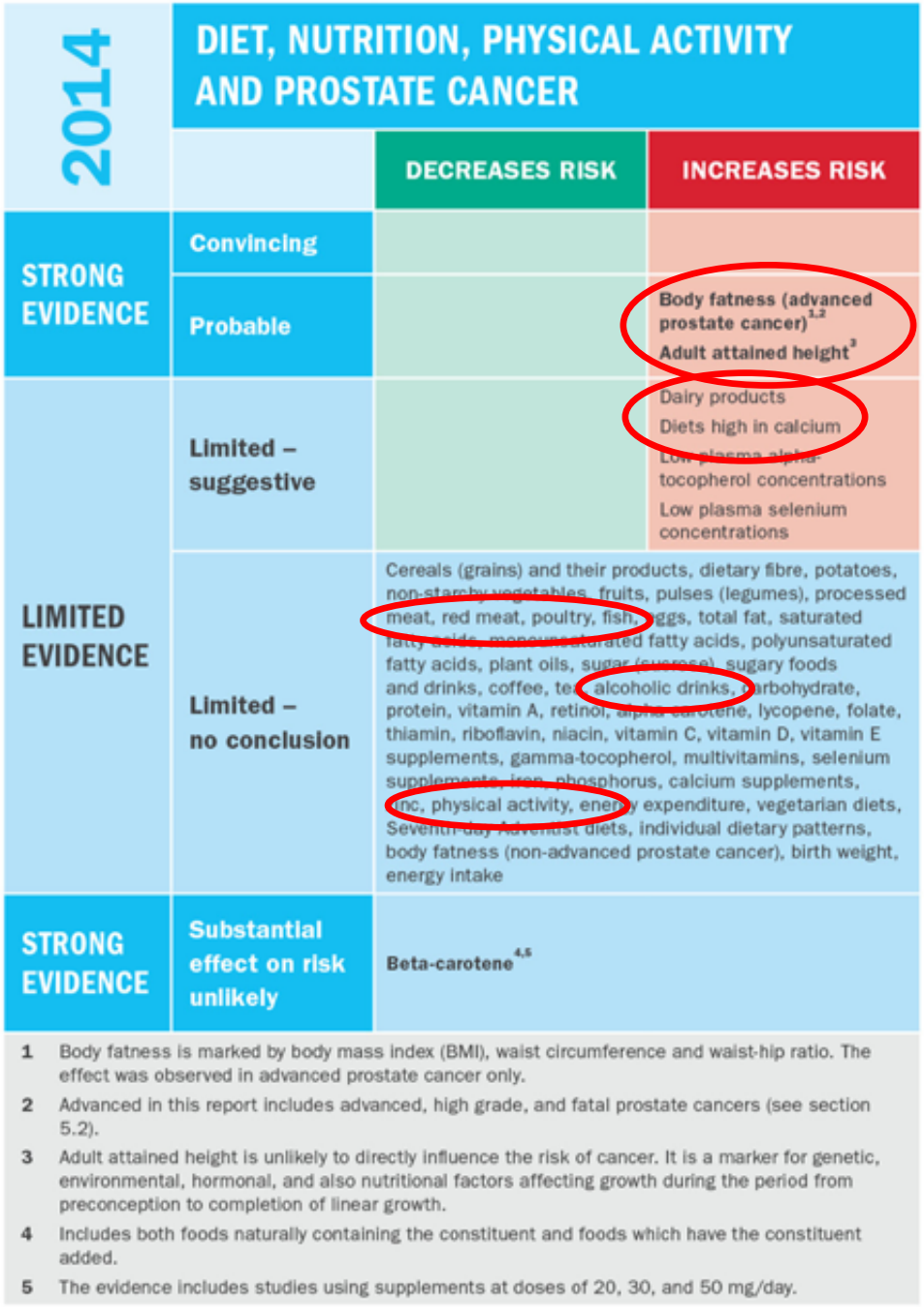
Blood	1	1.24 (0.76, 2.02)	1.04 (0.65, 1.67)		0.124
Cases, *n*	21	36	58	30	
Prostate	1	0.67 (0.39, 1.18)	0.48 (0.28, 0.82)		0.053
Cases, *n*	32	18	21	27	

- Rather small samples size ⇨ we cannot stratify by language region
- Still rather limited information on lifestyle and biomarkers
- Difficult to link SNC data with cancer registry (i.e, incidence) data, in particular large cantons such as ZH
- Is there any information from non-linked data?

Lohse T, Am J Clin Nutr 2016

Lifestyle and prostate cancer – what do we actually know? 2014 (most recent update)



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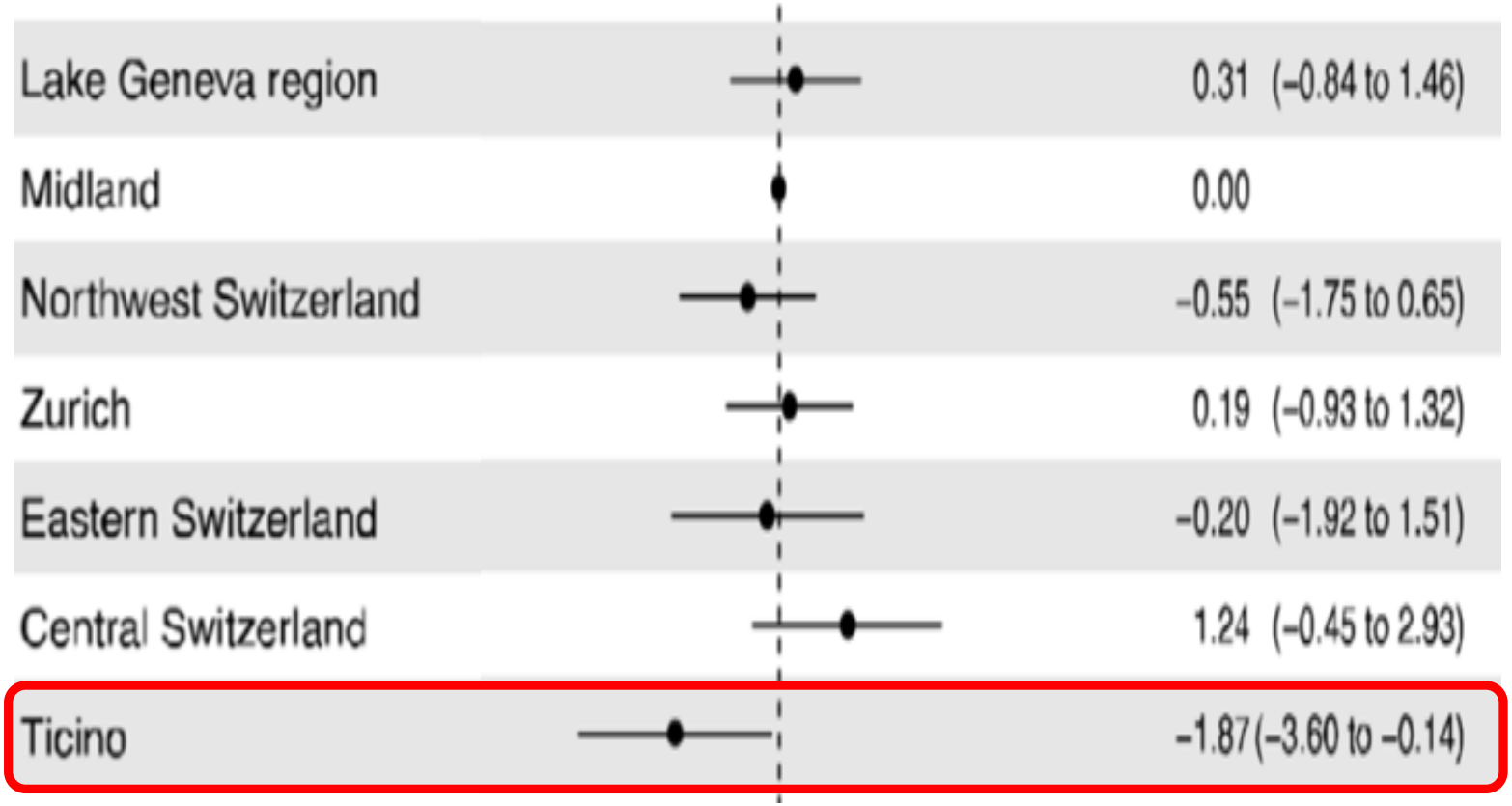
Body height by region (menuCH, 2014/15)



Vinci L, Econ Hum Biol 2019

Excess weight by region (menuCH, 2014/15)

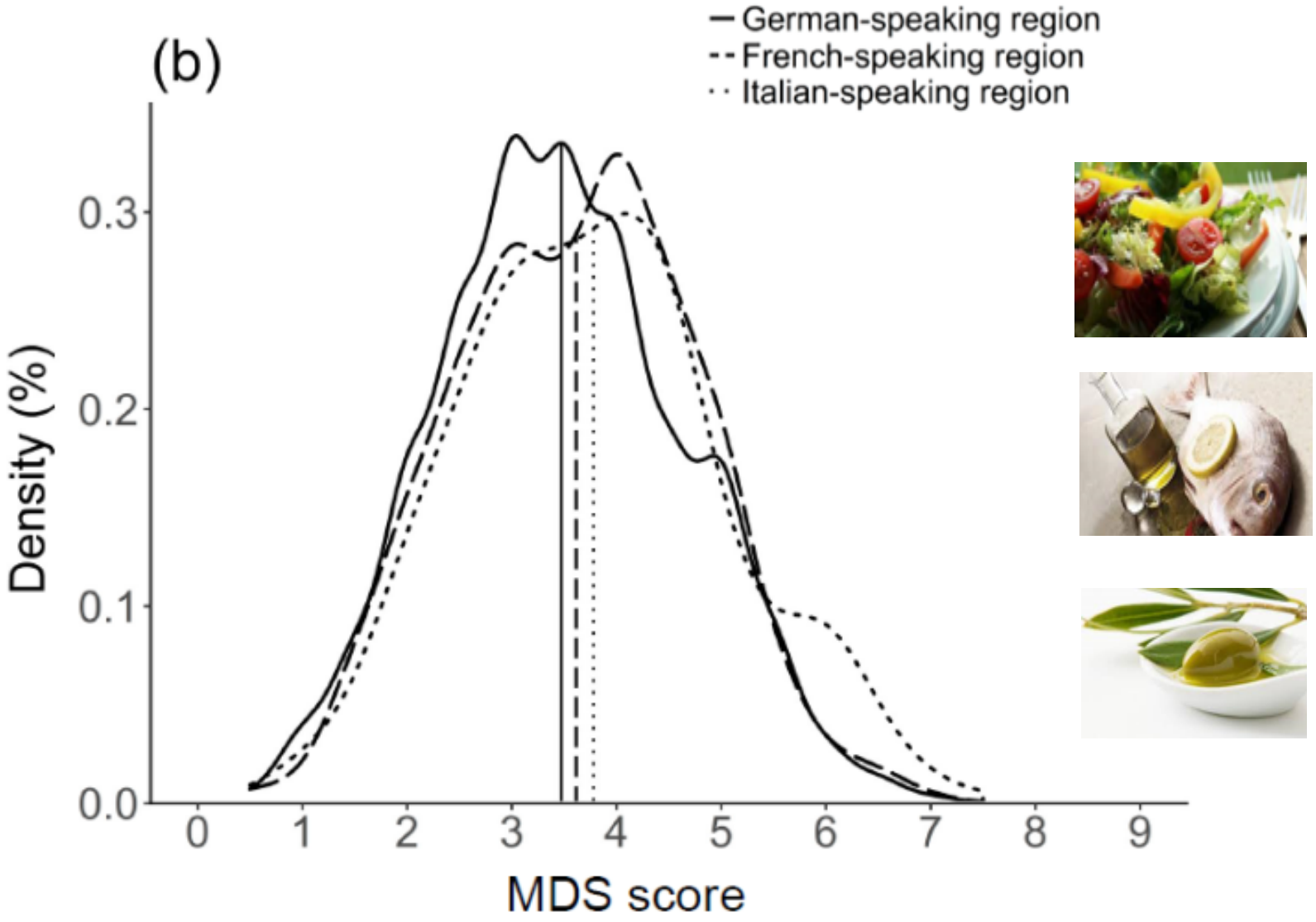
	Men		
	Overweight	Obesity	Excess weight
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Language region			
German	1.00	1.00	1.00
French	0.92 (0.71–1.21)	1.02 (0.90–1.16)	0.94 (0.69–1.29)
Italian	1.00 (0.97–1.04)	**1.17 (1.14–1.20)**	**1.05 (1.00–1.09)**

Differences in dietary and lifestyle habits Swiss Health Surveys 2002, 2007, 2012

Language region	German	Italian
Meat consumption > 5/week	28%	12%
Fish < 1/week	42%	25%
Milk/dairy > 1/day	65%	51%
Beer consumption per "event"	0.54 l	0.45 l
Wine consumption per "event"	0.19 l	0.16 l
		[drink more often]
Physically inactive	20%	39%
Current smoker	32%	34%

Richard A., Int J Vitam Nutr Res. 2016

Differences in dietary patterns (menuCH 2014/15)



Pestoni G, Nutrients 2019

Possible reasons for the differences observed

- Swiss health system is similar in all regions due to a general basic health insurance model
- Differences in screening habits do not explain differences (and change) in stage distribution
- Differences in lifestyle habits may affect differences in incidence and mortality rates
  - However, there is no clear pattern of a generally healthier lifestyle among men living in Ticino or men of Italian decent
  - Cross-sectional and ecological information!

Lessons learned

- Swiss health system is similar in all regions due to a general basic health insurance model
- Differences in screening habits do not explain differences (and change) in stage distribution
- Differences in lifestyle habits may contribute to differences in incidence and mortality rates
  - However, there is no clear pattern of a generally healthier lifestyle among men living in Ticino or men of Italian decent
  - Cross-sectional & ecological information
- Linkage of existing data, e.g. cancer registry information with existing information on risk factors

What does it take to examine the causes of cancer (and of differences in the burden of disease)?

This is some years old, but still true!

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University of Zurich[UZH]

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Thank you very much for your attention!

Sabine Rohrmann

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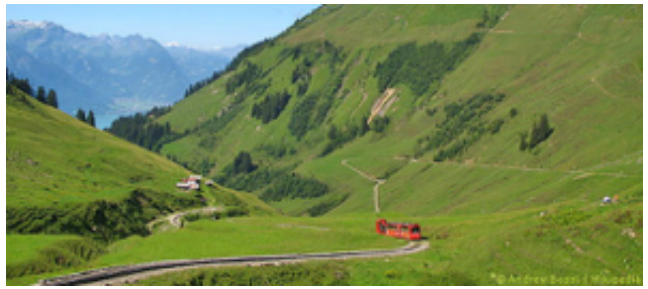
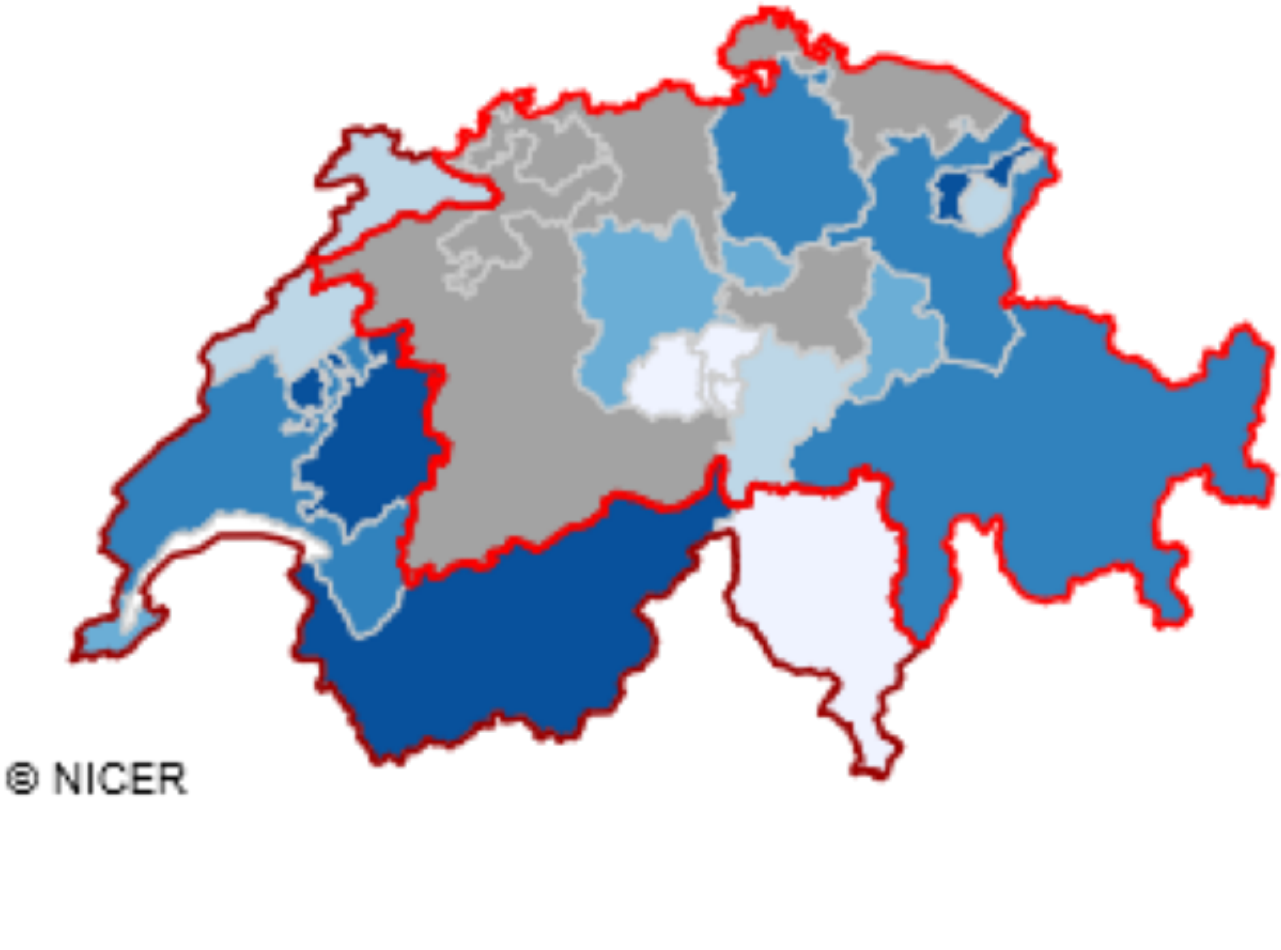


Prostate cancer incidence by canton in CH (age-standardized rates per 100,000, 2011-2015)



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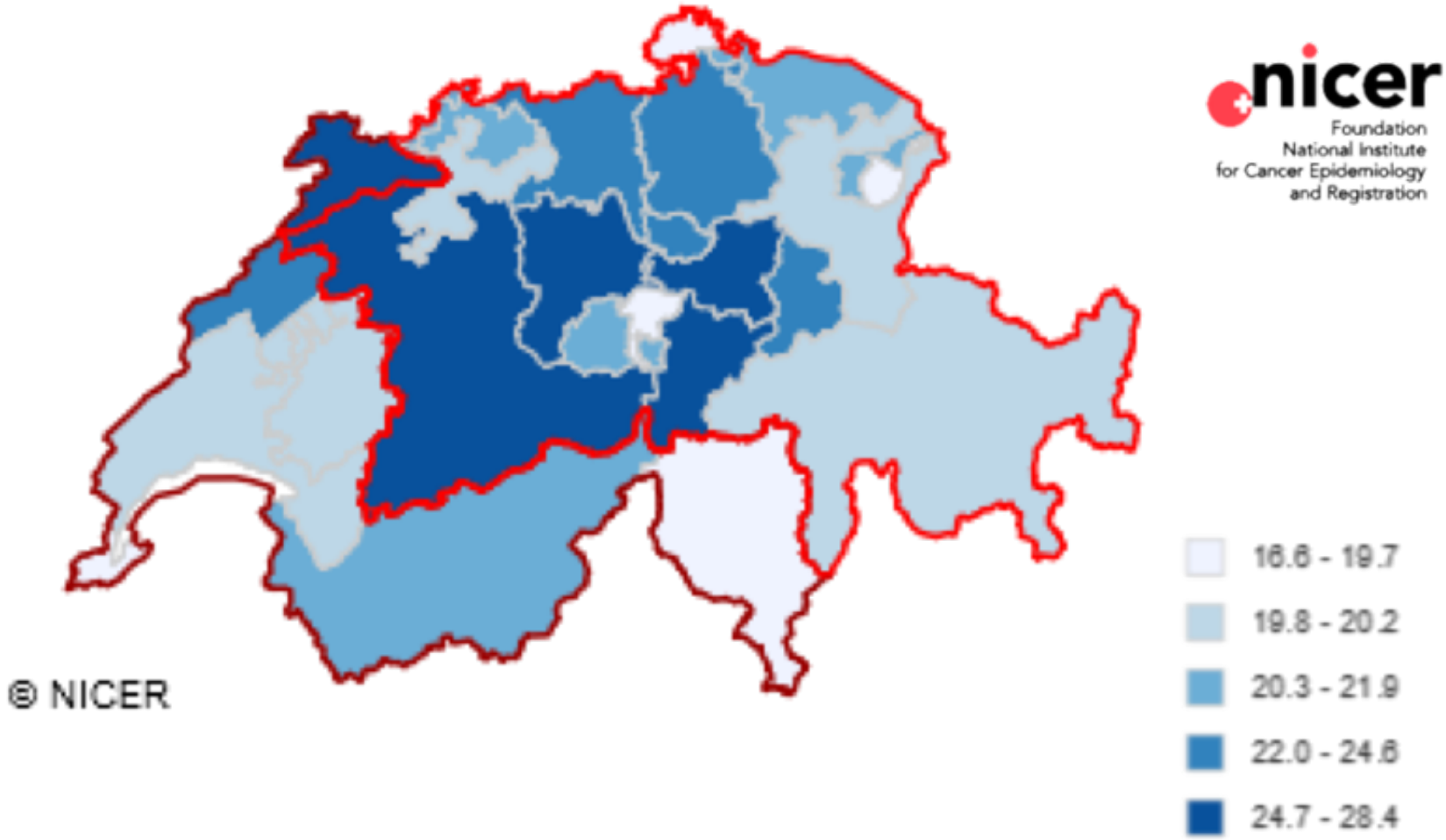
Prostate cancer mortality by canton in CH (age-standardized rates per 100,000, 2011-2015)



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Due to differences in prostate cancer screening?

Percentage of men, 40+ years old, who ever (or in the past 12 months) had a prostate examination;

Language region	ever	last 12 months	check-up*
German speaking part	53,2 (51,1–55,3)	25,1 (23,3–27,0)	76,1 (73,5–78,5)
French speaking part	51,6 (48,5–54,7)	25,9 (23,3–28,6)	76,8 (72,9–80,4)
Italian speaking part	57,0 (51,1–62,6)	29,1(24,5–34,2)	70,5 (63,2–76,9)

*men who had a prostate examination as part of health check-up

(Swiss Health Survey 2007)

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Differences in dietary habits (menuCH 2014/2015)

(mean, 2 24h recalls, men and women combined)

Food-Based Dietary Guidelines (FBDG) [1]	German	Italian	Diff. (*p*-Value) [4]
	Weighted % [3]	Weighted % [3]	Ger. vs. Ita.
Non-caloric beverages *≥1 L/day of water, tea and coffee*	82.6	79.8	0.340
Fruit and vegetables *≥5 portions/day: max. 1 portion can be provided by 2 dL of 100% fruit or vegetable juices*	18.1	17.2	0.824
Vegetables *≥3 portions/day: 1 portion =120 g, 30 g if dried, 2.5 dL of soup, and 100 g of sauce*	8.9	12.1	0.291
Fruit *≥2 portions/day: 1 portion = 120 g, 30 g if dried*	29.0	20.0	0.013
Dairy products *≥3 portions/day: 1 portion = 200 mL of milk, 175 g of yogurt or fresh cheese, 60 g of soft cheese and 30 g of hard cheese*	23.4	19.1	0.226
Total meat *≤35 g/day of prepared meat*[2]	23.4	19.7	0.340
Red meat *≤35 g/day of prepared meat*	64.8	63.3	0.703
Processed meat *≤15 g/day*	40.0	43.1	0.477
Vegetable oil *≥25 g/day*	11.8	24.5	<0.001*
Nuts, seeds, and olives *≥25 g/day*	6.7	2.4	0.110
Alcohol *≤30 g (♂) or ≤15 g (♀)* of pure alcohol	78.2	79.0	0.814

(Chatelan, A. Nutrients 2017)

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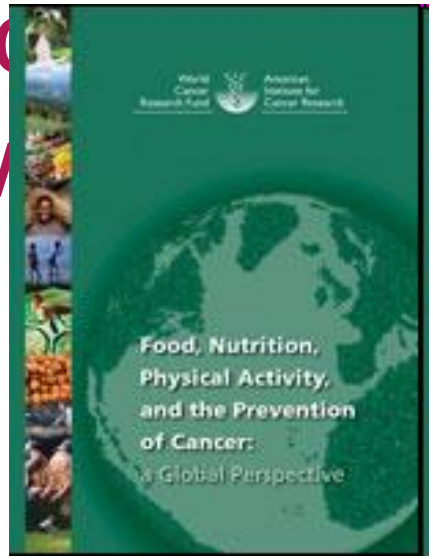
Lifestyle and prostate canc
what do we actually know

	DECREASES RISK	INCREASES RISK
Convincing		
Probable	**Foods containing lycopene[1,2]** **Foods containing selenium[1]** **Selenium[3]**	**Diets high in calcium[4,5]**
Limited — suggestive	Pulses (legumes)[6] Foods containing vitamin E[1] Alpha-tocopherol[7]	Processed meat[8] Milk and dairy products[5]
Limited — no conclusion	Cereals (grains) and their products; dietary fibre; potatoes; non-starchy vegetables; fruits; meat; poultry; fish; eggs; total fat; plant oils; sugar (sucrose); sugary foods and drinks; coffee; tea; alcohol; carbohydrate; protein; vitamin A; retinol; thiamin; riboflavin; niacin; vitamin C; vitamin D; gamma-tocopherol; vitamin supplements; multivitamins; iron; phosphorus; zinc; other carotenoids; physical activity; energy expenditure; vegetarian diets; Seventh-day Adventist diets; body fatness; abdominal fatness; birth weight; energy intake	



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