World Cancer Research Fund International
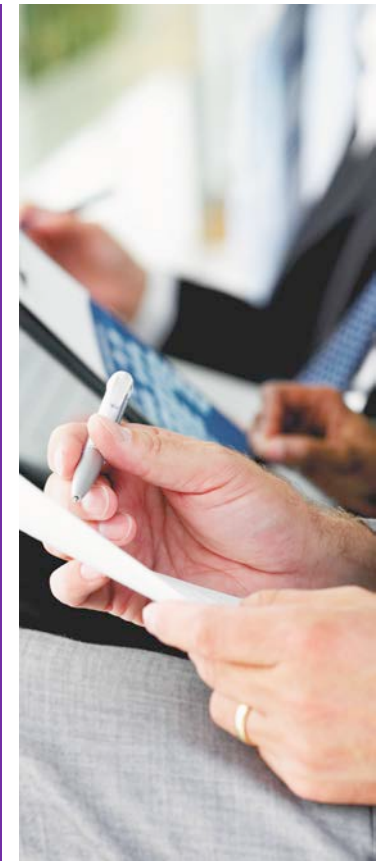
Diet, Nutrition, Physical Activity and Cancer: strength and consistency of the evidence

4 February 2016

Martin Wiseman

World Cancer Research Fund International & University of Southampton

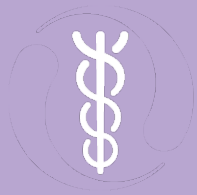**World Cancer Research Fund International**

CUP Continuous Update Project

Analysing research on cancer prevention and survival

Who we are

What we do

AICR

WCRF UK

WCRF Netherlands

WCRF Hong Kong
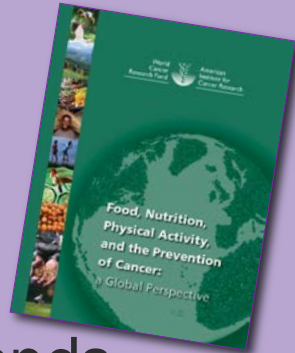
Fund research on the relationship of diet, nutrition, physical activity and body weight to cancer risk

Interpret the accumulated scientific literature to derive Cancer Prevention Recommendations

Educate people through our national Health Information programmes

WCRF International

CUP Continuous Update Project

Analysing research on cancer prevention and survival

Advocate effective policies to help people and populations to reduce their chances of developing cancer

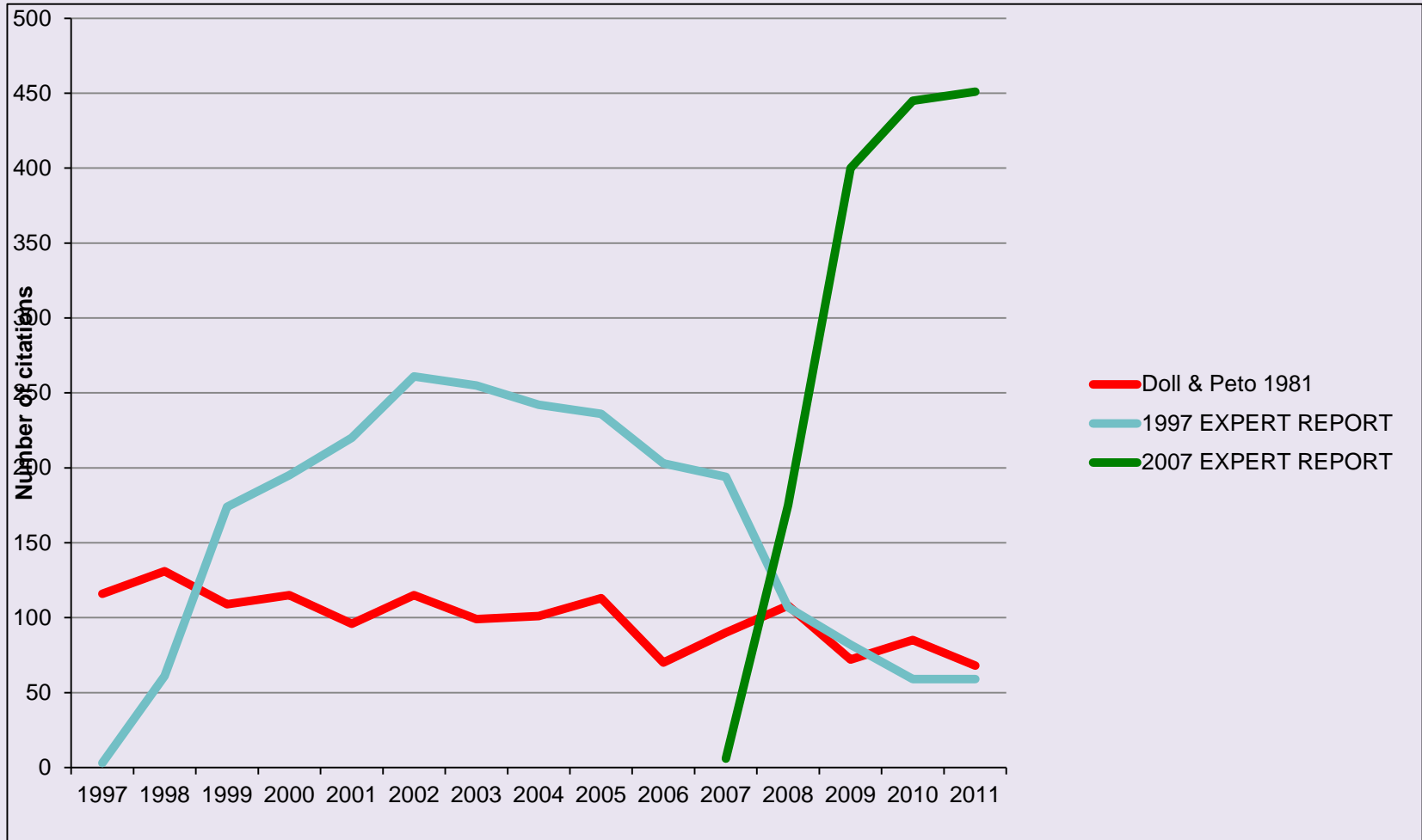Food, Nutrition and the Prevention of Cancer: a global perspective

Policy and Action for Cancer

Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective

Continuous Update Project 2011
Keeping the science current
Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective
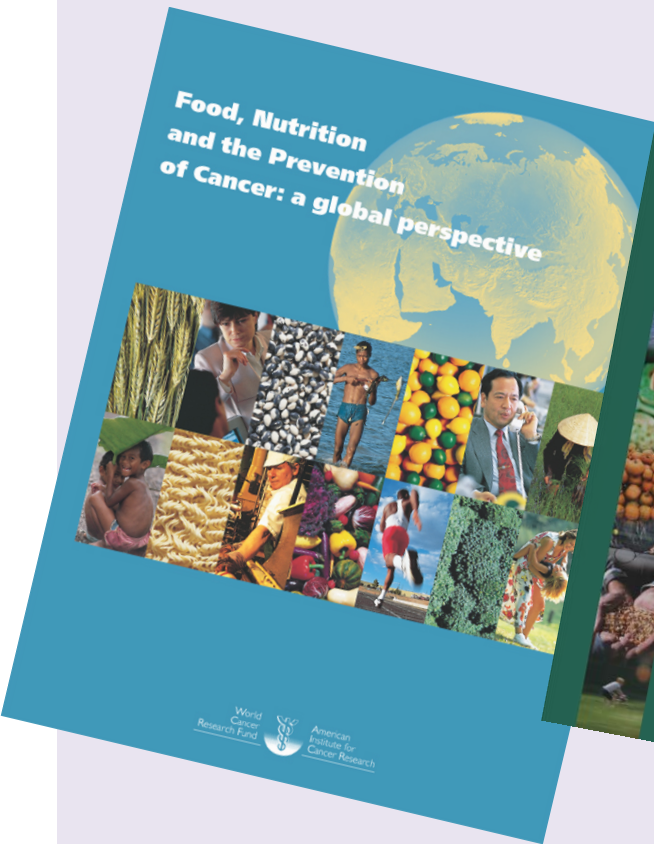
Journal citations
WCRF/AICR Reports

World Cancer Research Fund International

CUP — Continuous Update Project
Analysing research on cancer prevention and survival

Number of citations

Legend:
- Doll & Peto 1981
- 1997 EXPERT REPORT
- 2007 EXPERT REPORT

Global variation in cancer incidence

World Cancer Research Fund International

Breast

Colorectum

Globocan, WHO

www.wcrf.org
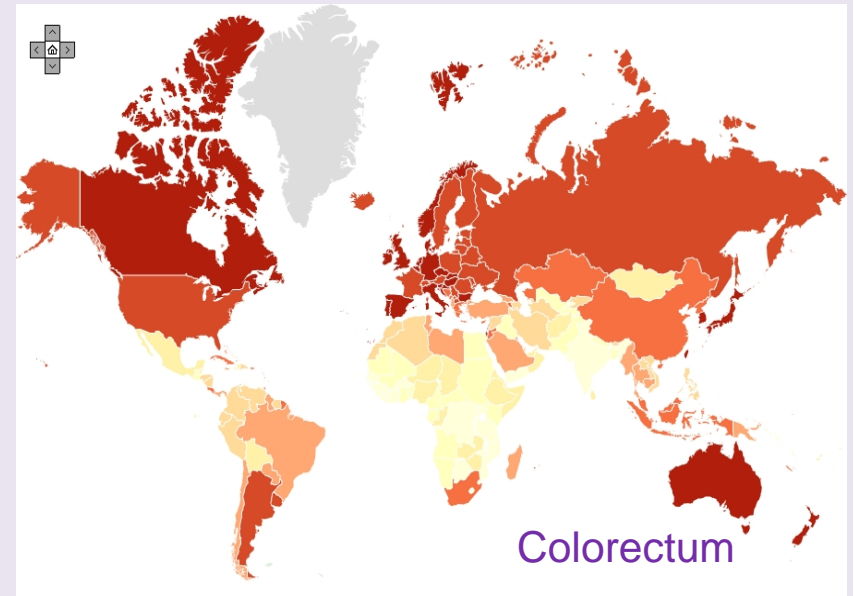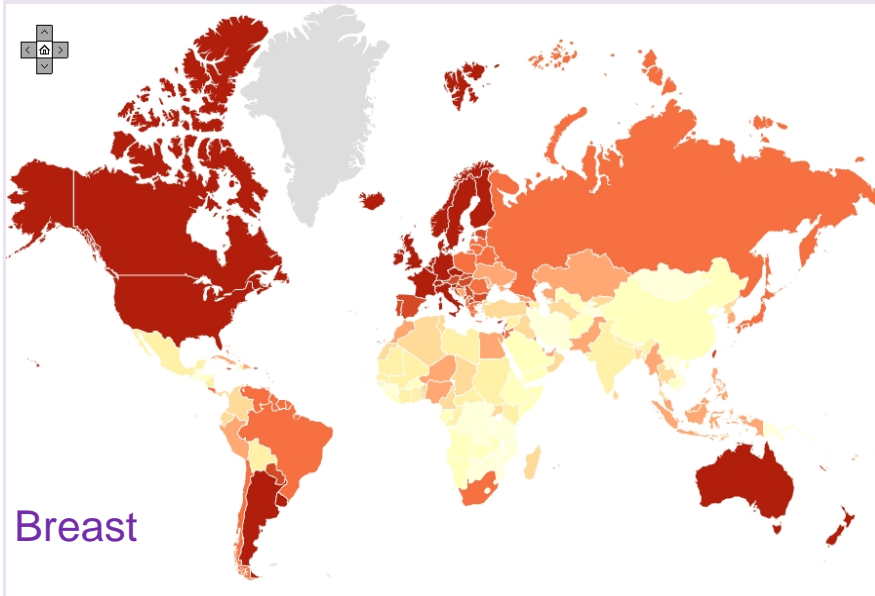
Migration data

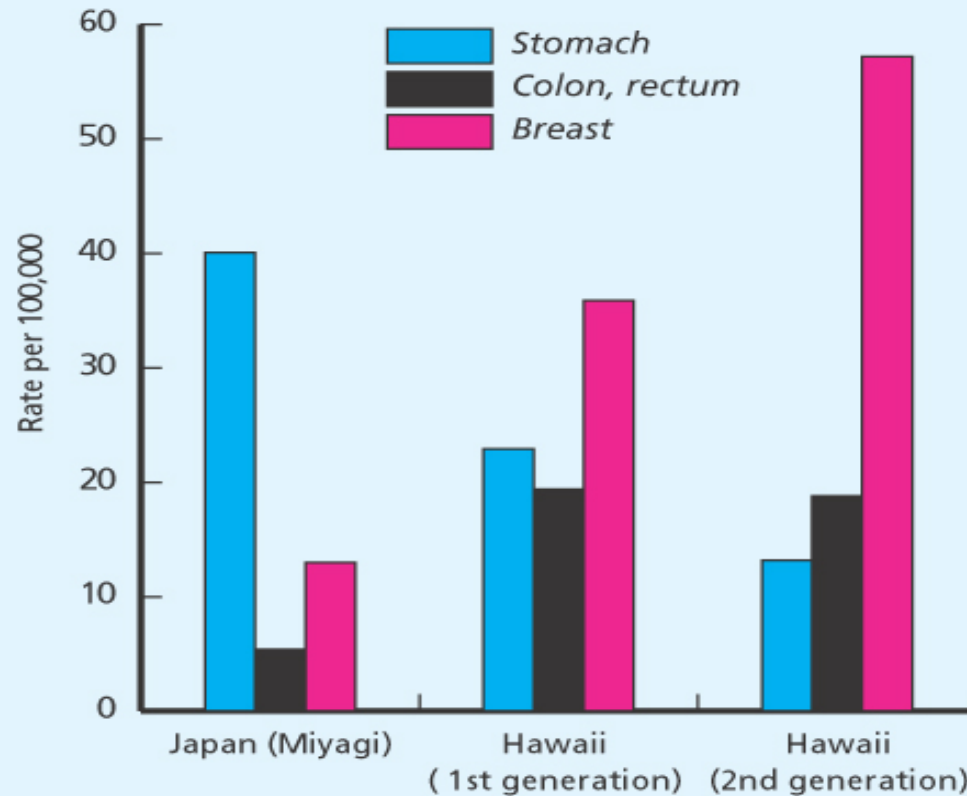Figure 1.2.20 Cancer incidence for selected cancers in Japanese women by generation in Hawaii and Japan, 1968–1977

Age-adjusted to the World Standard Population
(From Kolonel et al, 1980)

Cancer Incidence in Japan*

* Per 100,000, world population standard

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Two enabling characteristics for acquiring hallmarks

Hanahan & Weinberg (2011) Cell; Hanahan & Coussens (2012) Cancer Cell

CUP database

Second Expert Report 2007

Continuous Update Project 2013

Number of papers on cancer prevention

2015 estimate total ca 9000 papers

www.wcrf.org

1997 WCRF/AICR Expert Report – summary matrix

World
Cancer
Research Fund

American
Institute for
Cancer Research

Food, Nutrition,
Physical Activity,
and the Prevention
of Cancer:
a Global Perspective

Summary of 'convincing' and 'probable' judgements

Cancer sites (columns): Mouth, pharynx, larynx · Nasopharynx · Oesophagus · Lung · Stomach · Pancreas · Gallbladder · Liver · Colorectum[9] · Breast premenopause · Breast postmenopause · Ovary · Endometrium · Prostate · Kidney · Skin · Weight gain, overweight and obesity

Risk judgements conveyed by the chart (CD = convincing decreased risk; PD = probable decreased risk; PI = probable increased risk; CI = convincing increased risk):

Factor	Judgements
Foods containing dietary fibre	Colorectum: PD
Aflatoxins	Liver: CI
Non-starchy vegetables[1]	Mouth, pharynx, larynx: PD; Oesophagus: PD; Stomach: PD
Allium vegetables	Stomach: PD
Garlic	Colorectum: PD
Fruits[2]	Mouth, pharynx, larynx: PD; Oesophagus: PD; Lung: PD; Stomach: PD
Foods containing folate	Pancreas: PD
Foods containing lycopene	Prostate: PD
Foods containing selenium[3]	Prostate: PD
Red meat	Colorectum: CI
Processed meat	Colorectum: CI
Cantonese-style salted fish	Nasopharynx: PI
Diets high in calcium[4]	Colorectum: PD; Prostate: PI
Energy-dense foods[5]	Weight gain, overweight and obesity: PI
Low energy-dense foods	Weight gain, overweight and obesity: PD
Salt, salted and salty foods	Stomach: PI
Arsenic in drinking water	Lung: PI
Maté	Oesophagus: PI
Sugary drinks	Weight gain, overweight and obesity: PI
Alcoholic drinks[6]	Mouth, pharynx, larynx: CI; Oesophagus: CI; Liver: PI; Colorectum: CI (men) / PI (women); Breast premenopause: PI; Breast postmenopause: CI
Beta-carotene[7]	Lung: CI
Physical activity	Colorectum: CD; Breast postmenopause: PD; Endometrium: PD; Weight gain, overweight and obesity: CD
Sedentary living[8]	
Body fatness	Oesophagus: CI; Pancreas: CI; Gallbladder: PI; Colorectum: CI; Breast premenopause: PD; Breast postmenopause: CI; Endometrium: CI; Kidney: CI
Abdominal fatness	Pancreas: PI; Colorectum: CI; Breast postmenopause: PI; Endometrium: PI
Adult weight gain	Breast postmenopause: CI
Adult attained height	Pancreas: PI; Colorectum: CI; Breast premenopause: PI; Breast postmenopause: PI; Ovary: PI
Greater birth weight	Breast premenopause: PI
Lactation	Breast premenopause: CD; Breast postmenopause: CD
Being breastfed	Weight gain, overweight and obesity: PD

KEY

- Convincing decreased risk
- Probable decreased risk
- Probable increased risk
- Convincing increased risk

1 Includes evidence on foods containing carotenoids for mouth, pharynx, larynx; foods containing beta-carotene for oesophagus; foods containing vitamin C for oesophagus

2 Includes evidence on foods containing carotenoids for mouth, pharynx, larynx and lung; foods containing beta-carotene for oesophagus; foods containing vitamin C for oesophagus

3 Includes evidence from supplements for prostate

4 Evidence is from milk and studies using supplements for colorectum

5 Includes 'fast foods'

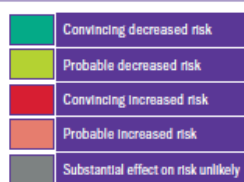6 Convincing harm for men and probable harm for women for colorectum

7 The evidence is derived from studies using supplements for lung

8 Includes evidence on televison viewing

9 Judgement for physical activity applies to colon and not rectum

World Cancer Research Fund · American Institute for Cancer Research

![World Cancer Research Fund International]

SUMMARY OF STRONG EVIDENCE ON DIET, NUTRITION, PHYSICAL ACTIVITY AND PREVENTION OF CANCER

Legend:
- ■ Convincing decreased risk (CD)
- ■ Probable decreased risk (PD)
- ■ Convincing increased risk (CI)
- ■ Probable increased risk (PI)
- ■ Substantial effect on risk unlikely (SU)

	MOUTH, PHARYNX, LARYNX (2007)	NASOPHARYNX (2007)	OESOPHAGUS (2007)	LUNG (2007)	STOMACH (2007)	PANCREAS (2012)	GALLBLADDER (2015)	LIVER (2015)	COLORECTUM (2011)	BREAST PREMENOPAUSE (2010)	BREAST POSTMENOPAUSE (2010)	OVARY (2014)	ENDOMETRIUM (2013)	PROSTATE (2014)	KIDNEY (2015)	SKIN (2007)
Foods containing dietary fibre									CD							
Aflatoxins								CI								
Non-starchy vegetables[1]	PD		PD		PD											
Allium vegetables					PD											
Garlic									PD							
Fruits[2]	PD		PD	PD	PD											
Red meat									CI							
Processed meat									CI							
Cantonese-style salted fish		PI														
Diets high in calcium[3]									PD							
Salt, salted and salty foods					PI											
Glycaemic load													PI			
Arsenic in drinking water				CI												PI
Maté			PI													
Alcoholic drinks[4]	CI		CI					CI	CI	PI	CI				PD	
Coffee						SU		PD					PD			
Beta-carotene[5]				CI										SU		SU
Physical activity[6]									CD				PD			
Body fatness[7]			CI			CI	PI	CI	CI	PD	CI	PI	CI	PI	CI	
Adult attained height[8]						PI			CI	PI	CI	CI		PI	PI	
Greater birth weight										PI						
Lactation										CD	CD					

NUTRITION AND CANCERS

- **ADIPOSITY**
  - BREAST (PM), COLORECTUM, ENDOMETRIUM, OESOPHAGUS, PANCREAS, GALLBLADDER, KIDNEY, OVARY, PROSTATE (ADVANCED), LIVER
- **PHYSICAL (IN)ACTIVITY**
  - COLON, BREAST, ENDOMETRIUM
- **MEAT – RED AND PROCESSED**
  - COLON, RECTUM
- **ALCOHOL**
  - MPL, BREAST, COLORECTUM, LIVER, OESOPHAGUS
- **PLANT FOODS (F&V, PULSES, WHOLEGRAINS)**
  - MPL, OESOPHAGUS, STOMACH, COLORECTUM (DF), LUNG
- **BREASTFEEDING**
  - BREAST (MOTHER), OBESITY (CHILD)

World Cancer Research Fund International

Obesity, physical activity and cancer

There is a strong link between being overweight or obese & an **increased risk** of 10 cancers:

◆ Liver
◆ Advanced prostate
◆ Ovarian
◆ Gallbladder
◆ Kidney
◆ Colorectal (bowel)
◆ Oesophageal*
◆ Postmenopausal breast
◆ Pancreatic
◆ Endometrial (womb)

There is a strong link between being physically active & a **decreased risk** of 3 cancers:

◆ Postmenopausal breast
◆ Colorectal (bowel)
◆ Endometrial (womb)

Top 10 countries* with the highest % of overweight or obese adults

◆ Mexico 71.3%
◆ United States 68.6%
◆ Chile 64.5%
◆ New Zealand 63.8%
◆ Australia 63.4%
◆ Israel 62.2%
◆ United Kingdom 61.9%
◆ Hungary 61.6%
◆ Ireland 61%
◆ Finland 59.2%
◆ Luxembourg 59.2%

1.9 billion adults worldwide are overweight or obese. This exceeds the population of China

Physical inactivity is the 4th leading cause of death worldwide

www.wcrf.org

Changes to conclusions for strong evidence since 2007 (1)

Change	Exposure	Cancer	From	To
Stronger	Foods containing fibre	Colorectum	Probable decreased	Convincing decreased
New conclusion	Coffee	Endometrium	No conclusion	Probable decreased
New conclusion	Glycaemic load	Endometrium	No conclusion	Probable increased
New conclusion	Body fatness	Ovary	No conclusion	Probable increased
No conclusion	Foods containing folate	Pancreas	Probable decreased	No conclusion
New conclusion	Body fatness	Prostate (advanced)	No conclusion	Probable increased
New conclusion	Adult attained height	Prostate	No conclusion	Probable increased

Changes to conclusions for strong evidence since 2007 (2)

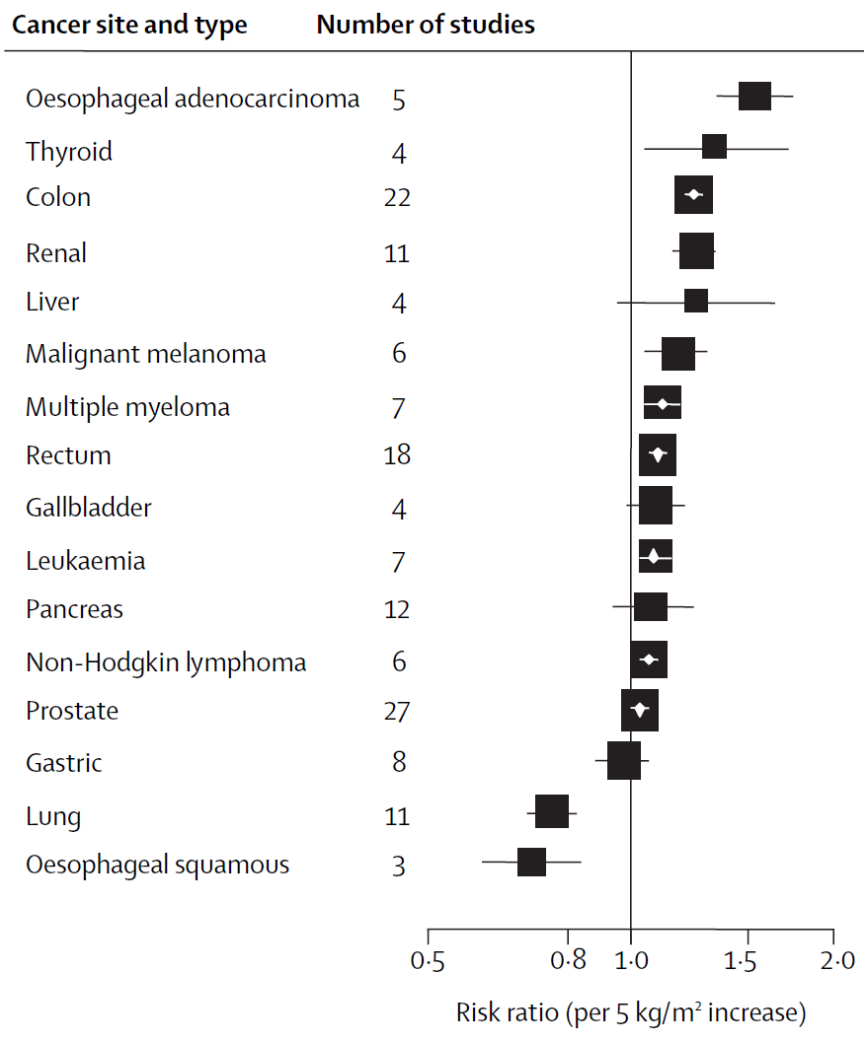| Change	Exposure	Cancer	From	To
New conclusion	Body fatness	Liver	Limited-suggestive	Convincing increased
New conclusion	Coffee	Liver	No conclusion	Probable decreased
Stronger	Adult attained height	Kidney	No conclusion	Probable increased
New conclusion	Alcohol	Kidney	Substantial effect on risk unlikely	Probable decreased
Stronger	Arsenic in drinking water	Bladder	Limited-suggestive	Probable increased

Significant shifts in emphasis

- Adiposity and activity vs foods and drinks
- Foods vs nutrients
- Whole diets vs individual foods
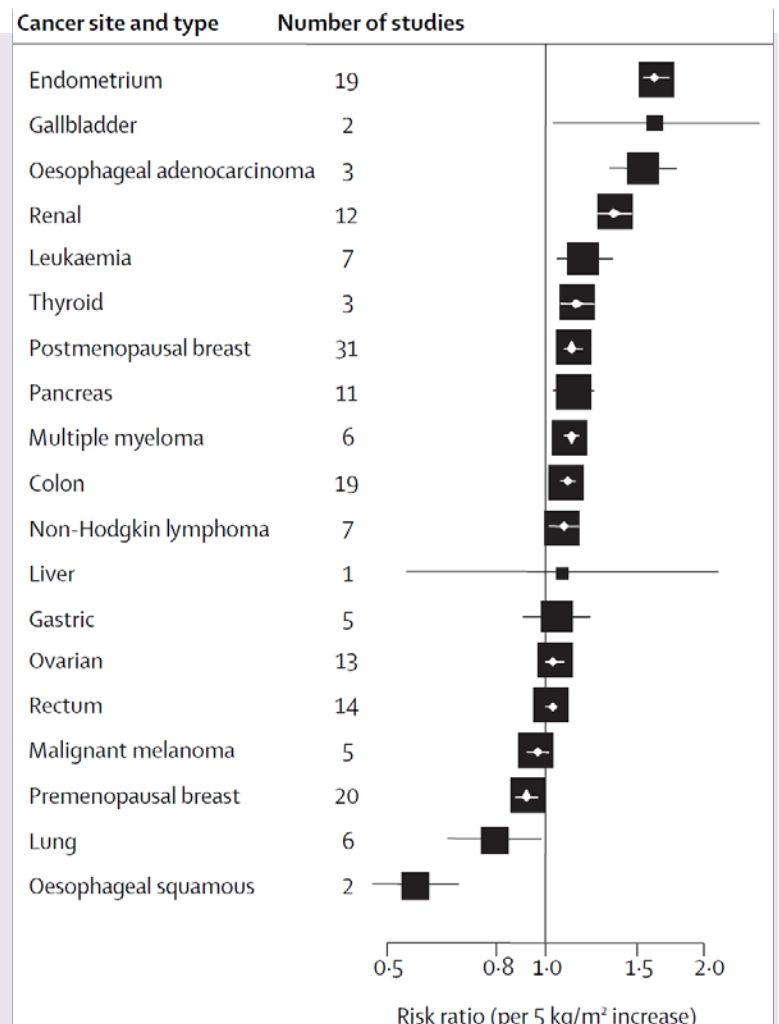- Plant foods vs fruit and veg
- Lifecourse (height)

Significant shifts in emphasis

- Adiposity and activity vs foods and drinks
- Foods vs nutrients
- Whole diets vs individual foods
- Plant foods vs fruit and veg
- Lifecourse (height)

- Individual recs vs the whole package
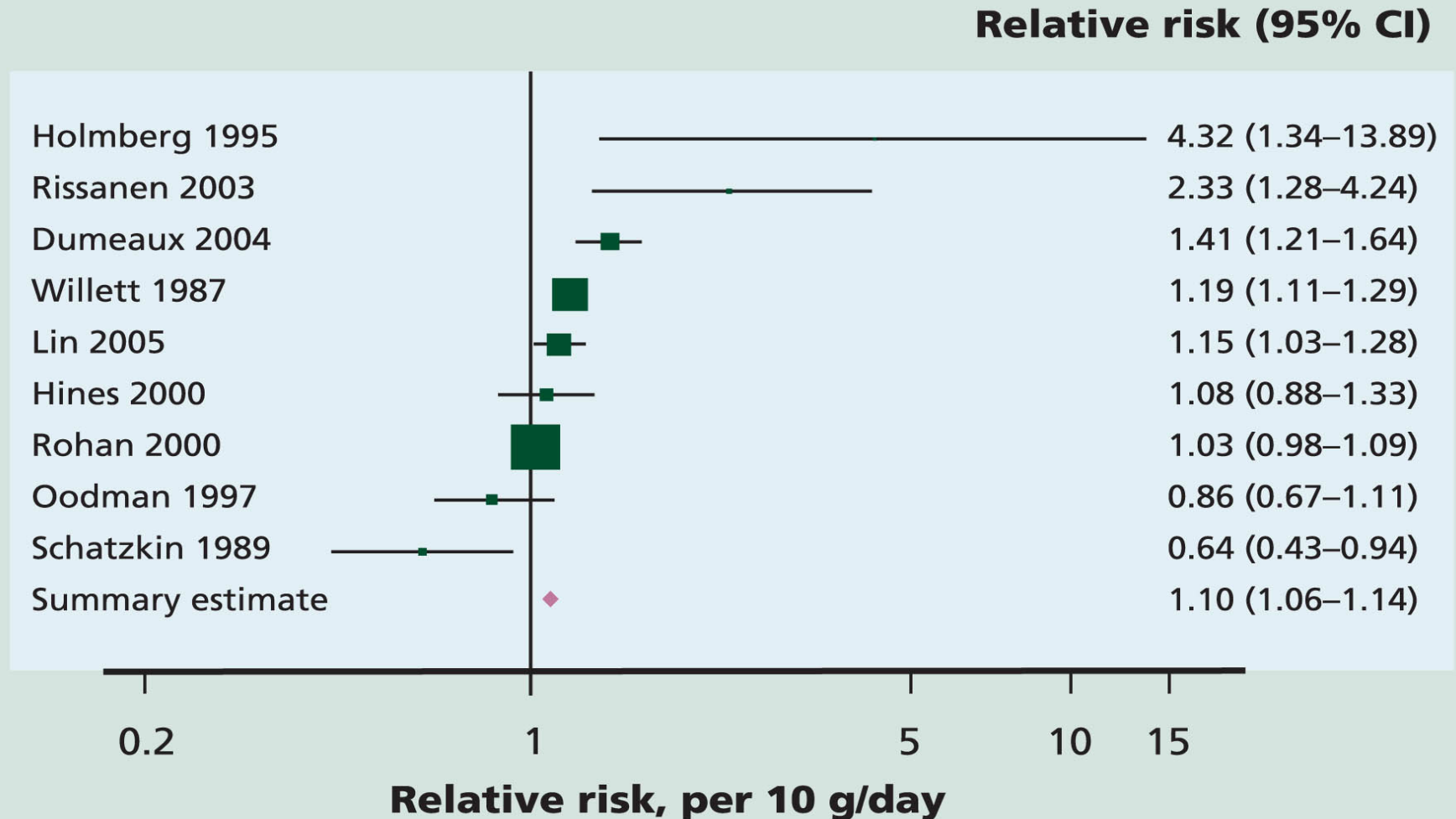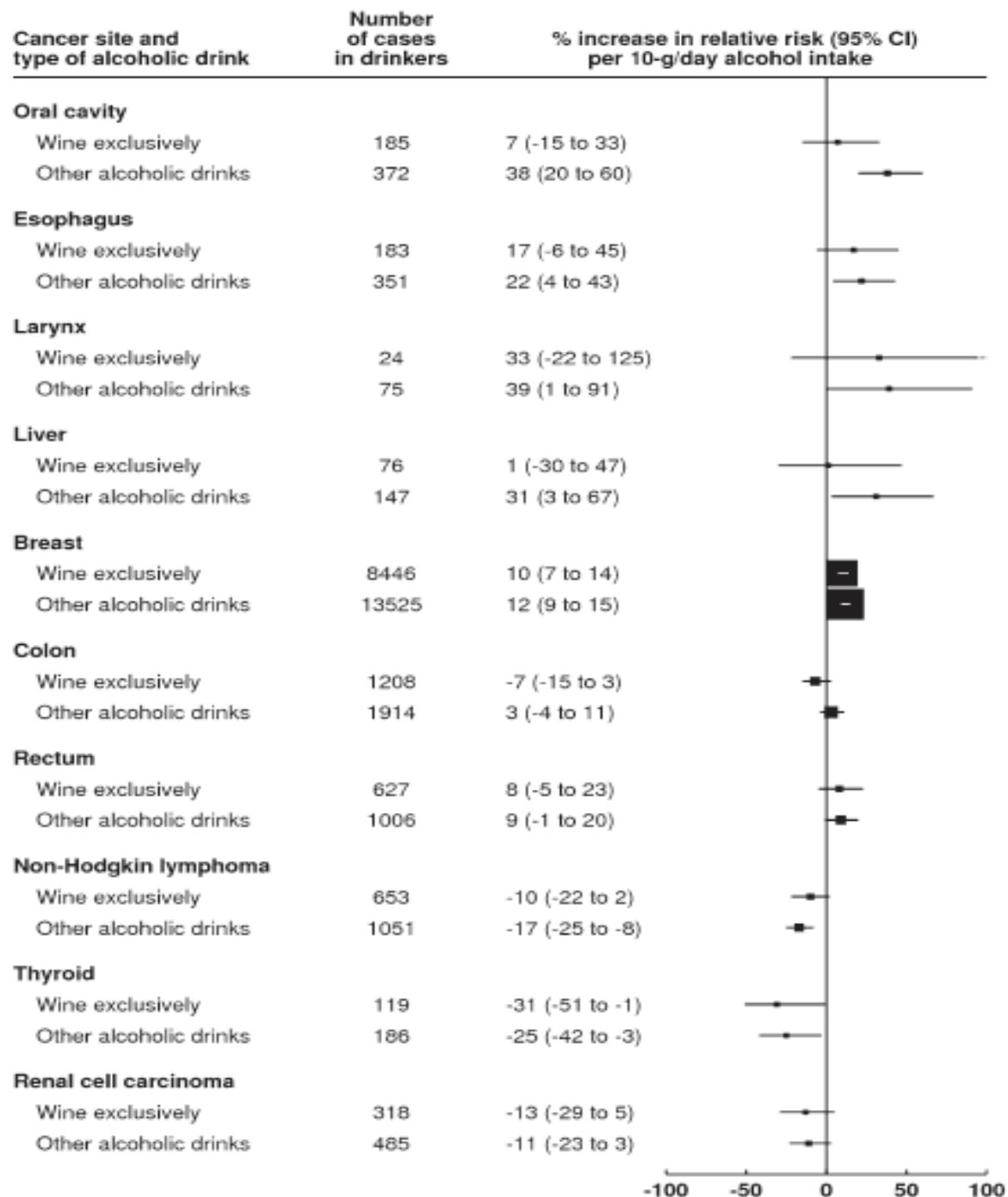
Body Mass Index and Cancer Risk

World Cancer Research Fund International

Men

Cancer site and type	Number of studies
Oesophageal adenocarcinoma	5
Thyroid	4
Colon	22
Renal	11
Liver	4
Malignant melanoma	6
Multiple myeloma	7
Rectum	18
Gallbladder	4
Leukaemia	7
Pancreas	12
Non-Hodgkin lymphoma	6
Prostate	27
Gastric	8
Lung	11
Oesophageal squamous	3

Risk ratio (per 5 kg/m² increase)

Women

Cancer site and type	Number of studies
Endometrium	19
Gallbladder	2
Oesophageal adenocarcinoma	3
Renal	12
Leukaemia	7
Thyroid	3
Postmenopausal breast	31
Pancreas	11
Multiple myeloma	6
Colon	19
Non-Hodgkin lymphoma	7
Liver	1
Gastric	5
Ovarian	13
Rectum	14
Malignant melanoma	5
Premenopausal breast	20
Lung	6
Oesophageal squamous	2

Risk ratio (per 5 kg/m² increase)

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Ethanol and breast cancer; cohort studies

Relative risk (95% CI)

Study	Relative risk (95% CI)
Holmberg 1995	4.32 (1.34–13.89)
Rissanen 2003	2.33 (1.28–4.24)
Dumeaux 2004	1.41 (1.21–1.64)
Willett 1987	1.19 (1.11–1.29)
Lin 2005	1.15 (1.03–1.28)
Hines 2000	1.08 (0.88–1.33)
Rohan 2000	1.03 (0.98–1.09)
Oodman 1997	0.86 (0.67–1.11)
Schatzkin 1989	0.64 (0.43–0.94)
Summary estimate	1.10 (1.06–1.14)

Relative risk, per 10 g/day

0.2   1   5   10   15

World Cancer Research Fund   American Institute for Cancer Research

Cancer site and type of alcoholic drink	Number of cases in drinkers	% increase in relative risk (95% CI) per 10-g/day alcohol intake
Oral cavity		
Wine exclusively	185	7 (-15 to 33)
Other alcoholic drinks	372	38 (20 to 60)
Esophagus		
Wine exclusively	183	17 (-6 to 45)
Other alcoholic drinks	351	22 (4 to 43)
Larynx		
Wine exclusively	24	33 (-22 to 125)
Other alcoholic drinks	75	39 (1 to 91)
Liver		
Wine exclusively	76	1 (-30 to 47)
Other alcoholic drinks	147	31 (3 to 67)
Breast		
Wine exclusively	8446	10 (7 to 14)
Other alcoholic drinks	13525	12 (9 to 15)
Colon		
Wine exclusively	1208	-7 (-15 to 3)
Other alcoholic drinks	1914	3 (-4 to 11)
Rectum		
Wine exclusively	627	8 (-5 to 23)
Other alcoholic drinks	1006	9 (-1 to 20)
Non-Hodgkin lymphoma		
Wine exclusively	653	-10 (-22 to 2)
Other alcoholic drinks	1051	-17 (-25 to -8)
Thyroid		
Wine exclusively	119	-31 (-51 to -1)
Other alcoholic drinks	186	-25 (-42 to -3)
Renal cell carcinoma		
Wine exclusively	318	-13 (-29 to 5)
Other alcoholic drinks	485	-11 (-23 to 3)

-100   -50   0   50   100

Figure 2. Estimated increase in relative risk (95% confidence interval) for selected cancer sites per 10-g/d increase in alcohol intake and by type of alcohol consumed (drinkers only). Analyses are adjusted for age, region of residence, socioeconomic status, body mass index, smoking, physical activity, use of oral contraceptives, and hormone replacement therapy. CI=confidence interval. "Other alcoholic drinks" is defined as drinkers of beer and/or spirits exclusively or a mixture of wine, beer, and/or spirits.

BREAST CANCER – MILLION WOMEN STUDY
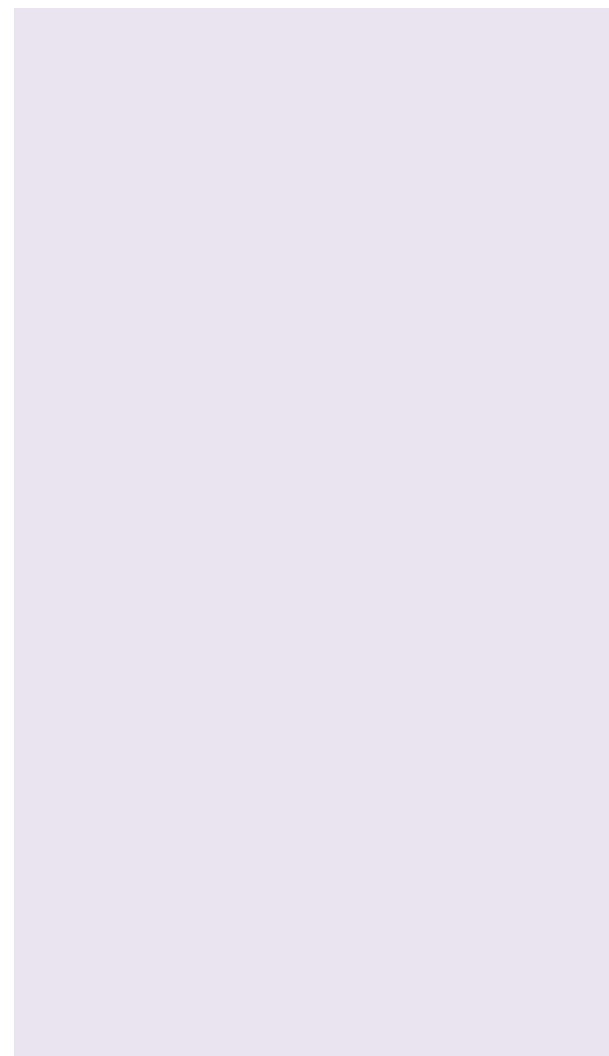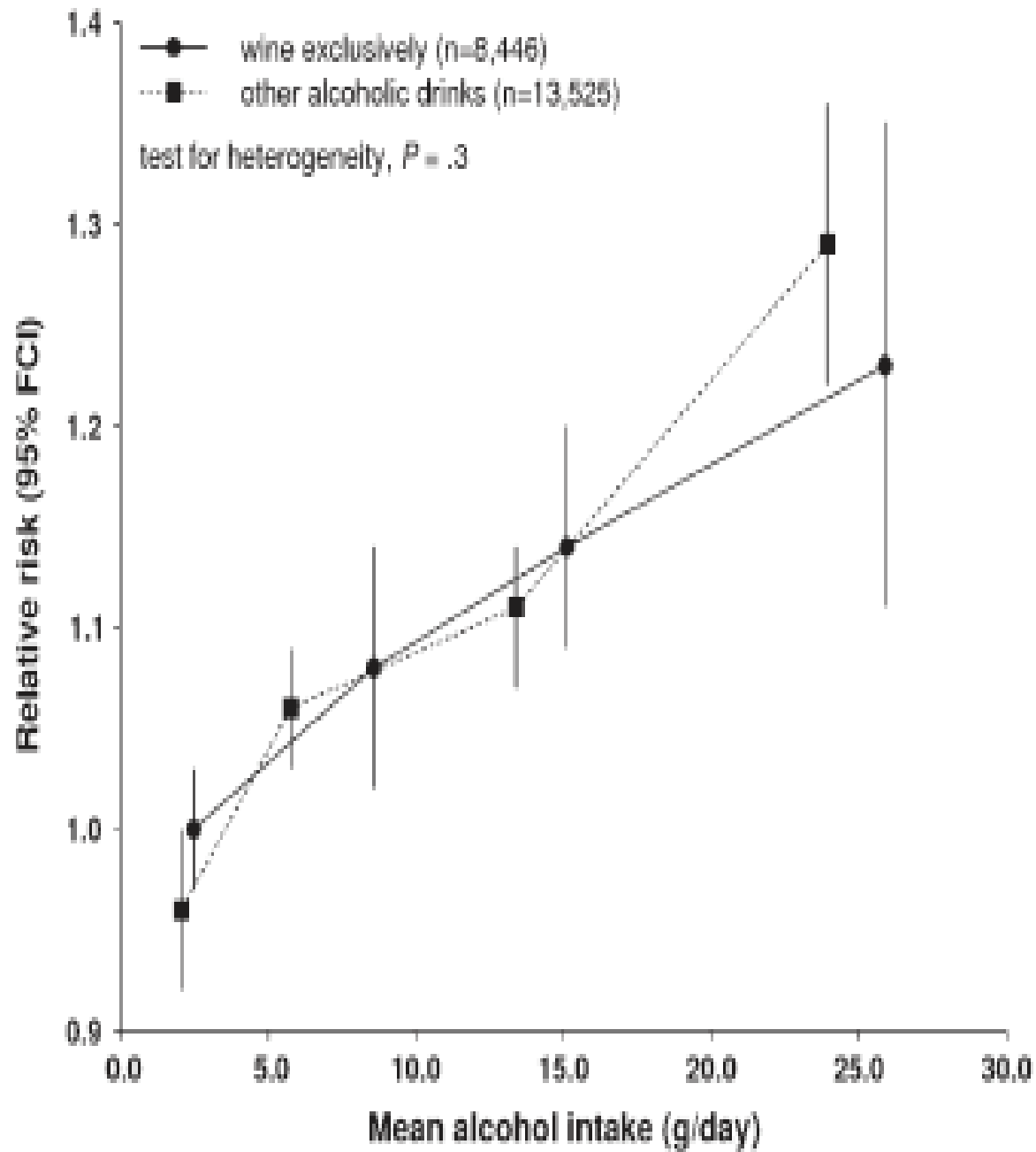
Alcohol Guidelines Review – Report from the Guidelines development group to the UK Chief Medical Officers

January 2016

3.   The group concluded[3] that there is significant new, good quality evidence available on the effects of alcohol consumption on health, which was not available at the time of the 1995 review. This applies for both men and women. In particular, stronger evidence has emerged that the risk of a range of cancers, especially breast cancer, increases directly in line with consumption of any amount of alcohol.

Alcohol related mortality - UK

SMR/100,000

Alcohol related mortality, UK countries, 1991-2005
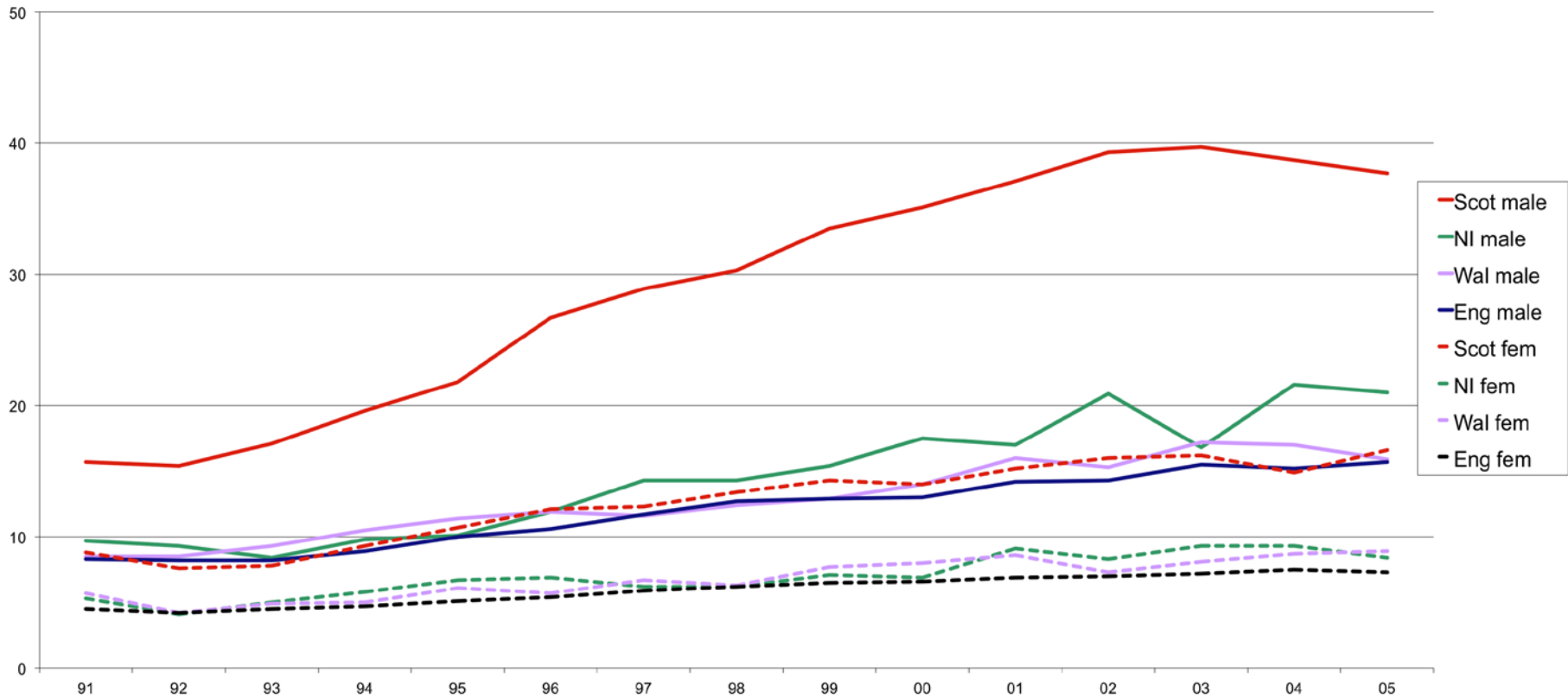
IARC Monographs evaluate consumption of red meat and processed meat

Lyon, France, 26 October 2015 – The International Agency for Research on Cancer (IARC), the cancer agency of the World Health Organization, has evaluated the carcinogenicity of the consumption of red meat and processed meat.

Red meat

After thoroughly reviewing the accumulated scientific literature, a Working Group of 22 experts from 10 countries convened by the IARC Monographs Programme classified the consumption of red meat as *probably carcinogenic to humans* (Group 2A), based on *limited evidence* that the consumption of red meat causes cancer in humans and *strong* mechanistic evidence supporting a carcinogenic effect.

This association was observed mainly for colorectal cancer, but associations were also seen for pancreatic cancer and prostate cancer.

Processed meat

Processed meat was classified as *carcinogenic to humans* (Group 1), based on *sufficient evidence* in humans that the consumption of processed meat causes colorectal cancer.

Reasons for uncertainty

- Measurement error
  - Diet, activity, anthropometry (cf adiposity)
  - Random error, systematic bias
- Study design
  - RCT vs cohort vs case control
  - Mechanistic
  - Population
  - Study size
- Confounding
  - Smoking
  - Nutrient vs food
  - Multiple collinearity eg PA
- Exposure homogeneity
- Small effect size

29 MARCH 2012 | VOL 483 | NATURE | 531
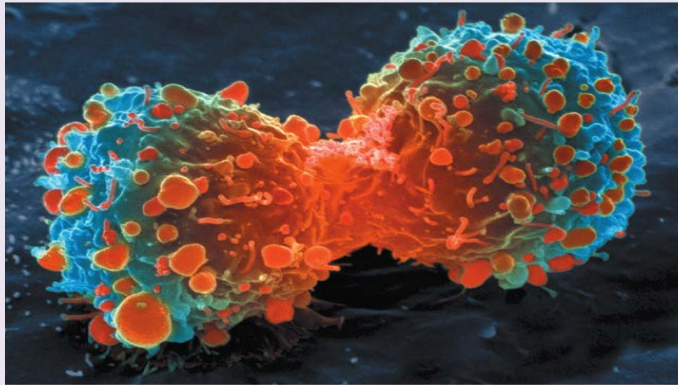
Many landmark findings in preclinical oncology research are not reproducible, in part because of inadequate cell lines and animal models.

Raise standards for preclinical cancer research

C. Glenn Begley and Lee M. Ellis propose how methods, publications and incentives must change if patients are to benefit.

- **Reproducibility**
- **Relevance of model**
- **Relevance of exposure**
- **Relevance of dose**
- **Route of administration**
- **Publication bias**

DIET, NUTRITION, PHYSICAL ACTIVITY AND LIVER CANCER

		DECREASES RISK	INCREASES RISK
STRONG EVIDENCE	Convincing		Aflatoxins[1] Alcoholic drinks[2] Body fatness[3]
	Probable	Coffee	
LIMITED EVIDENCE	Limited - suggestive	Fish Physical activity[4]	
	Limited - no conclusion	Cereals (grains) and their products, non-starchy vegetables, fruits, peanuts (groundnuts), meat and poultry, salted fish, tea, green tea, glycaemic index, calcium and vitamin D supplements, vitamin C, water source, low fat diet	
STRONG EVIDENCE	Substantial effect on risk unlikely		

1. Foods that may be contaminated with aflatoxins include cereals (grains), as well as pulses (legumes), seeds, nuts and some vegetables and fruits.
2. Based on evidence for alcohol intakes above around 45 grams per day (about 3 drinks a day). No conclusion was possible for intakes below 45 grams per day. There is insufficient evidence to conclude that there is any difference in effect between men and women. Alcohol consumption is graded by the International Agency for Research on Cancer (IARC) as carcinogenic to humans (Group 1) [2].
3. Body fatness is marked by body mass index (BMI).
4. Physical activity of all types.

Certainty is unattainable – degrees of uncertainty

Is the evidence strong enough to take action?

Evidence accrues and conclusions may change

Convincing is not the same as proof

The Panel emphasises the importance of not smoking and of avoiding exposure to tobacco smoke

RECOMMENDATIONS

BODY FATNESS
Be as lean as possible within the normal range of body weight

PHYSICAL ACTIVITY
Be physically active as part of everyday life

FOODS AND DRINKS THAT PROMOTE WEIGHT GAIN
Limit consumption of energy-dense foods
Avoid sugary drinks

PLANT FOODS
Eat mostly foods of plant origin

ANIMAL FOODS
Limit intake of red meat and avoid processed meat

ALCOHOLIC DRINKS
Limit alcoholic drinks

PRESERVATION, PROCESSING, PREPARATION
Limit consumption of salt
Avoid mouldy cereals (grains) or pulses (legumes)

DIETARY SUPPLEMENTS
Aim to meet nutritional needs through diet alone

BREASTFEEDING
Mothers to breastfeed; children to be breastfed

CANCER SURVIVORS
Follow the recommendations for cancer prevention

Our Cancer Prevention Recommendations

Be a healthy weight
Keep your weight as low as you can within the healthy range

Move more
Be physically active for at least 30 minutes every day, and sit less

Avoid high-calorie foods and sugary drinks
Limit high-calorie foods (particularly processed foods high in fat or added sugar, or low in fibre) and avoid sugary drinks

Enjoy more grains, veg, fruit and beans
Eat a wide variety of whole grains, vegetables, fruit and pulses such as beans

Limit red meat and avoid processed meat
Eat no more than 500g (cooked weight) a week of red meat, such as beef, pork and lamb. Eat little, if any, processed meat such as ham and bacon

For cancer prevention, don't drink alcohol
For cancer prevention, it's best not to drink alcohol. If you do, limit alcoholic drinks to two for men and one for women a day

Eat less salt and avoid mouldy grains & cereals
Limit your salt intake to less than 6g (2.4g sodium) a day by adding less salt and eating less food processed with salt

Avoid mouldy grains and cereals as they may be contaminated by aflatoxins

For cancer prevention, don't rely on supplements
Eat a healthy diet rather than relying on supplements to protect against cancer

If you can, breastfeed your baby
If you can, breastfeed your baby for six months before adding other liquids and foods

Cancer survivors should follow our Recommendations (where possible)

After cancer treatment, the best advice is to follow the Cancer Prevention Recommendations. Check with your health professional

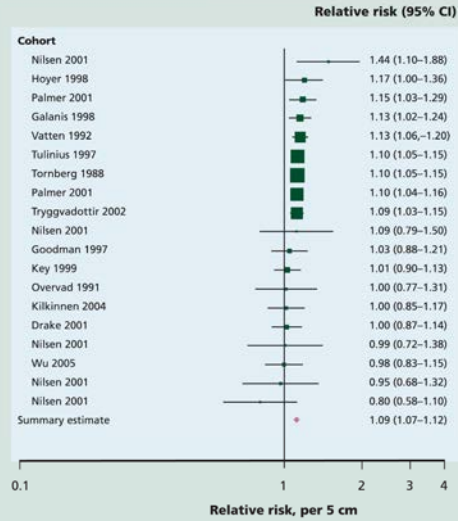# Estimates of cancer preventability by appropriate diet, nutrition, physical activity and body fatness

	USA	UK	BRAZIL	CHINA
Mouth, pharynx, larynx	63	67	63	44
Oesophagus	63	71	50	33
Lung	36	33	36	38
Stomach	47	45	41	33
Pancreas	19	15	11	8
Gallbladder	21	16	10	6
Liver	30	24	13	7
Colorectum	50	47	41	22
Breast	33	38	22	11
Ovary	5	4	3	1
Endometrium	59	44	37	21
Prostate (advanced)	11	9	5	4
Kidney	24	19	13	8
Total for these cancers	31	32	25	24
Total for all cancers	21	24	18	20

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IMPACT OF OFFSPRING SIZE AND GROWTH ON CANCER RISK - 2007

Height and breast cancer (age unspecified); cohort studies — Relative risk (95% CI), Relative risk, per 5 cm

Height and postmenopausal breast cancer; cohort studies — Relative risk (95% CI), Relative risk, per 5 cm
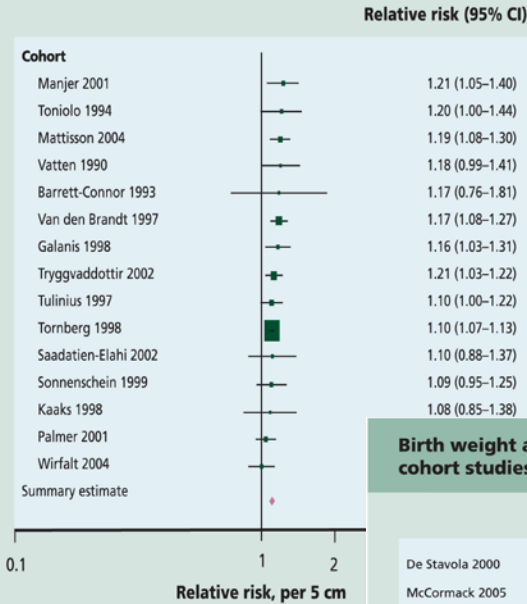
Height and colorectal cancer; cohort studies — Relative risk (95% CI), Relative risk, per 5 cm

Height and premenopausal breast cancer; cohort studies — Relative risk (95% CI), Relative risk, per 5 cm
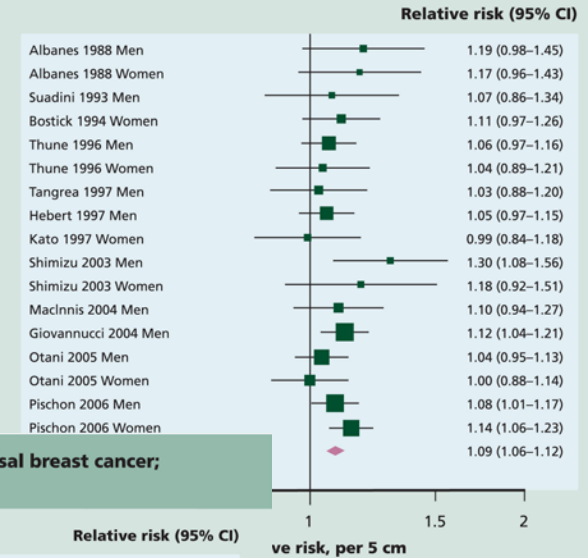
Birth weight and premenopausal breast cancer; cohort studies — Relative risk (95% CI), Relative risk, per kg
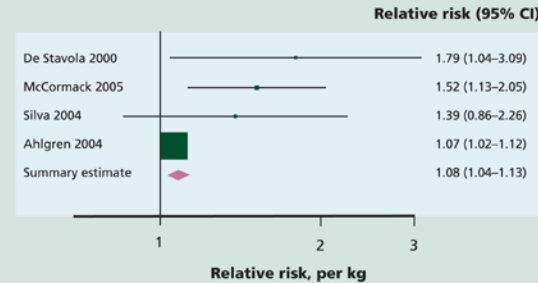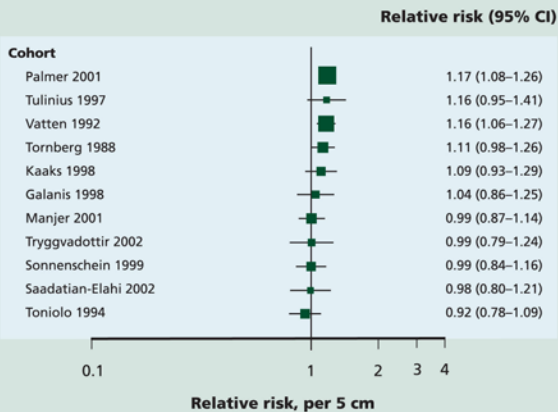
Height and ovarian cancer; cohort studies — Relative risk (95% CI), Relative risk, per 10 cm
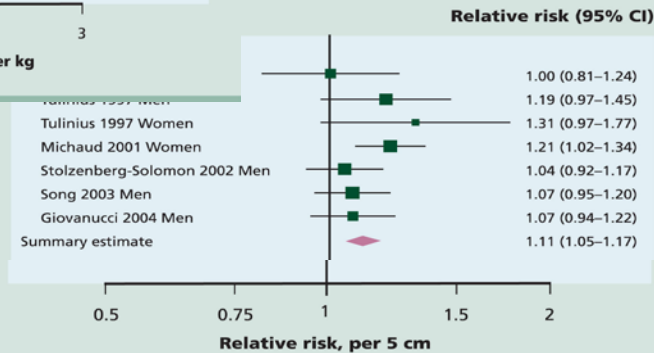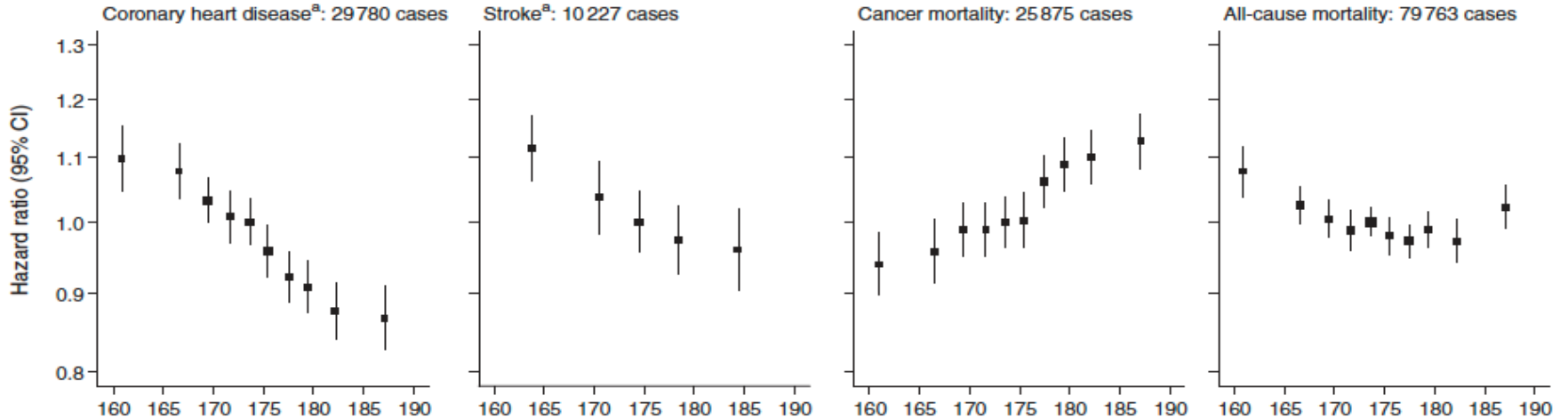
Height and cancer CUP 2015

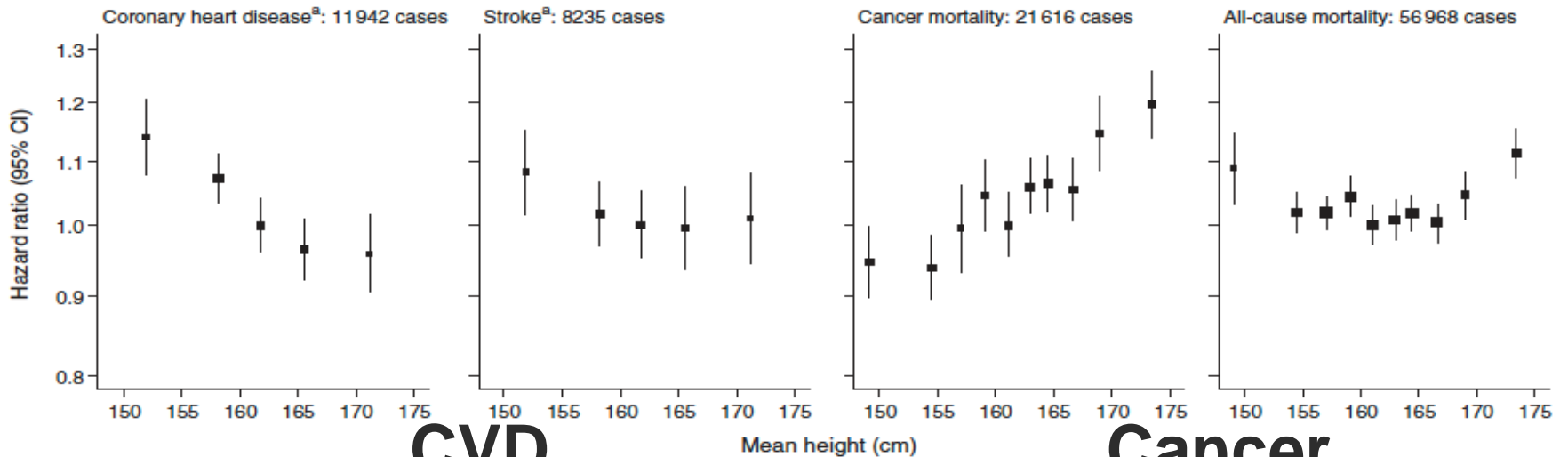Every 5 cm increment in height increases risk of cancers of:

- Kidney -10%
- Breast (pre-menopausal) - 9%
- Breast (post-menopausal) -11%
- Ovary - 8%
- Pancreas - 7%
- Colorectum - 5%
- Prostate – 4%

Height and risk of CVD and cancer

World Cancer Research Fund International

MALES:

Coronary heart disease[a]: 29 780 cases — Stroke[a]: 10 227 cases — Cancer mortality: 25 875 cases — All-cause mortality: 79 763 cases

FEMALES:

Coronary heart disease[a]: 11 942 cases — Stroke[a]: 8235 cases — Cancer mortality: 21 616 cases — All-cause mortality: 56 968 cases

Hazard ratio (95% CI)

Mean height (cm)

CVD   Cancer

www.wcrf.org

Bottom Line

The key messages are robust and generally agreed

- Be active, and don't be sedentary – and keep it up as long as possible

- Eat enough but not too much – don't get too thin or fat

- Eat food not pills

- Mostly from plants, emphasise wholegrains and pulses

- Avoid highly processed energy dense foods and sugar sweetened beverages (and alcohol, processed meat and salty foods)

- Grow appropriately from conception to adulthood

- Get your mother to be well nourished before getting pregnant. And to breastfeed you.

JOHN TUKEY

Far better an approximate answer to the *right* question, which is often vague, than an *exact* answer to the wrong question, which can always be made precise.

> *The future of data analysis*. Annals of Mathematical Statistics 1962

An approximate answer to the right question is worth a great deal more than a precise answer to the wrong question.

> – *Super Freakonomics*

The WCRF/AICR Continuous Update Reports
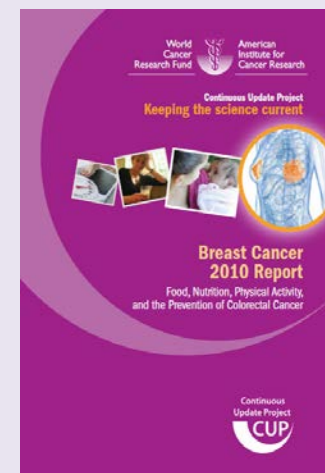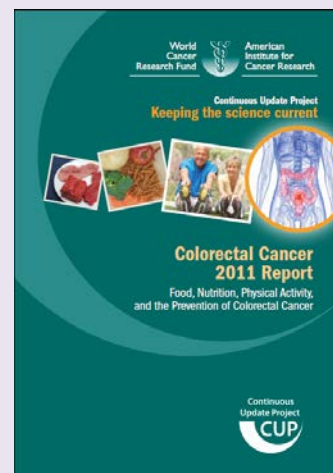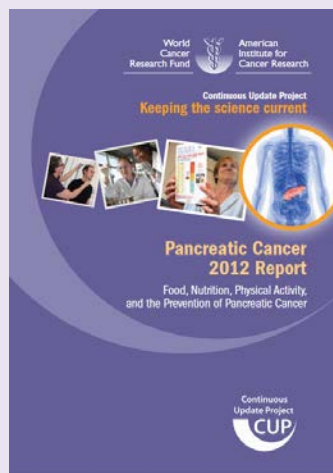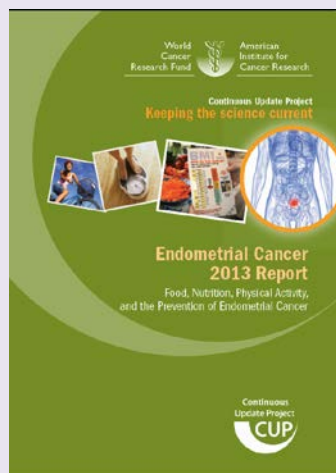
http://www.wcrf.org/cancer_research/cup/key_findings/index.php