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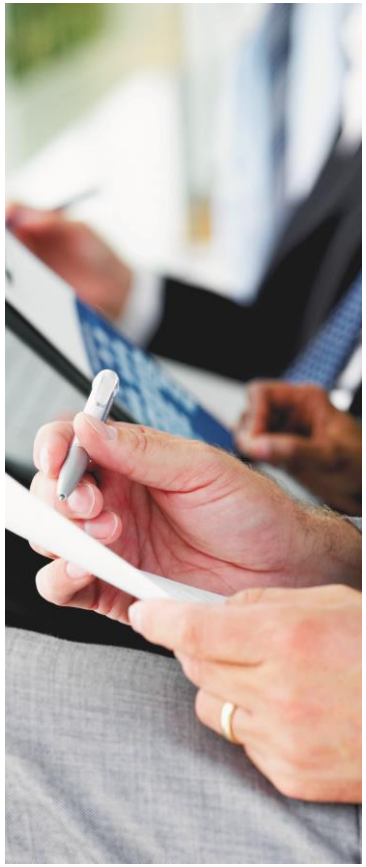
Diet, weight, physical activity and cancer

Dr Rachel Thompson, Head of Research Interpretation



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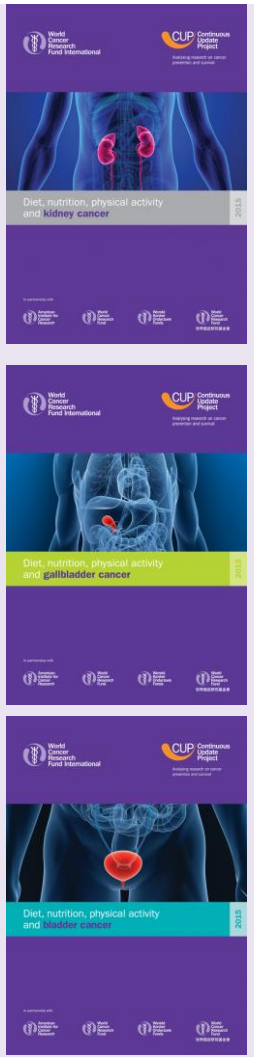
CUP Continuous Update Project

Analysing research on cancer prevention and survival

Outline

- World Cancer Research Fund network
- Continuous Update Project
- Recommendations for cancer prevention and evidence behind them
- Advice for people living with cancer
- Publications from WCRF in 2017



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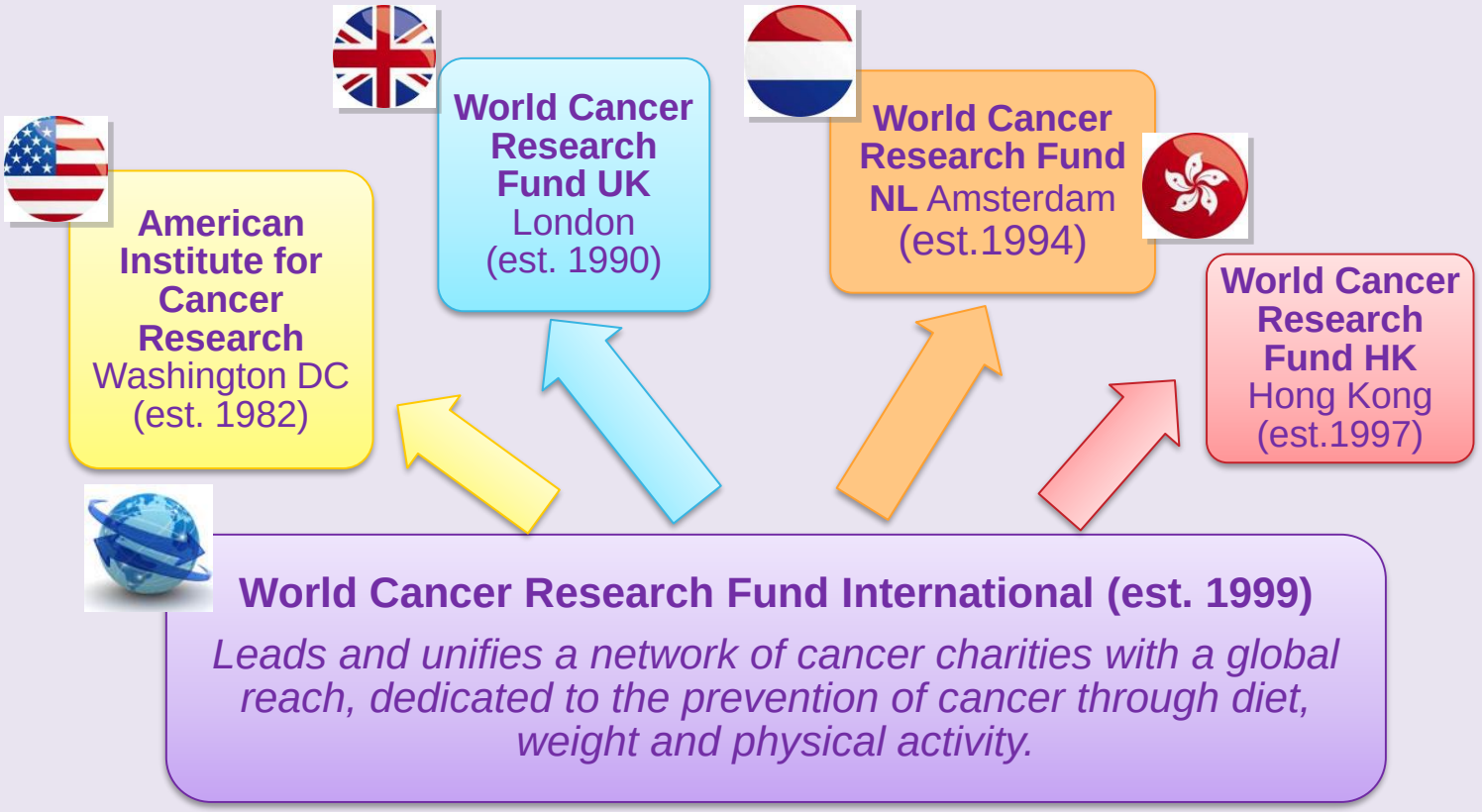
The World Cancer Research Fund Network



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WCRF: What we do

CUP Continuous Update Project

Analysing research on cancer prevention and survival

- We **fund research** on the relationship of diet, physical activity and body fatness to cancer risk
- We **interpret** the accumulated scientific literature in the field of cancer, diet, physical activity and body fatness, and use this to derive **Cancer Prevention Recommendations**
- We **educate** people through our national Health Information Departments
- We **advocate** wider implementation of effective policies through our international Policy and Public Affairs Department
- We do all this to **help people and populations to reduce their chances of developing cancer**

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Why cancer?

- Cancer **affects everyone in some way**
- Cancer is preventable – **about third of cases** of common cancers linked to diet, weight, physical activity
- Alongside smoking, **diet, weight and physical activity** are the most important factors affecting cancer risk
- A healthy lifestyle will also **prevent other diseases**

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Continuous Update Project

- The CUP analyses global cancer prevention and survival research linked to diet, nutrition and physical activity. Among experts worldwide it is a trusted, authoritative scientific resource, which underpins current guidelines and policy for cancer prevention
- It ensures the WCRF network Recommendations for Cancer Prevention are based on the latest evidence
- The CUP is produced in partnership with the American Institute for Cancer Research, World Cancer Research Fund UK, World Cancer Research Fund NL and World Cancer Research Fund HK.

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13 CUP reports so far

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AVAILABLE FOR DOWNLOAD at

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www.wcrf.org/cupreports

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Underlying principles

- Exposures include diet, nutrition (including body composition) and physical activity
- Cancers with some evidence of link with above
- Identify causal exposures - protective or adverse
- Use most robust methods for systematically reviewing evidence on epidemiology
- Epidemiological evidence of a link needs to be supported by biological mechanisms
- Transparency

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People involved in the CUP

- More than 100 scientists
- 17 countries

Team of researchers for the CUP at Imperial College London

CUP Panel of independent experts

- Includes CUP Expert Panel, researchers, peer reviewers, advisers and more

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CUP database

- World's largest central resource for scientific evidence on cancer, diet, weight and physical activity. It's continually updated as papers are published.
- *About 9,000 papers on prevention (17 cancers) and survival (breast cancer only)*

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Hierarchy of evidence

Pooled analyses and meta-analyses

RCT

Cohort

Case control

Ecological

Opinion

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CUP analyses

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Figure 3: Highest versus lowest analysis of intake of salt-preserved foods and stomach cancer

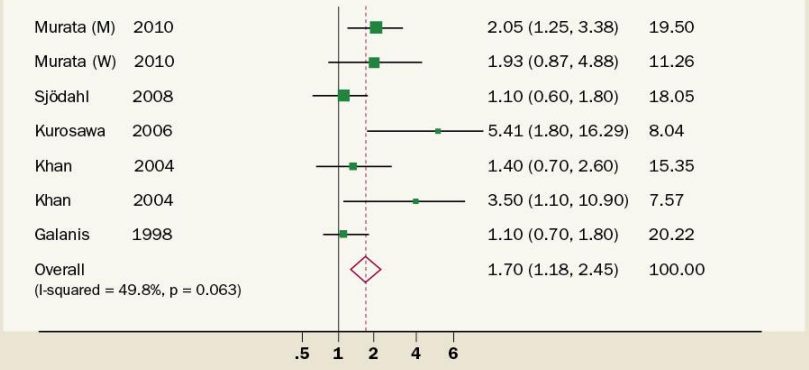


Figure 2: Dose-response meta-analysis of intake of salt-preserved vegetables and stomach cancer, per 0.5 serving (20 grams) per day

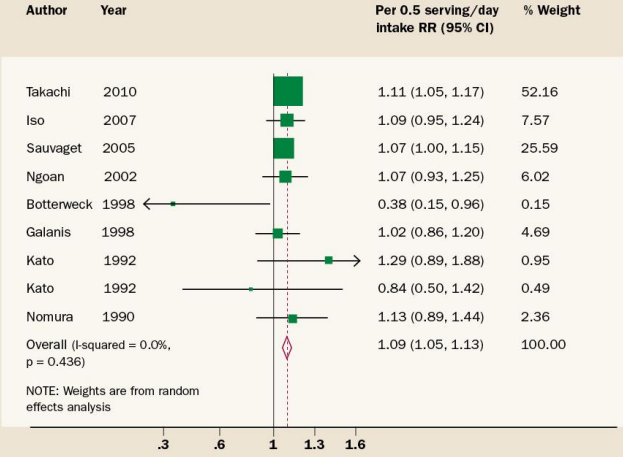


Figure 4: Dose-response meta-analysis of processed meat intake and stomach cancer, per 50 grams per day

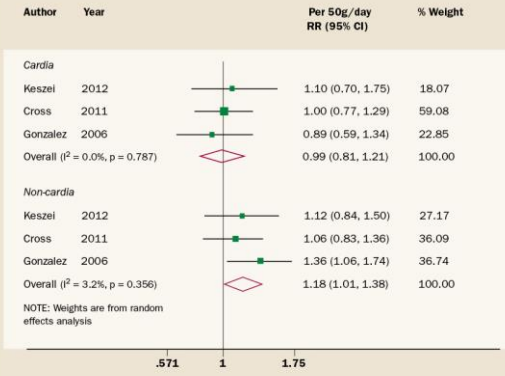
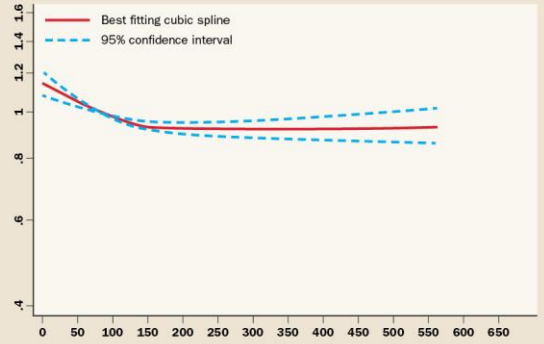


Figure 1: Non-linear dose-response association of fruit intake and stomach cancer



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CUP mechanisms work

For any exposure (e.g. red/processed meat) what is the mechanism that causes (or protects from) cancer?

Red/processed meat (exposure) →  → Colorectal cancer

?

Biological/Cellular Pathway

Epidemiological and mechanistic info together give more complete picture on risk factors for cancer

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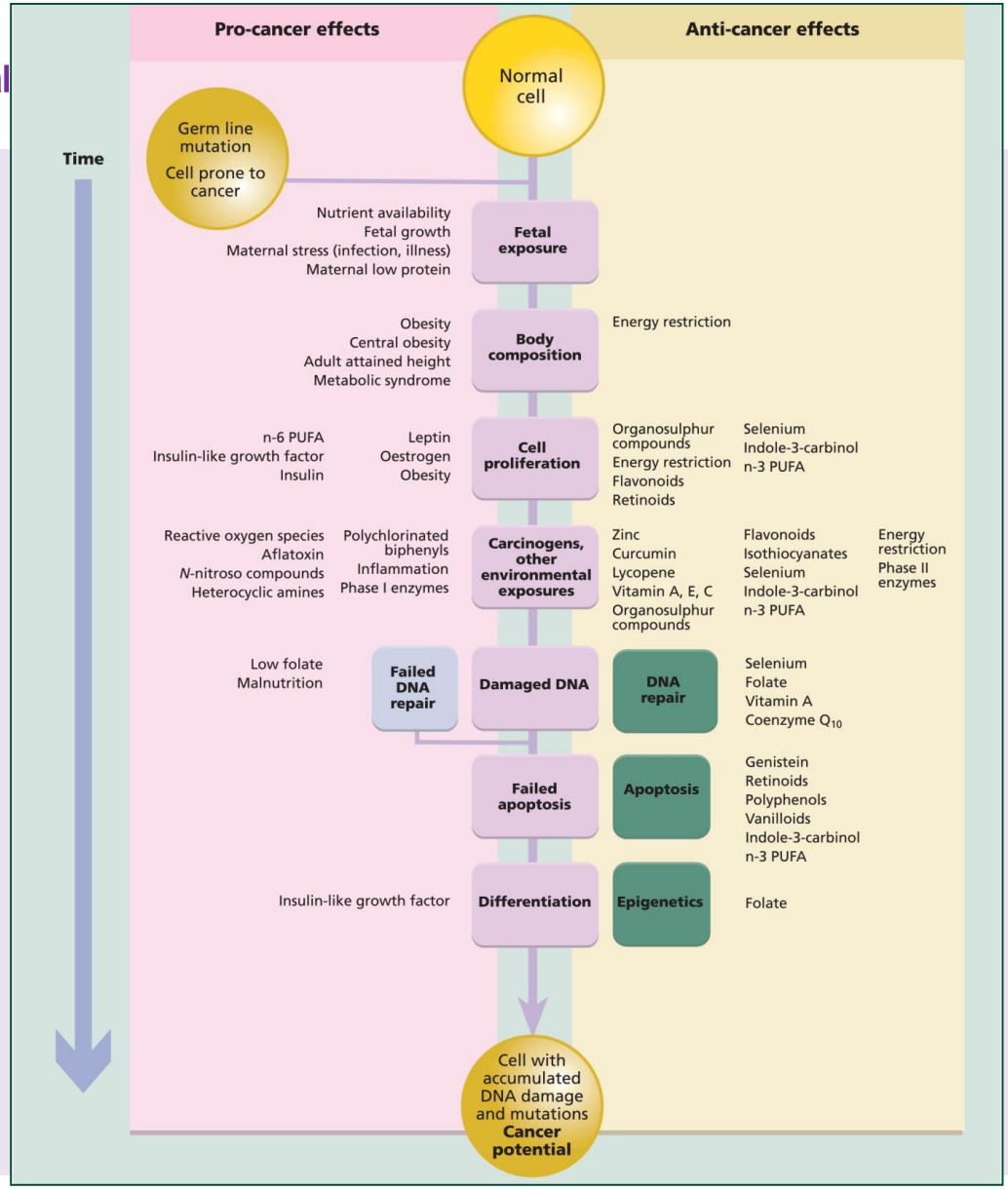
Impact of diet, nutrition & physical activity on cancer



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Grading criteria

Predefined requirements for

- Number and types of studies
- Quality of exposure and outcome assessment
- Heterogeneity within and between study types
- Exclusion of chance, bias or confounding
- Biological gradient
- Evidence of mechanisms
- Size of effect

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Grading the evidence

		Decreases risk	Increases risk
Strong evidence	Convincing	Basis for recommendations	
	Probable		
Limited evidence	Limited - suggestive		
	Limited – no conclusion		
Strong evidence	Substantial effect on risk unlikely		

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From conclusions to recommendations

- Exposures graded convincing or probable
- Basis for policies, programmes, personal choices
- Broad based - foods rather than nutrients
- Global
- Cancer in general
- Prevention of other diseases

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WCRF Cancer Prevention Recommendations and evidence behind them

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Be a healthy weight

BODY FATNESS		
	DECREASES RISK	**INCREASES RISK**
Convincing		Oesophagus (AC); pancreas; liver; colorectum; breast (postmenopause); endometrium; kidney
Probable	Breast (premenopause)	Stomach (cardia); prostate (advanced); gallbladder; ovary
Substantial effect on risk unlikely	None identified	

Overweight and obesity linked to increased risk of 11 cancers

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Body fatness as body mass index

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Cancer	RR per 5kg/m^2	Number of cohort studies
Endometrium	1.50 (1.42-1.59)	25
Oesophagus (adenocarcinoma)	1.48 (1.35-1.62)	9
Kidney	1.30 (1.25-1.35)	23
Liver	1.30 (1.16-1.46)	12
Gallbladder	1.25 (1.15-1.37)	8
Stomach (cardia)	1.23 (1.07-1.40)	7
Breast (postmenopause)	1.13 (1.08-1.18)	19
Pancreas	1.10 (1.07-1.14)	23
Colorectum	1.10 (1.04-1.16)	23
Prostate (advanced)	1.08 (1.04-1.12)	23
Ovary	1.06 (1.02-1.11)	25
Breast (premenopause)	0.93 (0.88-0.98)	16

Also reviewed waist circumference and waist-hip ratio

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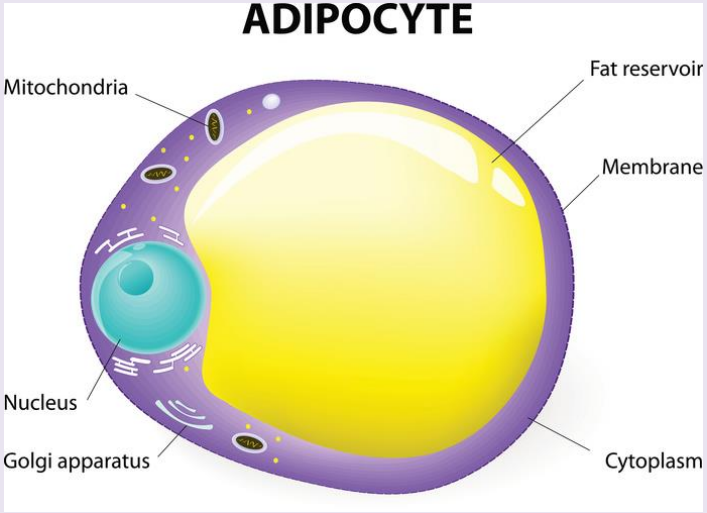
How does body fatness affect cancer risk?

- Fat in the body (adipose tissue) is active ➔ sends signals to the rest of the body and helps to control processes like growth, metabolism and reproductive cycles
- Three main ways that excess fat can affect cancer risk:
  - Oestrogen
  - Insulin and growth factors
  - Inflammation



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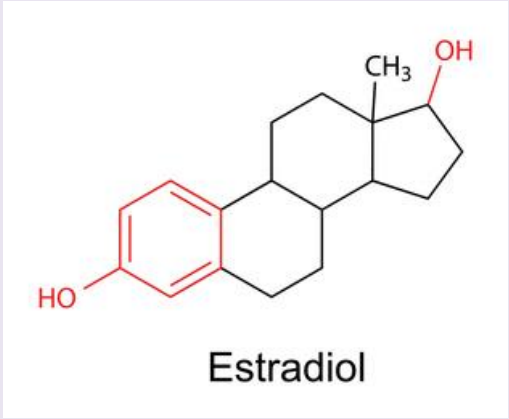
Oestrogen



Estradiol

Oestrogen – primary female sex hormone

Fat cells produce **OESTROGEN**

↑ fat means higher levels of oestrogen circulating

Promotes uncontrolled cell division

CANCER GROWTH

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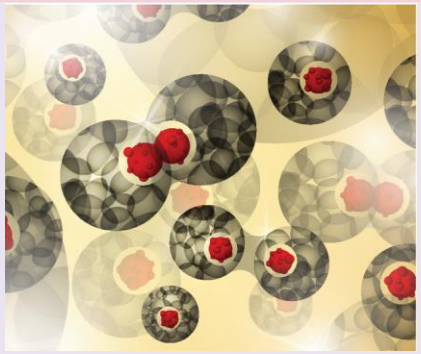
Insulin and growth factors

Insulin – hormone with a key role in the regulation of blood glucose levels

Cells resistant to effects of insulin

Pancreas produces ↑ insulin to compensate – 'hyperinsulinemia'



↑ insulin affects levels of certain growth factors

Promotes uncontrolled cell division

CANCER GROWTH

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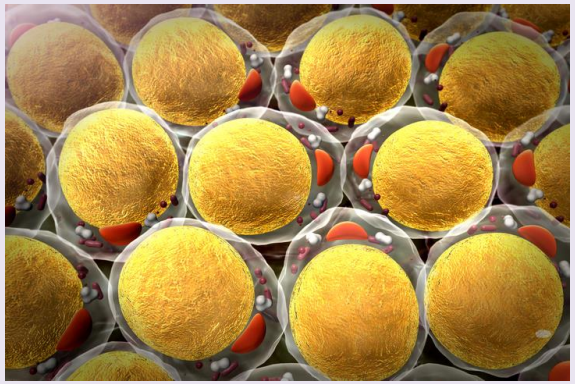
Inflammation



↑ Fat cells in the body

↓

Release specialised immune cells (macrophages)

→

Stimulates release of cytokines, which encourage cell division'

→

Promotes uncontrolled cell division

↓

CANCER GROWTH

Obese individuals often have chronic low-level inflammation

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Recommendation

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

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Move more

PHYSICAL ACTIVITY				
	DECREASES RISK		INCREASES RISK	
	Exposure	**Cancer/weight**	**Exposure**	**Cancer/weight**
Convincing	Physical activity	Overweight/obesity	Sedentary living	Overweight/obesity
Probable	Physical activity	Colon, breast (post), endometrium	Television viewing	Overweight/obesity
Substantial effect on risk unlikely	None identified			

Physical activity linked to a decreased risk of 3 cancers

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How does physical activity affect cancer risk?

- Physical activity can reduce the risk of some cancers through these general mechanisms:

  - Decreases body fat
  - Improves the body's sensitivity to insulin
  - Reduces inflammation
  - Improves immune function
  - Enhances DNA repair

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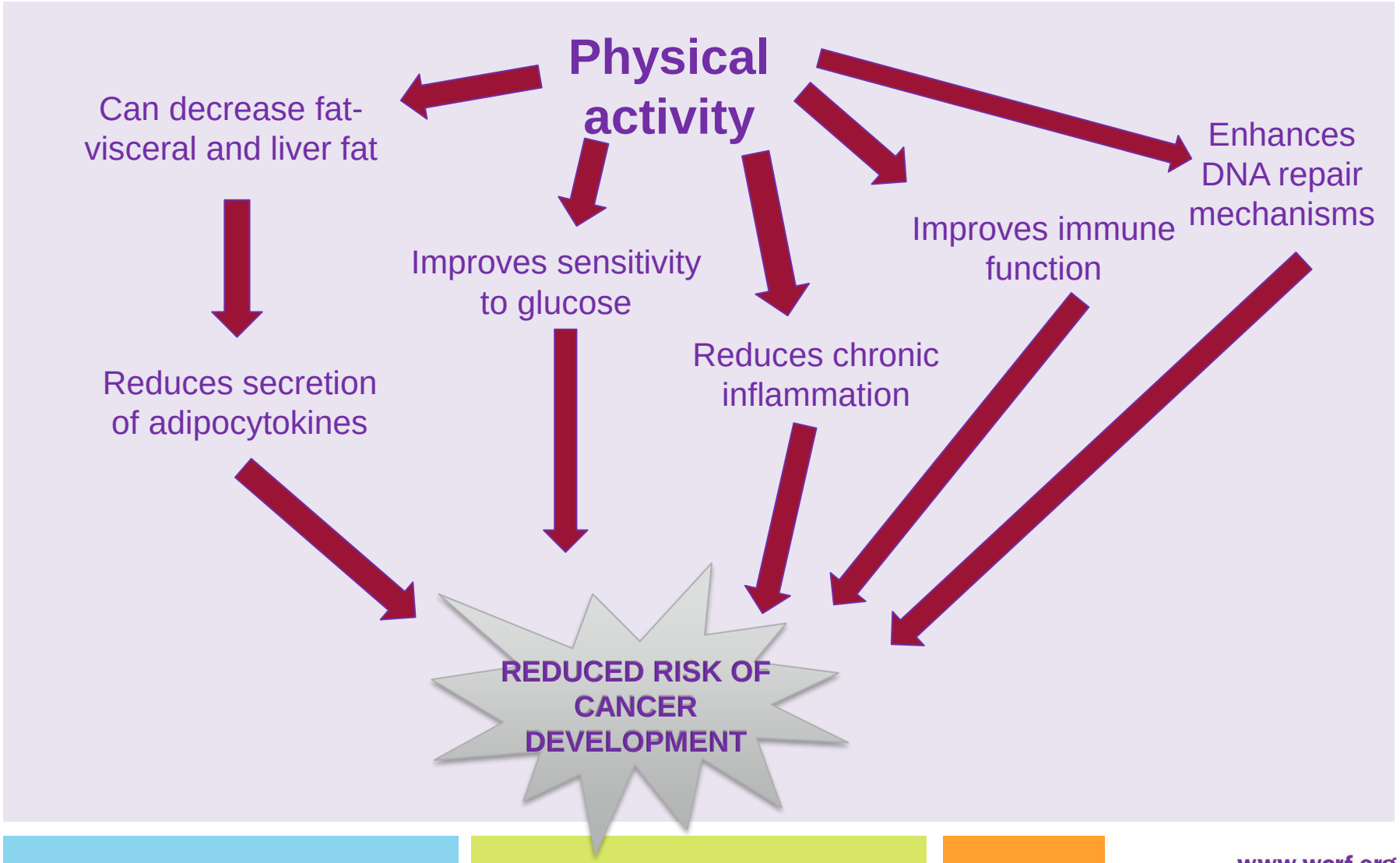

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Recommendation

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

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Avoid high calorie foods

HIGH ENERGY FOODS/GLYCAEMIC LOAD				
	DECREASES RISK		INCREASES RISK	
	Exposure	Cancer/weight	Exposure	Cancer/weight
Convincing				
Probable			Energy-dense foods Fast foods Glycaemic load	Overweight/obesity Overweight/obesity Endometrium
Substantial effect on risk unlikely	None identified			

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Avoid sugary drinks

NON-ALCOHOLIC DRINKS				
	DECREASES RISK		INCREASES RISK	
	Exposure	**Cancer/weight**	**Exposure**	**Cancer/weight**
Convincing			Arsenic in drinking water	Lung
Probable	Coffee	Liver & endometrium	Sugary drinks Arsenic in drinking water Mate	Overweight/obesity Bladder & skin Oesophagus (SCC)
Substantial effect on risk unlikely	Coffee - Pancreas			

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Recommendation

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

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Enjoy more grains, veg, fruits and beans; For cancer prevention don't rely on supplements

PLANT FOODS AND DIETARY SUPPLEMENTS				
	DECREASES RISK		INCREASES RISK	
	Exposure	**Cancer/weight**	**Exposure**	**Cancer/weight**
Convincing	Foods containing dietary fibre	Colorectum	High-dose beta-carotene supplements	Lung
Probable	Low-energy dense foods Vegetables Fruits Calcium supplements	Overweight/obesity Mouth/throat Lung & Mouth/throat Colorectum		
Substantial effect on risk unlikely	Foods and supplements containing beta-carotene – prostate and skin			

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Recommendations

- Eat a wide variety of whole grains, vegetables, fruits and pulses such as beans.
- Eat a healthy diet rather than relying on supplements to protect against cancer

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Limit red and avoid processed meat

ANIMAL FOODS				
	DECREASES RISK		INCREASES RISK	
	Exposure	**Cancer**	**Exposure**	**Cancer**
Convincing			Red meat Processed meat	Colorectum Colorectum
Probable	Milk	Colorectum	Processed meat Cantonese-style salted fish	Non-cardia stomach cancer Nasopharynx
Substantial effect on risk unlikely	None identified			

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Recommendation

- Eat less 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

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How do red & processed meats affect cancer risk?

- Red and processed meat can increase cancer risk through the following mechanisms:

  - Contain haem which promotes the formation of potentially carcinogenic compounds
  - Processed meat contains nitrates and nitrites

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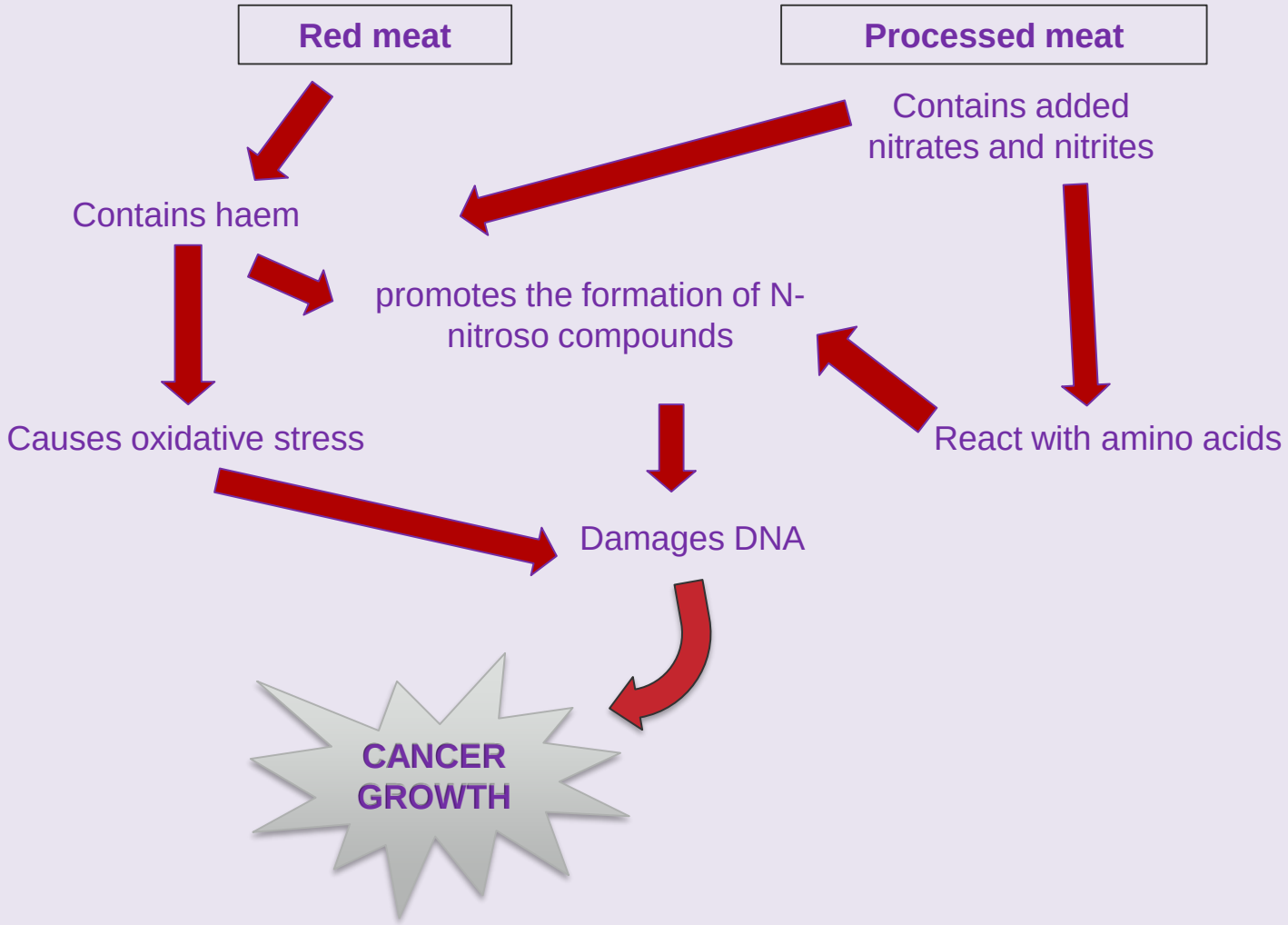

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Headlines from October 2015

SAUSAGES, bacon and burgers are as big a cancer threat as cigarettes, global health bosses are to rule.

Sausages 'give you cancer'

Processed meat to be ranked among most carcinogenic substances

Bacon and other processed meats cause cancer, claims WHO report

Farmers and the meat industry have expressed concern about the impact on sales if the organisation lists processed meat as a carcinogen

Bacon, burgers and sausages are a cancer risk, say world health chiefs: Processed meats added to list of substances most likely to cause disease alongside cigarettes and asbestos

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IARC/WHO: Carcinogenicity of the consumption of red meat and processed meat

- Processed meat: carcinogenic to humans (Group 1)
- Red meat: probably carcinogenic to humans (Group 2A)
- Evidence mainly for colorectal
- Some evidence for processed meat and stomach cancer; red meat with pancreatic and prostate cancer
- A working group of 22 experts reviewed about 800 studies

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For cancer prevention, don't drink alcohol

ALCOHOLIC DRINKS		
	DECREASES RISK	**INCREASES RISK**
Convincing		Mouth/throat; oesophagus (SCC); liver; colorectum (men); breast (pre & post)
Probable	Kidney	Stomach; colorectum (women)
Substantial effect on risk unlikely	None identified	

Alcohol consumption linked to an increased risk of 6 cancers

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Alcohol (as ethanol)

Cancer	RR per 10g/d	Number of cohort studies	Threshold
Oesophagus (squamous cell carcinoma)	1.25 (1.12-1.41)	6	
Colorectum	1.10 (1.06-1.13)	8	
Breast (premenopause)	1.09 (1.01-1.17)	5	
Breast (postmenopause)	1.08 (1.05-1.11)	13	
Mouth/throat	N/A	2	
Stomach	1.02 (1.00-1.04)	23	From 45g/d
Liver	1.04 (1.02-1.06)	14	From 45g/d
Kidney	0.92 (0.86-0.97)	7	Up to 30g/d

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How does alcohol affect cancer risk?

- There are several theories for how alcohol interacts with our bodies to increase cancer risk:

  - Causes direct damage to DNA
  - Carries carcinogens into cells
  - Interferes with vitamin A metabolism
  - Indirect association: can be associated with increased body fatness

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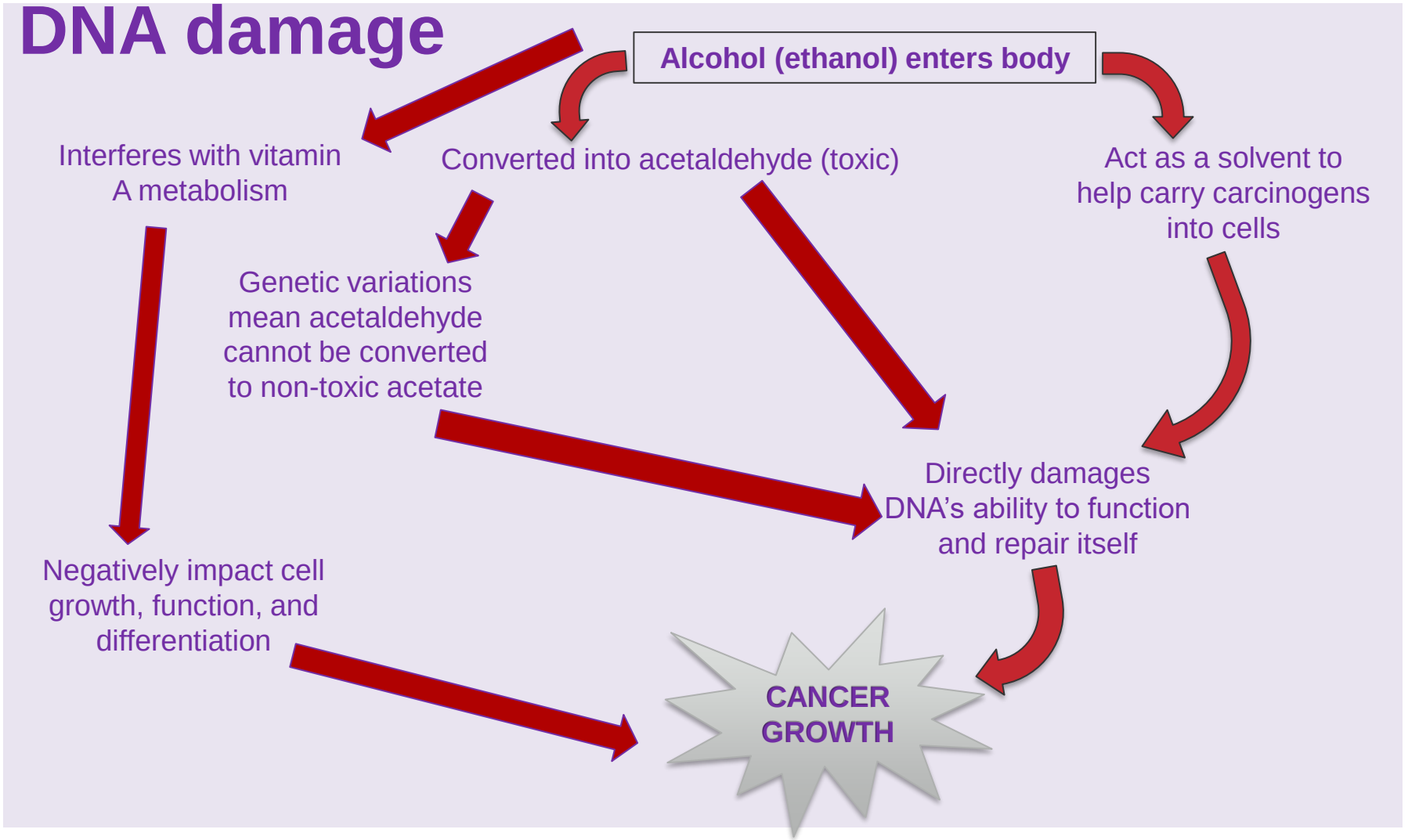
DNA damage



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Recommendation

For cancer prevention, it's best not to drink alcohol. If you do, limit alcoholic drinks and follow national guidelines

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Eat less salt; avoid mouldy grains and cereals

PRESERVATION AND CONTAMINATION				
	DECREASES RISK		INCREASES RISK	
	Exposure	Cancer	Exposure	Cancer
Convincing			Aflatoxins	Liver
Probable			Foods preserved by salting Processed meat Cantonese-style salted fish	Stomach Colorectum; stomach (non-cardia) Nasopharynx
Substantial effect on risk unlikely	None identified			

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Recommendation

Limit your salt intake to less than 6g 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

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If you can, breastfeed your baby

LACTATION/BEING BREAST FED				
	DECREASES RISK		INCREASES RISK	
	Exposure	**Cancer/weight**	**Exposure**	**Cancer/weight**
Convincing				
Probable	Lactation Being breastfed	Breast (pre and post) Overweight/obesity		
Substantial effect on risk unlikely	None identified			

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Recommendation

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

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Growth and development

GROWTH AND DEVELOPMENT				
	DECREASES RISK		INCREASES RISK	
	Exposure	Cancer	Exposure	Cancer
Convincing			Adult attained height	Colorectum, breast (post), ovary
Probable			Adult attained height Greater birth weight	Pancreas, breast (pre), prostate, kidney Breast (pre)
Substantial effect on risk unlikely	None identified			

No recommendation

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Adult attained height and other diseases

Cause of death	RR per 6.5 cm
Any	0.97 (0.96-0.99)
Vascular	0.94 (0.93-0.96)
Cancer	1.04 (1.03-1.06)
Other	0.92 (0.90-0.94)

From Emerging Risk Factors Collaboration – pooled analysis of 1 million adults (Wormser et al, 2012)

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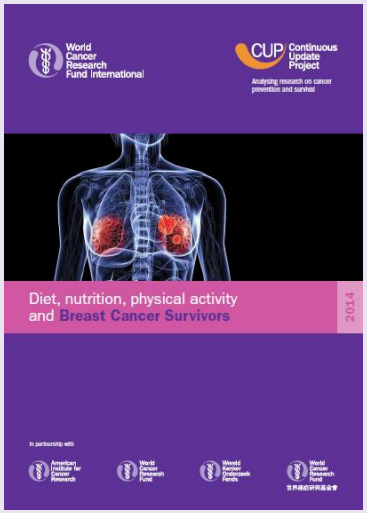
Breast cancer survivors



- Although there were significant associations between some exposures and outcomes, incomplete adjustment for potential confounders restricted the ability to ascribe causality
- CUP Panel concluded that evidence is limited

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Criteria for study inclusion

- Medline, EMBASE and the Cochrane Library CENTRAL searched
- Randomised controlled trials
  - ≥ 50 women
  - ≥ 6 months follow-up
- Prospective cohort (follow-up) studies
- Primary analysis, secondary analysis or ancillary analysis of randomised controlled trials or follow-up studies in breast cancer survivors

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Analysing research on cancer

DIET, NUTRITION, PHYSICAL ACTIVITY AND BREAST CANCER SURVIVAL (BY TIMEFRAME)

	Timing of exposure assessment	BEFORE DIAGNOSIS		LESS THAN 12 MONTHS AFTER DIAGNOSIS		12 MONTHS OR MORE AFTER DIAGNOSIS	
		DECREASES RISK	INCREASES RISK	DECREASES RISK	INCREASES RISK	DECREASES RISK	INCREASES RISK
		Exposure Outcome	Exposure Outcome	Exposure Outcome	Exposure Outcome	Exposure Outcome	Exposure Outcome
STRONG EVIDENCE	Convincing						
	Probable						
LIMITED EVIDENCE	Limited-suggestive	Physical activity — All mortality, BC mortality Foods containing fibre — All mortality	Body fatness — All mortality, BC mortality[2], 2nd BC Total fat — All mortality Saturated fatty acids — All mortality		Body fatness — All mortality, BC mortality[2], 2nd BC	Physical activity — All mortality Foods containing fibre — All mortality Foods containing soy — All mortality	Body fatness — All mortality
	Limited-no conclusion[1]	Fruits, vegetables, foods containing folate, foods containing soy, carbohydrate, glycaemic index, glycaemic load, protein, dietary supplements, alcoholic drinks, dietary patterns, underweight, body fatness (premenopause), adult attained height, energy intake		Foods containing fibre, carbohydrate, protein, total fat, saturated fatty acids, alcoholic drinks, physical activity, underweight, body fatness (premenopause), adult attained height, energy intake		Fruits, vegetables, foods containing fibre, foods containing folate, foods containing soy, carbohydrate, glycaemic index, glycaemic load, protein, total fat, saturated fatty acids, alcoholic drinks, dietary patterns, physical activity, body fatness, underweight, height, energy intake	
STRONG EVIDENCE	Substantial effect on risk unlikely						

All mortality, All cause mortality; BC mortality, breast cancer mortality; 2nd BC, Second primary breast cancer

STRONG: Evidence strong enough to support a judgement of a convincing or probable causal relationship and generally justify making recommendations

LIMITED: Evidence that is too limited to justify making specific recommendations

1 Includes various exposure-outcome combinations where evidence was available but too limited to draw conclusions. For more details of the outcomes related to the exposures listed here, see the full Breast Cancer Survivors SLR

2 Postmenopause only

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DIET, NUTRITION, PHYSICAL ACTIVITY AND BREAST CANCER SURVIVAL (BY OUTCOME)

	Outcome	ALL CAUSE MORTALITY				BREAST CANCER MORTALITY				SECOND PRIMARY BREAST CANCER			
		DECREASED RISK		INCREASED RISK		DECREASED RISK		INCREASED RISK		DECREASED RISK		INCREASED RISK	
		Exposure	Timeframe	Exposure	Timeframe	Exposure	Timeframe	Exposure	Timeframe	Exposure	Timeframe	Exposure	Timeframe
STRONG EVIDENCE	Convincing												
	Probable												
LIMITED EVIDENCE	Limited-suggestive	Physical activity	Before diagnosis ≥12 months after diagnosis	Body fatness	Before diagnosis <12 months after diagnosis ≥12 months after diagnosis	Physical activity	Before diagnosis	Body fatness[1]	Before diagnosis <12 months after diagnosis			Body fatness	Before diagnosis <12 months after diagnosis
		Foods containing fibre	Before diagnosis ≥12 months after diagnosis	Total fat	Before diagnosis								
		Foods containing soy	≥12 months after diagnosis	Saturated fatty acids	Before diagnosis								
STRONG EVIDENCE	Substantial effect on risk unlikely												

STRONG: Evidence strong enough to support a judgement of a convincing or probable causal relationship and generally justify making recommendations
LIMITED: Evidence that is too limited to justify making specific recommendations

1 Post menopause only

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Recommendation

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

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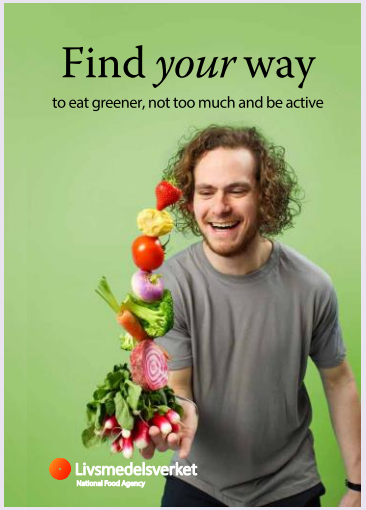
CUP impact: general



- Information from CUP used in major reports

  e.g. by Nordic Nutrition Recommendations,

  Scientific Advisory Committee on Nutrition, UK;

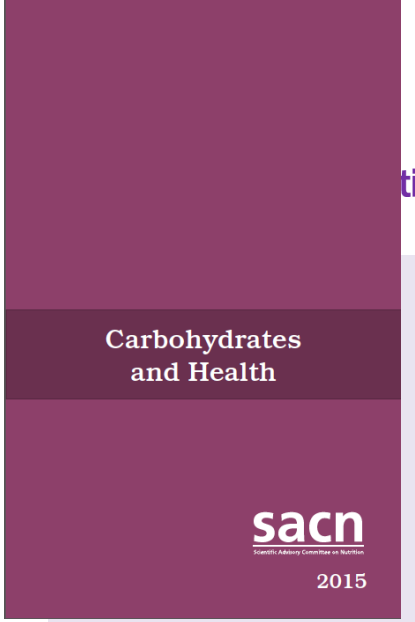
  IARC, Australian Government, US Dietary Guidelines

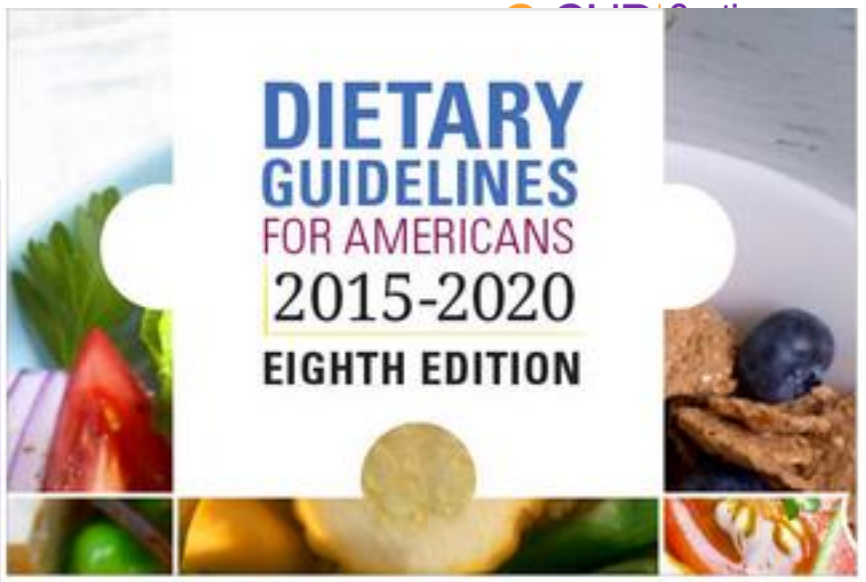
- Evidence that following WCRF Cancer Prevention Recommendations decreases risk of cancer and other diseases

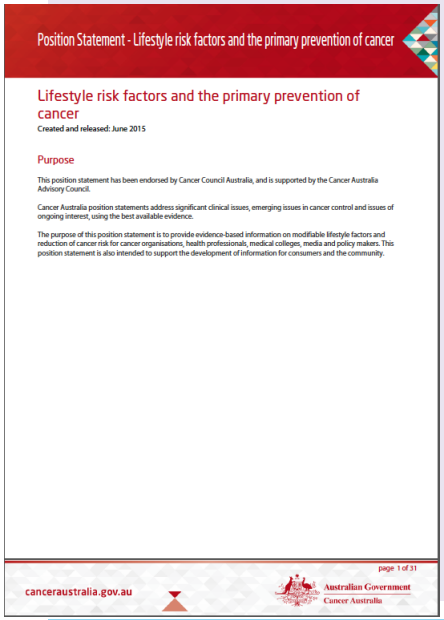
Beyond CUP

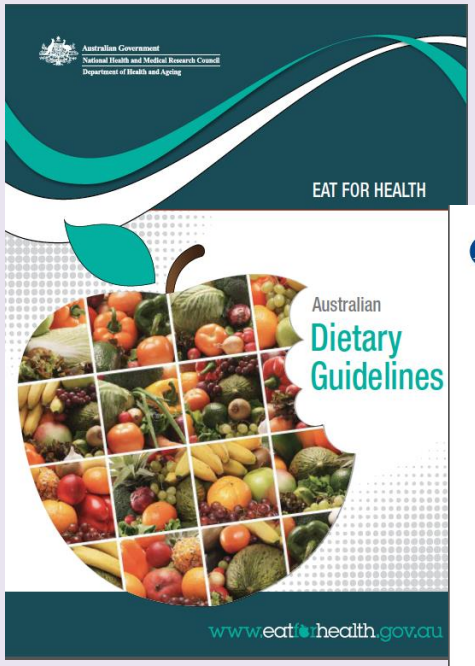
- New methodology - mainstream approach to review mechanistic studies
- Inform direction of future research in area of diet/physical activity/weight and cancer

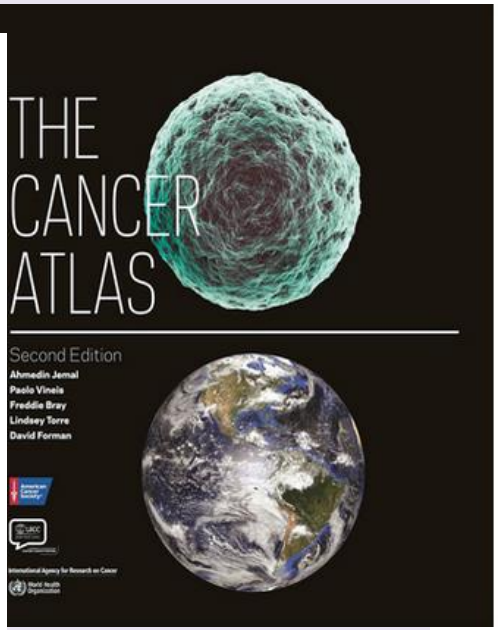
tional











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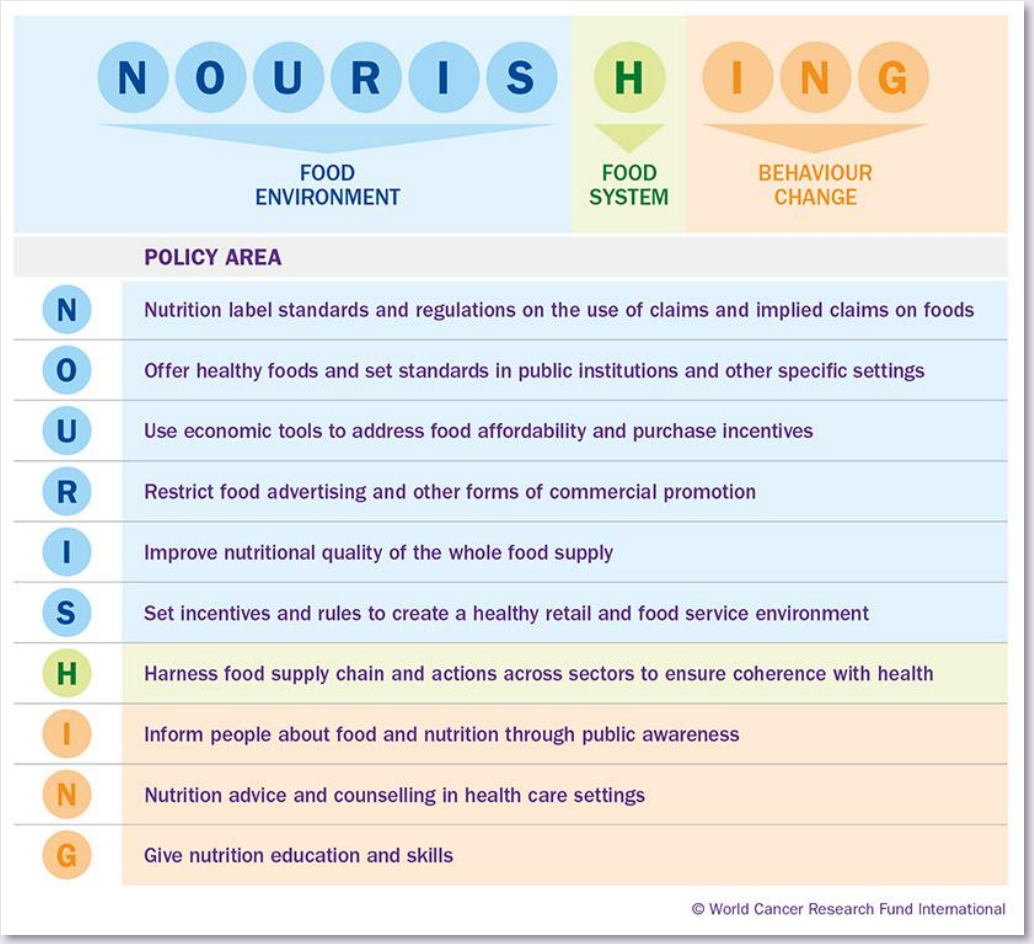
NOURISHING framework



	POLICY AREA
N	Nutrition label standards and regulations on the use of claims and implied claims on foods
O	Offer healthy foods and set standards in public institutions and other specific settings
U	Use economic tools to address food affordability and purchase incentives
R	Restrict food advertising and other forms of commercial promotion
I	Improve nutritional quality of the whole food supply
S	Set incentives and rules to create a healthy retail and food service environment
H	Harness food supply chain and actions across sectors to ensure coherence with health
I	Inform people about food and nutrition through public awareness
N	Nutrition advice and counselling in health care settings
G	Give nutrition education and skills

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NOURISHING framework

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- **Aim**: formalise a comprehensive package of policies to promote healthy diets and reduce obesity and non-communicable diseases (NCDs)

- **For:**
- Policymakers
  - To identify where action is needed to promote healthy diets
  - Select and tailor options suitable to different populations
  - Assess if an approach is sufficiently comprehensive
- Researchers
  - To identify the evidence available for different policies, identify research gaps and as a resource for policy monitoring and evaluation
- Civil society organisations
  - To monitor what governments are doing around the world, benchmark progress and hold them to account

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NOURISHING policy database

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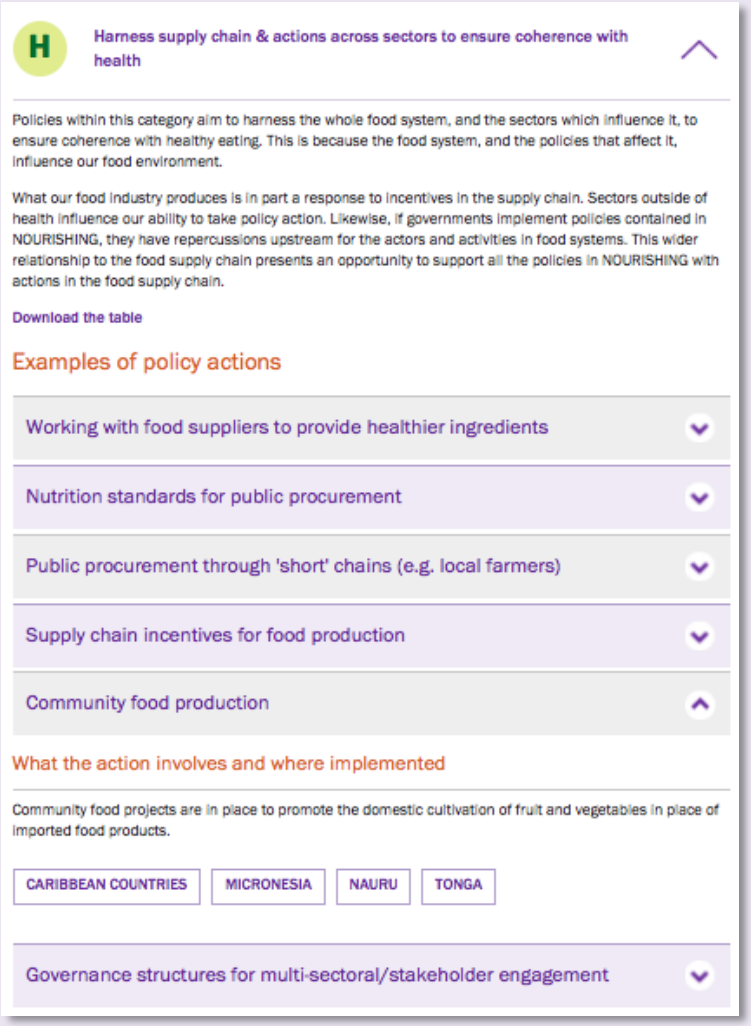

360 implemented policies across 126 countries

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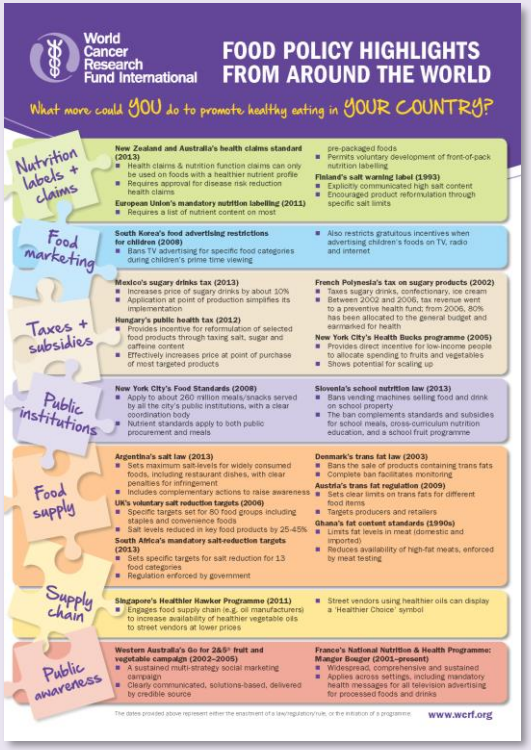
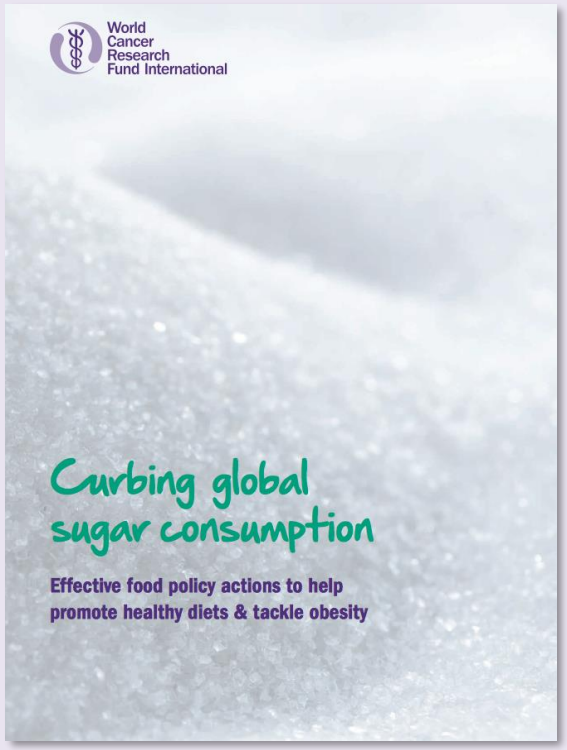
Recent policy briefs



2014



2015

2016

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Continuous Update Project 2017

- **New publications:**

Cancer reports for breast and colorectum

- **Review of cancer prevention recommendations**

Diet, nutrition, physical activity and cancer: a global perspective

- **Systematic review methods for mechanisms**

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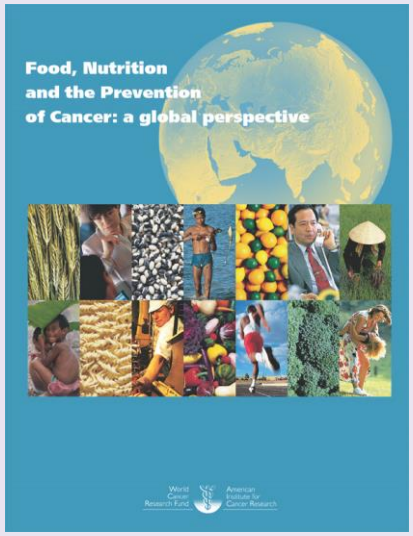
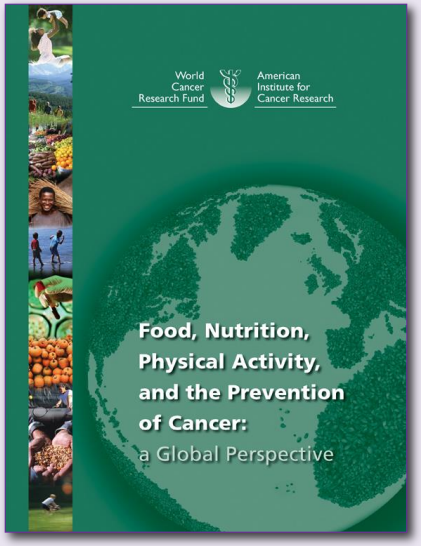
New Expert Report

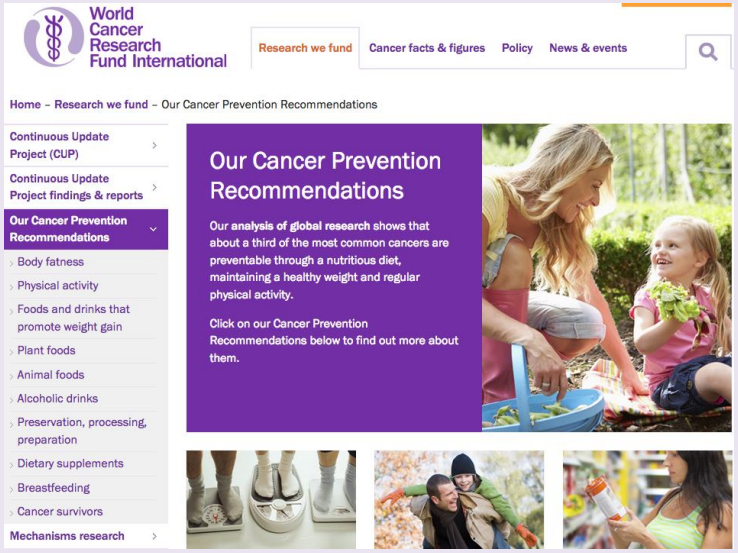
1997



2007



2017



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Contents

- Cancer prevention recommendations
- Evidence by diet, weight, physical activity
- Evidence by cancer (CUP cancer reports)
- Determinants of weight
- Cancer process, methods, background
- New preventability estimates
- Printed summary report focusing on cancer prevention recommendations

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For further information

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