Mashhad University of Medical Sciences

Nutrition in the prevention of cancer

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Learning Objectives

- To understand the ***potential of nutrition*** in cancer prevention;
- To understand ***specific behaviors*** that can modify cancer risk;
- To gather insights into the role of ***gene-diet interaction*** in determining response to dietary components.

Contents

KEY MESSAGES

Key Messages

Cancer is a

preventable

disease;

Key Messages

Environmental factors

play a *prominent role* in

increasing

cancer risk;

Key Messages

Diet

physical activity

and

maintenance of a ***healthy weight***

can **prevent 40% of all cancers**;

Key Messages

Fruit,
vegetables,
and **fibre**

have a **protective effect,**

whereas

high-temperature cooked
red meat
and
processed meat

increase the risk of developing cancer;

Key Messages

There is **no evidence** that

vitamin supplements

help to prevent cancer.

1. INTRODUCTION

1. Introduction

Cancer

Genetic origin

Environmental

Cancer is a disease

largely caused by environmental factors

1. Introduction

Rather than winning the

"war on cancer"

we are facing a

global cancer epidemic

1. Introduction

Cancer death projections updates 2008 (IARC):

Between ***1975*** and ***2000*** cancer cases ***doubled***
Will ***double*** again between ***2000*** and ***2020***
Nearly ***triple*** by ***2030***

In **2010**, **cancer** was due to become the
leading cause of death worldwide

1. Introduction

Almost **two-thirds of all cancers can be prevented** by

Lifestyle modifications

Physical **activity**

Proper **diet**

And maintenance of a **healthy weight**

Public health policies, **government programs** and **research funding**

From **cancer treatment and diagnosis** to

Primary cancer prevention

If we want to ***halt current growing trends***

2. CANCER NUMBERS

2. Cancer Numbers

In **2002**,

more than **10 million** **new cases of cancer** were recorded worldwide,

with nearly **7 million** **cancer deaths**.

These numbers are destined to grow

Projections estimate an almost **tripling** of **new cases** by **2030**,

with approximately **13 to 17 million** **deaths**

2. Cancer Numbers

Such a **dramatic increase** can only be partly attributable to

a ***growing global population***,

an ***increase in life expectancy***

and

progress in diagnosis and screening

2. Cancer Numbers

The rising incidence of cancers

In fact, is documented across

All age categories,

Including **children** and **adolescents**,

*The **fetus** being particularly vulnerable to exogenous factors.*

2. Cancer Numbers

Of **particular concern** is the

Steady raise in **childhood** cancers observed over the

past three decades,

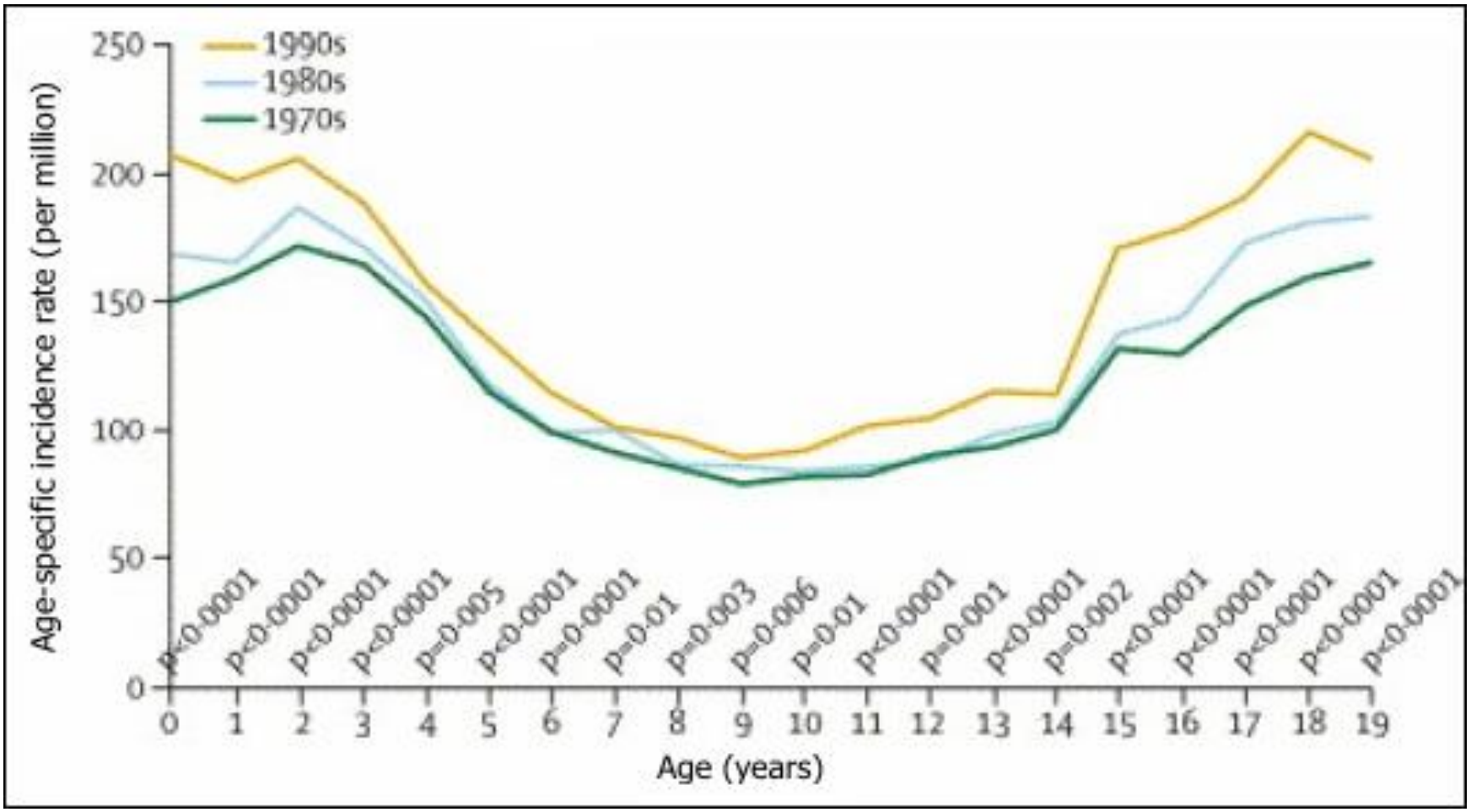
And the ***acceleration of this trend***,

With a documented **1 percent** in **children**

And **1.5 percent** in **adolescents**

Average annual increase

Age-specific incidence rates of cancer in children and adolescents in Europe



Steliarova-Foucher E. et al, Lancet 2004

2. Cancer Numbers

The **economic burden of cancer**

is substantially **increasing**

In the year **2008**,

The **National Institutes of Health**

Estimated **overall annual total costs of cancer** in

2007

In the **U.S.**

At **$219.2 billion**

2. Cancer Numbers

Of note

in **2007**, **six million** **new cases of cancer**

(more than half of the

eleven million cases reported worldwide),

occurred in **low-** and **middle-income** countries

which simply

lack the resources to **sustain the economic costs**
associated with

cancer screening and **treatment**

3. CANCER IS A PREVENTABLE DISEASE

3.1 Cancer and the Environment

3.2 Evidence from Ecological Studies

3.3 When More is Better

3. Cancer is a Preventable Disease

During the **past few decades**,

A **broad range of in-depth studies** have provided

Conclusive evidence on

The **pivotal role** of

Food and **nutrition** (or **specific food constituents**),

In cancer prevention.

3. Cancer is a Preventable Disease

The combined scientific data derived from

Epidemiological,

Interventional and

Experimental studies

Concerning

Food, ***nutrition***, ***overweight***, ***physical activity***

And other ***environmental*** factors,

Clearly suggest that,

At least to a certain degree,

Cancer is a *preventable disease*.

3. Cancer is a Preventable Disease

Worryingly enough, it has been recently pointed out that in spite of a general **scientific consensus on the importance of a healthy diet for cancer prevention**, the ***eating habits of pre-adolescents and adolescents are not aligned with dietary recommendations.***

3. Cancer is a Preventable Disease

These **discrepancies** between

expert recommendations on diet and cancer

and **actual dietary practices** in the **young**

point to the *need for more research* to

better promote the

translation of science into practice

3. Cancer is a Preventable Disease

In **1997** the WCRF/AICR published its **first report** on

Food, Nutrition and the Prevention of Cancer: a Global Perspective, which has become the most authoritative statement on the topic

in **2007** review of the **updated** literature resulted in the publication of a **second WCRF/AICR document** entitled ***Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective***

3. Cancer is a Preventable Disease

The first report:

"cancer is principally caused by **environmental factors**, of which the most important are

tobacco, **diet** and factors **related to diet**,

including **body mass** and **physical activity**, and **exposures in the workplace** and elsewhere".

The same report concluded that

30 to 40 percent of all cancers

are directly linked to **dietary choices**.

3. Cancer is a Preventable Disease

Since the mid **1990s** there has been a dramatic increase in the amount of literature on this subject, concerning particularly the effects of

overweight,

obesity

and

physical activity

3. Cancer is a Preventable Disease

Review of the new data confirmed that

approximately **40% of all cancers** are linked to

poor diet, **physical inactivity**, and **excessive body weight**.

If we apply these percentages to the *more than 12 million* **new cancers** that occurred in **2007** worldwide

we can estimate that *over 4 million people*

could have been **spared the tragedy of cancer**

by the very feasible approach of **eating**, **weight control** and **exercise** outlined in the report recommendations.

3. CANCER IS A PREVENTABLE DISEASE

3.1 Cancer and the Environment

3.2 Evidence from Ecological Studies

3.3 When More is Better

3.1 Cancer and the Environment

For **decades** research has looked into the **genetics of cancer** to find solutions to the cancer riddle.

The discovery of

Oncogenes

tumor suppressor

DNA repair

and ***cancer susceptibility genes***

has led in the past to the conclusion that

cancerogenesis is a purely endogenous genetic process.

3.1 Cancer and the Environment

More recently, however, advances in the field of

Epigenomics

Transcriptomics

proteomics

and ***metabolomics***

have given a wider picture of the ***cancer process***, which is presently considered

the result of a complex interaction between

cells and **environmental** factors.

3. CANCER IS A PREVENTABLE DISEASE

3.1 Cancer and the Environment

3.2 Evidence from Ecological Studies

3.3 When More is Better

3.2 Evidence from Ecological Studies

Ecological studies examine

relationships between **environmental** factors and **disease**

among

populations rather than individuals.

3.2 Evidence from Ecological Studies

The cancer pattern (the distribution of different cancers) varies

between **countries** and **populations**

Some cancers are more prevalent in ***lower income*** countries,

others in ***higher income*** countries.

3.2 Evidence from Ecological Studies

Also, cancer patterns change ***in time within countries*** and populations,

for instance, if countries become **more urbanized** and **industrialized**, or if populations **migrate** to other countries.

highlight the important role of

environmental factors

as cancer risk modifiers.

3.2 Evidence from Ecological Studies

Studies on ***migrant population*** have provided some of the most compelling evidence, suggesting

not only that the

main causes of cancer are environmental,

but that

food, ***nutrition*** and ***maintenance of a healthy weight***

each plays a major role.

3.2 Evidence from Ecological Studies

Assessment of **breast cancer** risk in women who have **migrated** from countries with a low incidence of breast cancer to countries with high breast cancer rates is a typical example of migrant studies.

3.2 Evidence from Ecological Studies

In foreign-born Hispanics who moved to the San Francisco Bay Area, ***breast cancer risk*** was **50% lower** than in U.S.-born Hispanics.

The risk increased with

increasing **duration** of residence in the U.S.

and with **decreasing age at migration**

3.2 Evidence from Ecological Studies

Similarly, **stomach cancer** mortality in migrants from the Former Soviet Union (FSU), **a high-risk area**, to Germany and Israel *remained elevated* after migration but *started to decline* during a study period ranging from **1990 to 2005** in **Germany** and from **1990 to 2003 in Israel**.

3.2 Evidence from Ecological Studies

Converging mortality rates between migrants and the general population in Germany and Israel are such that mortality from stomach cancer among migrants from the FSU is ***expected to reach rates similar to those of the host countries in a few years***

3.2 Evidence from Ecological Studies

More data from recent migrant studies demonstrate that in second-generation immigrants, cancer incidence rates generally become similar to those of the host country.

This was shown in first- and second-generation immigrants to **Denmark**, a country with a **high-incidence** of **testicular cancer**.

3.2 Evidence from Ecological Studies

In first-generation immigrants testicular cancer risk was much lower than that in native-born Danes and reflected risk in the countries of origin, whereas the risk in second-generation immigrants was similar to that in natives of Denmark.

The fact that risk in first-generation immigrants was not modified by age at immigration or duration of stay, argues for a substantial influence of **environmental factors limited to exposure in early life**, most probably in **utero exposure**, in the development of testicular cancer.

3.2 Evidence from Ecological Studies

Ecological and migrant studies consistently indicate that the main determinants of cancer patterns are modifiable, and that ***environmental exposure during prenatal and early life has a fundamental role in cancer induction***. Such conclusions are supported by the results of thousands of epidemiological and experimental studies, thoroughly reviewed in the first and second WCRF/AICR expert report, which have highlighted the pivotal role of patterns of food, nutrition, body composition and physical activity in cancer control. As more is learned about how early life factors relate to childhood, adolescent and adult cancer risk, appropriate dietary interventions can be ***developed and targeted to the short-terms of pregnancy and early postnatal life before trying to alter diets and behaviors over longer periods of time***.

3. CANCER IS A PREVENTABLE DISEASE

3.1 Cancer and the Environment

3.2 Evidence from Ecological Studies

3.3 When More is Better

3.3 When More is Better

The interaction between environmental factors, diet, nutritional status, lifestyle and the incidence of cancer and other chronic diseases is presently being tested in the largest prospective cohort study ever undertaken, the ***European Prospective Investigation of Cancer (EPIC)***, a long-running study of diet and health. Study recruitment was carried out between 1993 and 1999 and follow up planned for at least ten years.

3.3 When More is Better

Dietary information and blood was collected from over half a million **(520,000) individuals living in ten European countries:**

Denmark, France, Germany, Greece, Italy, The Netherlands, Norway, Spain, Sweden and the United Kingdom.

While the trial and its analysis is still ongoing, some of the key results already published show how several environmental factors are seemingly having a pivotal role on cancer incidence.

The **combined impact of four healthy behaviors**:

Not smoking,

Not being physically inactive,

Moderate alcohol intake

And consumption of at ***least five fruit*** and ***vegetable servings***

a day

Predicts a 4-fold difference in

Total mortality in men and women

3.3 When More is Better

The trends reported in the study, while being strongest for **deaths from cardiovascular disease**, were also apparent for **deaths from cancer** and from other causes.

The magnitude of the combined impact resulting from these four behaviors translated into an estimate of being **14 years younger than chronological age**, which was significantly a greater effect than that expected from each individual risk factor, indicating that health behaviors act **synergistically** on pathways implicated in maintenance of proper biological functions.

3.3 When More is Better

On the same lines are the results of a

longitudinal study conducted on elderly European individuals aged **70-90 years**,

which investigated ***single*** and ***combined*** effect of

four factors:

Mediterranean diet,

being physically active,

moderate alcohol use,

and **non-smoking**,

on all-cause and cause-specific mortality.

3.3 When More is Better

During a **10-year follow-up**, individuals with **2, 3 or 4 healthy behaviors** had less than **half** the mortality rate from

all causes

coronary heart disease

cardiovascular diseases

cancer and from other causes

than those with 0 or 1 such behavior.

3.3 When More is Better

For **cancer specific mortality**,

60% of deaths during the **10-year follow-up** period

were associated with

not adhering to this low-risk pattern

The **more healthy behaviors adopted by individuals**, the

lower the risk of cancer-specific mortality

4. RESULTS FROM THE SECOND WCRF/AICR EXPERT REPORT

Major findings of the report:

Dietary fiber from

unrefined cereals, legumes,

vegetables and fruits

probably protects against

colorectal cancer.

Major findings of the report:

mechanisms which may explain:

increasing **fecal weight**

decreasing **transit time**

binding to **carcinogens**

alteration of the **gut environment** through lowering of fecal **pH**

stimulation of bacterial **fermentation**

production of **short chain fatty acids**, particularly **butyrate**,

capable of inducing **apoptosis**

cell cycle arrest

cell differentiation

Major findings of the report:

Although such mechanisms are plausible, the report concluded that the presence of ***confounder variables*** cannot be excluded.

Of note, results of a recent prospective study of **63,550 men and women** recruited in the **EPIC-Oxford study** in the UK in the **1990s**,showed that unlike

total cancer incidence, which is *lower in vegetarians*

compared to non vegetarians,

colorectal cancer incidence is *significantly higher*

in vegetarians compared to meat eaters

Major findings of the report:

There is ample and consistent evidence that

Foods contaminated with

Aflatoxins

Are a cause of liver cancer

Major findings of the report:

Aflatoxins are a type of **mycotoxins** classified as

human carcinogens (group 1) by the IARC

Contamination involves mainly

cereals and **legumes** (especially **peanuts**), followed by

nuts and **seeds**,

and is more frequent in countries with

damp climates and ***poor storage conditions***

Major findings of the report:

Non starchy vegetables and fruits

probably protect against

upper aereodigestive tract

(mouth, pharynx, larynx, oesophagus and stomach)

cancer

Major findings of the report:

While the majority of studies show **decreased risk** of these cancers with **increased intake of fruits and vegetables**, the overall evidence remains **contradictory.**

A possibility is that there ***may be a threshold of fruit and vegetable intake*** below which cancer risk is increased.

Still, **most countries** have adopted national recommendations for consumption of ***five or more servings per day of fruits and vegetables***;

Major findings of the report:

There is a significant

inverse association between

fruit consumption and lung cancer risk in both

smokers and nonsmokers,

while high vegetable intake

significantly decreases lung cancer risk in current smokers

Major findings of the report:

Among individual plant foods, plant food groups and food constituents,

Apples

Pears

citrus fruit

cruciferous vegetables

and **carotenoids** from foods

appear the ***most protective toward lung cancer risk***

Major findings of the report:

The ***possible protective effects***

of **fruit** and **vegetables**

might involve their **high levels of micronutrients**

(including ***antioxidants***),

which can decrease

DNA damage by scavenging for oxygen radicals

Major findings of the report:

Red meat* and *processed meat

(meat preserved by smoking, curing, salting, or by the addition of preservatives)

is a cause of colorectal cancer

Major findings of the report:

Milk* and more significantly *dietary calcium

***(from dairy foods, vegetables, nuts, pulses* and**

fish or meat cooked on the bone)

protects* from *colorectal cancer

Major findings of the report:

Total cheese intake may however

increase **colon cancer risk**,

and high dietary intake of ***calcium*** is a **probable cause** of

prostate cancer

The evidence is consistent with a

dose-response relationship

Major findings of the report:

There is ***limited evidence*** that

diets high in **fats**

may be a cause of

postmenopausal breast cancer

Major findings of the report:

On the other hand growing evidence supports the

protective role of a

high ω-3 to ω-6 fatty acid ratio

, which has been associated with a

reduced risk of cancer, especially **breast cancer**, and

with **improved prognosis**

Major findings of the report:

Excessive

salt and sodium intake

in general can increase the risk of

stomach cancer

Major findings of the report:

There is a strong, significant association between exposure to water contaminated with inorganic arsenic - arising from **agricultural** and **industrial** practices or naturally occurring - and increased lung cancer risk.

Major findings of the report:

Consumption of alcohol, including wine, significantly increases the risk of cancer in the upper aerodigestive tract (oral cavity, pharynx, larynx, oesophagus), the colorectum and the breast.

Major findings of the report:

Regarding supplements, the report confirms that **high dose beta-carotene** supplements **increase lung cancer risk**,

that **calcium** probably **protects** against **colorectal cancer**,

and that **selenium** at specific doses and in selected individuals probably **protects** against **prostate** cancer, and possibly against **lung** and **colorectal** cancer.

Major findings of the report:

Overweight and **obesity** is a **cause of cancer** of the

colorectum,

breast (in post-menopausal women),

endometrium,

oesophagus,

pancreas

and **kidney**

5. FOOD CONTAMINANTS AND FOOD ADDITIVES

5. Food Contaminants and Food Additives

Thousands of chemical substances, some of them with carcinogenic properties, contaminate the food supply.

They include chemicals added to modify

flavour, **colour**, **stability** or **texture**,

residues of **pesticides**,

and **drugs** given to animals.

The majority of these substances has never been tested for carcinogenicity.

5. Food Contaminants and Food Additives

In addition, **chemical contaminants** may be formed during food **preparation** or find their way into foods during industrial **processing** and **packaging**.

Food can also be contaminated by **naturally occurring carcinogens** such as **mycotoxins** from mould growth, and **aflatoxin** is a **definite cause of liver cancer**, as previously reported.

5. Food Contaminants and Food Additives

Among all substances, effects of **acrylamide** recently gained momentum as a potential public health concern.

Acrylamide is a proven **rodent carcinogen** and *probable human carcinogen*. In *Europe* its concentration in ***water*** is strictly regulated to maximum levels of **0.1 microgram per liter.**

5. Food Contaminants and Food Additives

Biochemical analysis showed that during food processing at **temperatures above 120°C**, **free asparagine** and **sugars** react together with the formation of acrylamide.

Acrylamide levels in food vary widely **depending** on the **manufacturer**, the **cooking time**, and the **method** and **temperature** of the cooking process.

6. PROTECTIVE DIETARY COMPONENTS

6. Protective Dietary Components

Phytochemicals confer particular properties to foods, such as taste and color and possess in various degrees

anti-oxidant,

anti-carcinogenic,

anti-inflammatory,

immunomodulant

and **antimicrobial** effects.

6. Protective Dietary Components

According to their **chemical structure** and **functional characteristics** they are grouped in different families which include:

Carotenoids

Isothiocyanates

Flavonoids

Curcuminoids

Carotenoids

This family of compounds comprises the **pro-vitamin A alpha-carotene**, **beta-carotene** and **beta-cryptoxanthin**, as well as **lycopene**, **lutein** and **zeaxanthin**.

Carotenoid-rich foods include **carrots**, **apricots**, **peaches**, **cantaloupe melon**, **sweet potatoes**, **winter squash**, **kale**, **spinach**, **romaine lettuce** and **broccoli**.

Consuming

five or more servings of fruit and vegetable per day

provides approximately

three to six milligrams of beta-carotene.

Carotenoids

Foods containing **carotenoids**

protect against

upper aerodigestive tract cancers

lung and **prostate** cancer

(**lycopene**).

Carotenoids

The protective effects of dietary carotenoids upon lung cancer risk stimulated randomized trials of high dose (20-30 milligrams per day) synthetic beta-carotene for lung cancer prevention in smokers. Results of these trials, reviewed in a recent meta-analysis, revealed however that

high dose synthetic beta-carotene supplementation in current smokers ***increases*** **lung cancer risk** and **lung cancer death**

Isothiocyanates

This class of sulphur-containing phytochemicals occur naturally as glucosinolate conjugates in cruciferous vegetables, which are released through hydrolyses by the enzyme myrosinase after plant cell rupture.

Isothiocyanates are found in cruciferous vegetables such as **broccoli**, **cauliflower**, **kale**, **turnips**, **collards**, **Brussel sprouts**, **cabbage**, **radishes**, and **watercress**, and are responsible for the typical flavours of these vegetables.

Isothiocyanates exert **anti-cancer properties** by inhibiting cell **proliferation** and inducing **apoptosis**; they are also potent inducers of the liver's Phase II enzymes, involved in carcinogen detoxification.

Flavonoids

Flavonoids are polyphenolic compounds ubiquitously found in plants and which are responsible for their **pigmentation**.

These compounds exert many biological effects including **immunomodulatory**, **anti-inflammatory** and **antioxidant** activity.

Flavonoids

Antioxidant activity is greatly enhanced by the presence of vitamin C.

Quercetin is the most abundant dietary flavonol, is a potent antioxidant and also directly inhibits expression of CYP1A1, a cytochrome P450 enzyme involved in toxins metabolism, with resultant decrease in DNA adduct formation. Elevated CYP1A1 activity has been linked to increased lung cancer risk in smokers. Several studies have found an inverse relationship between intake of foods containing quercetin and **lung** cancer risk, depending especially on CYP1A1 genotype (38).

Curcuminoids

Curcuminoids are polyphenolic pigments present in the spice Turmeric derived from the rhizomes of *Curcuma longa*. Curcumin is the principal curcuminoid in turmeric and is a potent **anti-inflammatory** and **chemopreventive** agent. Curcumin inhibits NF-kB -dependent gene transcription, induces apoptosis in a variety of cancer cell lines and inhibits VEGF-mediated angiogenesis in human intestinal endothelial cells.

Curcuminoids

Anti-cancer activity has been demonstrated in several animal models. Robust preclinical data and an excellent safety profile has led curcumin into phase I and II clinical trials to test its potential chemopreventive activity in human colon cancer. **Results are awaiting.**

7. CANCER SURVIVORS

7. Cancer Survivors

Lifestyle interventions are important aspects of survivorship care, as cohort studies have suggested that engagement in

physical **activity**

or adherence to a **healthy diet**

may impact on overall quality of life as well as on disease-specific and overall health outcomes in certain tumour types

8. CONCLUSIONS

8. Conclusions

Panellists of the second expert report have reviewed all available literature on the topic and concluded that about **40% of all cancers are linked to** poor diet**,** physical inactivity **and excessive** body weight**.**

In the previous report, smoking was judged responsible for approximately another **30%** of all cancer deaths

Environmental factors, therefore, are the most important aetiological influences on cancer risk.

The second expert report recommendations

maintaining a body mass index of between

21 and 23

(until now, the standard recommended range has been 18.5 to 24.5);

The second expert report recommendations

exercising moderately;

The second expert report recommendations

limiting consumption of

alcohol,

energy-dense foods

and **refined carbohydrates**;

The second expert report recommendations

Avoiding sugary beverages;

The second expert report recommendations

increasing intake of

vegetables and **fruits**

to at least **five** portions per day;

The second expert report recommendations

Increasing intake of **whole cereals**

(mainly in an unprocessed form) and **legumes**;

The second expert report recommendations

consuming **fast foods** sparingly, if at all;

The second expert report recommendations

limiting intake of salty and sodium-processed foods to less than

5 g of salt or 2 g of sodium per day;

The second expert report recommendations

limiting consumption of

red meats

and **avoiding** processed meats;

The second expert report recommendations

After treatment,

cancer survivors should

follow these recommendations

for cancer prevention.

Many thanks…