World Cancer Research Fund

American Institute for Cancer Research

CUP Continuous Update Project

Analysing research on cancer prevention and survival

Diet, Nutrition, Physical Activity and Cancer: a Global Perspective

A summary of the Third Expert Report

World Cancer Research Fund International

World Cancer Research Fund UK

Wereld Kanker Onderzoek Fonds

World Cancer Research Fund
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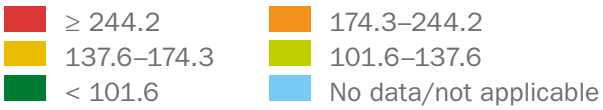
Cover illustration: Estimated incidence (per 100,000 persons per year) of all cancers (excluding non-melanoma skin cancer) in men and women, worldwide, in 2012



Data source: GLOBOCAN 2012
Map production: International Agency for Research on Cancer (http://gco.iarc.fr/today)
World Health Organization

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Preface

The World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) can be credited with great foresight and perspicacity in setting an ambition over 25 years ago to better define the relationship between diet, nutrition and physical activity, and cancer. Against a seemingly impossible challenge, their perseverance to progressively untangle a complex series of inter-relationships has been extraordinary.

Among a number of players seeking to better understand the factors that account for chronic non-communicable diseases, WCRF and AICR have identified a special need within a unique space. This report marks the most recent contribution in this remarkable journey and sets the stage for a further agenda that likely will see substantial impact on the prevention of cancer, which is set to become the most common affliction across the globe.

The First Expert Report, published in 1997, was informed by a body of evidence that was based very much upon anecdotal and ecological experience. It was generally considered that this evidence was not strong and for many not sufficiently persuasive to command wide agreement. It did however help identify a need and set the task of collating and interpreting a literature that at best could be considered contentious.

The difficulties were clear in that untangling any relationship was a far from simple task, given the multiple cancer sites and many varied exposures that of themselves were poorly characterised. The evidence tended to be fragmentary and difficult to interpret with confidence, given the long period of time over which the exposure had to operate before the evident appearance of a disease. Drawing a secure relationship between the two was inherently testing.

This early experience was drawn on directly in preparation for the second report in 2007. For this, major emphasis was placed upon the need to organise the evidence using a structured approach and for this evidence to be systematically interrogated, thereby giving greater security to the conclusions and recommendations. Further, the participation internationally of a wide scientific community knowledgeable in the range of considerations of relevance ensured that the different perspectives and emphases could be embraced to resolve major differences of opinion. Thus, the interpretation was more secure than had been achieved previously and commanded wide respect.

The 2007 Second Expert Report set a landmark and standard. Most importantly it clarified the value of a structured process for the collection and review of the available evidence thereby facilitating our ability to arrive at secure judgements with confidence. Further, it defined with greater clarity the nature and extent of what was known with confidence, and what was not known but of seeming importance. Of itself, this helped to direct attention to focus on the nature of the research that needed to be done. This has acted as a stimulus to many others who by organising their work and research within a common framework enable direct comparison, add value to each other and ensure that the whole is greater than the sum of the parts.

The creation of and support for the Continuous Update Project (CUP) during the last ten years marks a further remarkable commitment to a reliable process for the capturing of all relevant new evidence and enabling its up-to-date interrogation in 'real time'. Because the CUP has embedded the value of a structured and systematic approach, it has continued to enable scientists from disparate backgrounds to share knowledge and reach agreed interpretation. The increased number of cohort studies and the better quality of evidence has informed the reflections of the CUP. The recommendations made today are very securely based.

This has considerable value in presenting to policymakers and the wider public a consistent message of what can be done with confidence to prevent cancer. It also raises the challenge of how to better understand what people who have already experienced cancer might do to improve their life. There has been a progressive need to identify the factors that account for variability in risk and the response to treatment. Out of this concern for people living with cancer has emerged the considerable opportunities for deeper understanding offered by studies with a focus on secondary prevention and a clearer understanding of the underlying biological mechanisms.

The relatively simple statements that emerge as recommendations represent a massive commitment of effort from many people within a highly skilled organisation. I would specifically like to show appreciation to those who have given their time readily to act as peer reviewers or have participated in the Expert Panel. The way the judgements have been made, through a shared interactive process in which depth of experience has been used to assess nuanced considerations, has been exceptional.

The Panel's task was made possible only because of the outstanding quality of the material that they were given to consider. This was completely dependent upon the quality of the CUP team at Imperial College London, and the management of this by the scientific Secretariat at WCRF and AICR. The ongoing infrastructural support from WCRF and AICR, which allowed the space and time for careful, considered reflection in a conducive environment, is a valued and remarkable commitment from a charity.

Together this community of people have given their time and shared effort to arrive at a series of recommendations which we believe to be extremely robust and of relevance across the globe. We anticipate that the recommendations will inform policy, advice and practice. Further, they help set the stage for the next generation of enquiry in which a deeper understanding of mechanisms, and experience from better structured approaches to nutrition care in people with cancer, will enable ever greater ability to prevent and treat the disorder. Thereby, this will justify the trust placed in science from the many who in one way or another have supported the work of WCRF and AICR.

All who have enabled and participated in this process deserve our sincere and heartfelt thanks. The work has been carried out with the good grace, strong commitment, and endless good humour and persistence necessary for completing a difficult and complex task. The reward for this effort is in the knowledge that the current recommendations, if followed, will ensure less risk of cancer and better health for many.

Alan Jackson
CUP Panel Chair

Contents

Key

References to the different parts of the full Third Expert Report, available online at dietandcancerreport.org, are highlighted in purple.

References to other sections in this Summary are highlighted in **bold**.

Introduction

The Third Expert Report

The Third Expert Report, *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective*, from World Cancer Research Fund and American Institute for Cancer Research (see **Box 1**) brings together the very latest research, findings and Cancer Prevention Recommendations from the Continuous Update Project (CUP) – see **Box 2**.

The Third Expert Report builds on the groundbreaking achievements of the First and Second Expert Reports, published in 1997 and 2007 respectively. Like its predecessors, the Third Expert Report provides a comprehensive analysis, using the most meticulous of methods, of the worldwide body of evidence on preventing and surviving cancer through diet, nutrition and physical activity, and presents the latest global Cancer Prevention Recommendations.

The Third Expert Report, including this Summary, will help people who are keen to know how to prevent cancer and improve survival after a diagnosis. It may be particularly useful to:

Researchers
...when studying specific cancers and for guiding plans for future studies.

Medical and health professionals
...by providing reliable, up-to-date recommendations on preventing and surviving cancer to share with patients.

Policymakers
...when setting public health goals and implementing policies that prioritise cancer prevention and help people to follow the Recommendations.

Civil society organisations, including cancer organisations
...when benchmarking progress and holding governments to account.

The media
...by providing authoritative and trusted information on cancer prevention and a source of comment.

People looking to reduce their risk of cancer or live well after a diagnosis
...the Recommendations together constitute a blueprint for reducing cancer risk through changing dietary patterns, reducing alcohol consumption, increasing physical activity, and achieving and maintaining a healthy body weight – including after a diagnosis of cancer.

The entire contents of the Third Expert Report, including this Summary, are freely available online at dietandcancerreport.org. For an outline of the contents, including how this Summary and the online full report relate to each other, please see **Table 1** (pages 10 to 11). This Summary has been produced to provide an overview of the full online report.

Newly published studies will continue to be added to the CUP evidence database and reviewed as part of the ongoing CUP. In between the Expert Reports, regular reports of the evidence and the CUP Expert Panel's conclusions are published. The Cancer Prevention Recommendations are reviewed and updated at regular intervals, based on the latest evidence.

Box 1: World Cancer Research Fund and American Institute for Cancer Research (WCRF/AICR)

World Cancer Research Fund | American Institute for Cancer Research

What we do

We investigate the causes of cancer and help people to understand what they can do to prevent it as well as improve survival and quality of life after a cancer diagnosis.

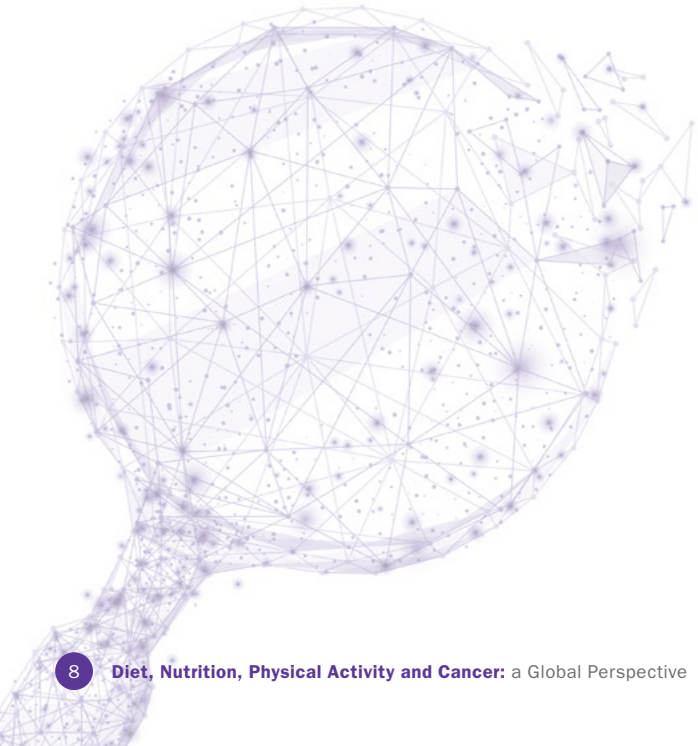
How we do this

We fund scientific research into the links between cancer and lifestyle, particularly diet, nutrition and physical activity.

We analyse all the research in this area from around the world to ensure our messages are current and based on the most accurate evidence.

We give people practical, easy-to-understand advice about how to reduce their risk of cancer.

We promote collaboration between the nutrition and cancer research communities, and work with governments and decision-makers to influence policy.



Box 2: The Continuous Update Project (CUP)

The Continuous Update Project (CUP) is a rigorous, systematic and ongoing programme to gather, present, analyse and judge the global research on how diet, nutrition and physical activity affect cancer risk and survival, and to make Cancer Prevention Recommendations.

Among experts worldwide, the CUP is a trusted, authoritative scientific resource which underpins current dietary guidelines and helps inform policy on cancer prevention and survival.

Scientific research from around the world is continually added to the CUP's unique database, which is held and systematically reviewed by a team of scientists at Imperial College London. This invaluable database is available to researchers on request.

An independent multi-disciplinary panel of experts, the CUP Panel, carries out ongoing evaluations of this evidence and uses its findings to update the Cancer Prevention Recommendations (see **Section 5: Recommendations and public health and policy implications** in this Summary).

Through this process, the CUP ensures that everyone, including scientists, policymakers, health professionals and members of the public, has access to the most up-to-date information on how to reduce the risk of developing cancer. The CUP also helps to identify priority areas for future research.

The CUP is led and managed by World Cancer Research Fund International in partnership with the American Institute for Cancer Research, on behalf of World Cancer Research Fund UK, Wereld Kanker Onderzoek Fonds and World Cancer Research Fund HK.

For more information on the robust approach taken in the CUP, see **Section 2: Judging the evidence** in this Summary.

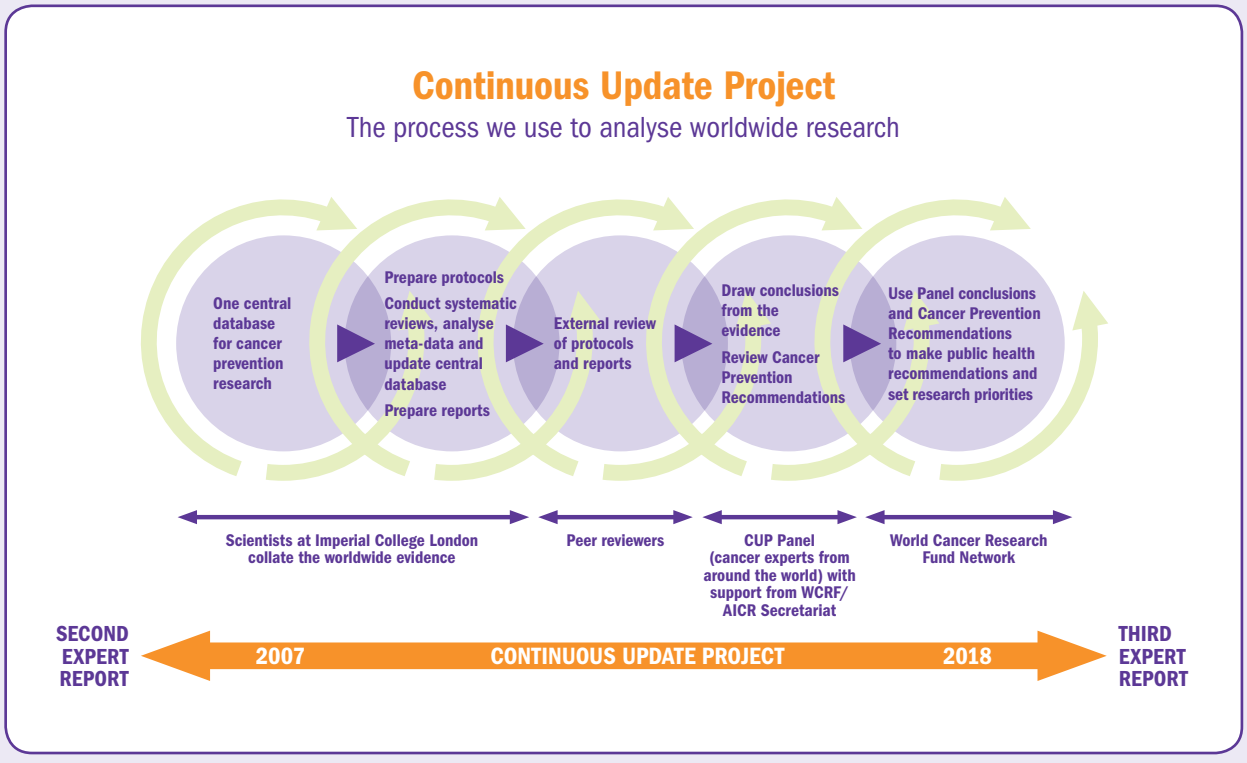


Table 1: Contents of the Third Expert Report and this Summary

The full Third Expert Report, *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective*, is available online at dietandcancerreport.org **It comprises the components listed below:**	**Abbreviated information from different parts of the Third Expert Report is available in this Summary as listed below:**
A summary of the Third Expert Report Overview of the whole report, with a particular focus on the Cancer Prevention Recommendations and on public health and policy implications. See right column.	This publication is the Summary of the Third Expert Report. The Summary is available online at dietandcancerreport.org and can also be ordered in print.
Cancer trends Cancer statistics (available online only).	Not included in this Summary.
The cancer process Summarises the wealth of evidence on how diet, nutrition and physical activity can influence the biological processes that underpin the development and progression of cancer.	**Section 1:** Diet, nutrition, physical activity and the cancer process
Judging the evidence Outlines the rationale and methodology of the CUP, describing the rigorous scientific processes involved in gathering, presenting, assessing and judging evidence.	**Section 2:** Judging the evidence
Exposures sections ***Collating evidence and judgements by exposure*** Each of the 10 exposure sections covers definitions and background information, issues relating to interpretation of the evidence, the evidence itself (from epidemiological studies featured in CUP systematic literature reviews and from research into biological mechanisms) and judgements on the evidence. • **Wholegrains, vegetables and fruit and the risk of cancer** • **Meat, fish and dairy products and the risk of cancer** • **Preservation and processing of foods and the risk of cancer** • **Non-alcoholic drinks and the risk of cancer** • **Alcoholic drinks and the risk of cancer** • **Other dietary exposures and the risk of cancer** • **Physical activity and the risk of cancer** • **Body fatness and weight gain and the risk of cancer** • **Height and birthweight and the risk of cancer** • **Lactation and the risk of cancer**	**Section 3:** The evidence for cancer risk: a summary matrix

The full Third Expert Report, *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective*, is available online at dietandcancerreport.org **It comprises the components listed below:**	**Abbreviated information from different parts of the Third Expert Report is available in this Summary as listed below:**
CUP cancer reports and systematic literature reviews (SLRs) ***Collating evidence and judgements by cancer*** CUP cancer reports, which summarise the CUP systematic literature reviews, focus on a particular cancer site, covering trends in incidence and survival, pathogenesis, other established causes, methodology, issues relating to interpretation of the evidence, the evidence itself (from epidemiological studies featured in CUP systematic literature reviews and from research into biological mechanisms) and judgements on the evidence. Diet, nutrition, physical activity and: • **cancers of the mouth, pharynx and larynx** • **nasopharyngeal cancer**[1] • **oesophageal cancer** • **lung cancer** • **stomach cancer** • **pancreatic cancer** • **gallbladder cancer** • **liver cancer** • **colorectal cancer** • **breast cancer** • **ovarian cancer** • **endometrial cancer** • **cervical cancer**[2] • **prostate cancer** • **kidney cancer** • **bladder cancer** • **skin cancer**[1] • **breast cancer survivors**	**Section 3:** The evidence for cancer risk: a summary matrix
Diet, nutrition and physical activity: Energy balance and body fatness[1] Presents information, evidence and judgements on exposures that increase or decrease the risk of weight gain, overweight and obesity.	**Section 3:** The evidence for cancer risk: a summary matrix
Survivors of breast and other cancers Presents information on current knowledge of the importance of diet, nutrition and physical activity for cancer survivors, with a particular emphasis on breast cancer. Also includes current advice and research priorities.	**Section 4:** Survivors of breast and other cancers
Recommendations and public health and policy implications Presents the latest Cancer Prevention Recommendations, with information on the reasons behind each Recommendation. Also includes other findings of the CUP relating to regional and special circumstances, as well as public health and policy implications, along with a new policy framework.	**Section 5:** Recommendations and public health and policy implications
Changes since the 2007 Second Expert Report Important shifts in emphasis since the 2007 Second Expert Report (webpage only).	**Section 6:** Changes since the 2007 Second Expert Report
Future research directions Outlines areas where further research is needed.	**Section 7:** Future research directions

[1] Systematic literature review available now; report not yet published.
[2] Systematic literature review available now; no report being published.

The Recommendations for Cancer Prevention

The Recommendations for Cancer Prevention featured in the Recommendations and public health and policy implications[1] part of the Third Expert Report and in **Section 5** of this Summary are based on the findings of the CUP – a rigorous systematic review of the evidence relating diet, nutrition and physical activity to the incidence of cancer, and outcomes after a diagnosis, as well as an expert review of biological pathways (mechanisms) that could plausibly explain links between exposures and cancer.

The Recommendations take the form of a series of general statements that constitute a comprehensive package of behaviours that, when taken together, promote a healthy pattern of diet and physical activity to reduce cancer risk, to be used by individuals, health professionals, communities and policymakers, as well as the media.

A significant body of evidence (from large population studies) has accumulated since the 2007 Second Expert Report showing that following a dietary pattern close to the 2007 WCRF Cancer Prevention Recommendations reduces the risk of new cancer cases, dying from cancer and dying from all causes [1–3]. These findings demonstrate that the Recommendations work in real-life settings.

Regional and special circumstances

Some findings of the CUP are not suitable for inclusion in the global Recommendations even though evidence is judged to be strong. For example, the evidence may relate to foods or drinks that are relevant only in discrete geographical locations. These findings are presented in **Section 5.2: Regional and special circumstances**. Where appropriate, locally applicable actions are recommended.

Acknowledging the 'causes of the causes' of disease

The goal of the Recommendations is to help people make healthy choices in their daily lives to reduce the risk of cancer and other non-communicable diseases (NCDs) and to be beneficial for cancer survivors.

However, simply informing people of lifestyle factors that cause, or protect against, cancer and making recommendations about healthy behaviours are by themselves insufficient to bring about substantial, sustained changes in behaviour.

Although people's choices are influenced by their knowledge, attitudes and beliefs, these are poor predictors of behaviour. Much behaviour is not the result of active choice but is instead a passive reflection of social norms and wider upstream factors (the 'causes of the causes' of disease). These may be social or economic, or relate to the physical or other environment, and may operate at local, national or global levels.

[1] The Recommendations and public health and policy implications part of the Third Expert Report is available online at wcrf.org/cancer-prevention-recommendations

The importance of public health policy

Governments have a prime responsibility, in protecting the health of their citizens, to create environments that are conducive to health.

The effectiveness of efforts to change diet and physical activity depends substantially on policies that influence the upstream factors and social norms that are the main determinants of people's behaviour. The prevention of cancer depends on creating an environment that encourages lifelong healthy eating and a physically active lifestyle. Public health policies that prioritise prevention, in the form of laws, regulations and guidelines, are critical (see **Section 5.3. Public health and policy implications** in this Summary).

The rising burden of cancer – a global issue

Cancer causes one in eight deaths worldwide [4] and has overtaken cardiovascular disease (CVD) as the leading cause of death in many parts of the world [5, 6]. The global cancer burden is expected to increase to 21.7 million new cases and 13 million deaths by 2030, mainly owing to an ageing population [4]. Incidence rates of cancer vary widely by country, with total cancer rates highest in high-income countries [7].

More people are living with and surviving cancer than ever before, at least in part because of earlier detection and the increasing success rates of treatment for several cancers [8]. Globally, in 2012, an estimated 32.6 million people were living with cancer [9].

The overall economic cost of cancer is astonishing: globally, the total cost of cancer in 2030, including direct medical costs, non-medical costs and income losses, is projected to be US$458 billion [10]. As well as being expensive, treatment of cancer is not always successful and many treatment options are unavailable in low- and middle-income countries.

The economic costs of cancer, as well as the financial burden of treating other NCDs, pose a significant challenge to patients, families, communities and governments around the world, especially in low- and middle-income countries facing multiple burdens of disease [11].

Many cases of cancer can be prevented

Cancer can affect anyone, but some people are at higher risk than others. Although some risk factors, such as inherited mutations, are fixed, a range of modifiable lifestyle and environmental factors can have a strong influence on cancer risk, meaning many cases of cancer are preventable. Between 30 and 50 per cent of all cancer cases are estimated to be preventable through healthy lifestyles and avoiding exposure to occupational carcinogens, environmental pollution and certain long-term infections [12].

Avoiding tobacco in any form, together with appropriate diet, nutrition and physical activity, and maintaining a healthy weight, have the potential over time to reduce much of the global burden of cancer. However, with current trends towards decreased physical activity and increased body fatness, the global burden of cancer can be expected to continue to rise until these issues are addressed, especially given projections of an ageing global population. If current trends continue, overweight and obesity are likely to overtake smoking as the number one risk factor for cancer.

For information on how cancer develops, and the influence of diet, nutrition and physical activity, see **Section 1: Diet, nutrition, physical activity and the cancer process** in this Summary.

Wider benefits of cancer prevention: non-communicable diseases and the environment

Trends in cancer rates are part of a broader global phenomenon of increases in NCDs, including cancer, diabetes and chronic respiratory disease and, at least in low- and middle-income countries, CVDs. Different NCDs share common underlying risk factors including diet, overweight and obesity, physical inactivity, alcohol consumption, tobacco use and certain long-term infections (for example, *Helicobacter pylori*). Therefore, approaches to preventing cancer can provide benefits across a range of NCDs.

Moreover, it is increasingly recognised that policy actions conducive to health are consonant with those needed to create a sustainable ecological environment.

Prioritising prevention

The case for prioritising the prevention of cancer is strong: cancer can take a heavy personal toll on those affected, and the global burden of cancer is high and rising, yet many cases of cancer are preventable. What is more, preventing cancer has additional benefits both for other common NCDs and even for the environment.

Prevention of additional cancers and other NCDs remains important after a diagnosis of cancer, hence the Recommendation for cancer survivors – people who have been diagnosed with cancer, including those who have recovered from the disease. (See **Section 4: Survivors of breast and other cancers** and **Section 5.1: Recommendations for Cancer Prevention** in this Summary.)

By providing a comprehensive analysis of the worldwide body of evidence on preventing and surviving cancer through diet, nutrition and physical activity, and presenting the latest global Cancer Prevention Recommendations, the Third Expert Report (including this Summary) ensures that governments, civil society and individuals are equipped with the knowledge needed to prioritise cancer prevention and reduce the number of deaths from preventable cancers.

Diet, nutrition, physical activity and the cancer process

1

For further information, see the more detailed **The cancer process** part of the Third Expert Report available online at **wcrf.org/cancer-process**

1.1 What is cancer and how does it develop?

This section summarises the wealth of evidence on how diet, nutrition and physical activity (see **Box 3**) can influence the biological processes that underpin the development and progression of cancer. Some of the more technical terms that are not explained here are included in the **Glossary**.

To help explain what cancer is, how it develops, and how nutrition and physical activity influence this, some key concepts are outlined in **Sections 1.1.1** to **1.1.6**.

1.1.1 Cancer develops from rogue cells, with genetic changes, that acquire capabilities known as the 'hallmarks of cancer'

There are several hundred types of cancer, arising from different tissues. Even tumours arising from the same tissue are increasingly recognised as comprising several different subtypes. What characterises cancer is a shared constellation of abnormal cell behaviours, such as rapid cell division and invasion of surrounding tissue, which are linked to changes in DNA.

Cancer develops when the normal processes that control cell behaviour fail and a rogue cell becomes the progenitor of a group of cells that share its abnormal behaviours or capabilities. This generally results from accumulation of genetic damage in cells over time (see **Box 4**). The cancer cell is a critical part of a tumour but only one of several important types of cell that create the tumour microenvironment (see **Box 5**).

Box 3: Diet, nutrition, physical activity and body fatness

Nutrition is the set of integrated processes by which cells, tissues, organs and indeed a whole organism acquire the energy and nutrients needed to function normally and have a normal structure. Nutrition is important throughout life, allowing an organism to grow, develop and function according to the template defined by the genetic code in the organism's DNA.

Ultimately, all the energy and nutrients needed for the life-sustaining biochemical reactions that take place in an organism – for metabolism – come from the diet. Some, known as essential nutrients, must be consumed ready-made; the body can synthesise others from various components of the diet.

The diet also contains many substances that are not nutrients (not necessary for metabolism) but can nevertheless influence metabolic processes. These include common chemicals such as phytochemicals, dietary fibre and caffeine, as well as some harmful substances such as arsenic.

Physical activity is any movement using skeletal muscle. It is more than just exercise; it also includes everyday activities such as standing, walking, domestic work and even fidgeting. Appropriate physical activity creates a metabolic environment in the body that reduces susceptibility to some cancers.

The amount and type of physical activity can influence the body's overall metabolic state, as well as total requirements for energy, which in turn can impact on the amount of food (and nutrients) that can be consumed without storing excess energy as fat. Excess energy intake that is not balanced by physical activity leads to positive energy balance and ultimately weight gain and higher body fatness. When we talk about nutrition in this report this includes body composition which encompasses body fatness.

Box 4: Genetic damage and cancer

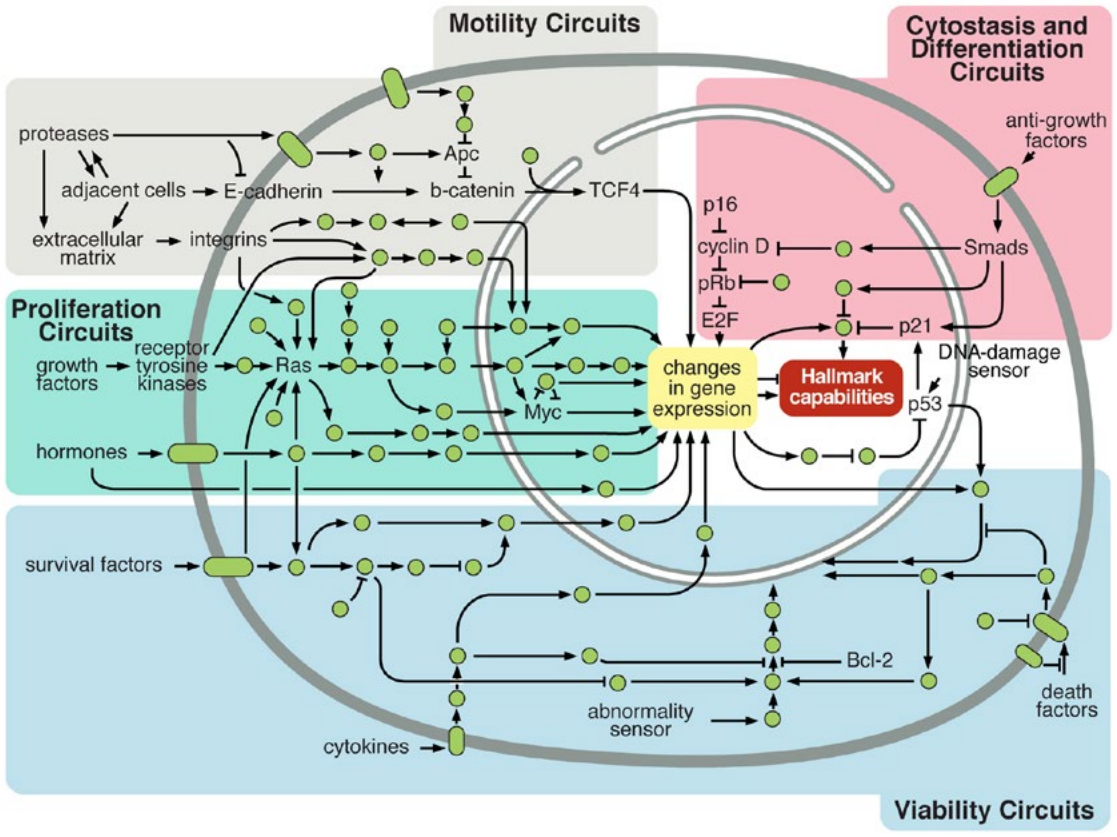
The rogue capabilities of cancer cells generally result from the accumulation of genetic damage – to cells' DNA – over time. This damage tends to involve multiple mutations and epigenetic changes.

Mutations are permanent changes to the DNA sequence, which are inherited by daughter cells when cells divide. Epigenetic changes affect the structure of DNA in other ways (for example, extra methyl groups may be added). These changes, while reversible, can still be passed on when cells divide.

Mutations can have potentially beneficial effects, which underpins the possibility of evolution by natural selection. Some are neutral. Others, like those linked to cancer, are harmful. A mutation may lead to the production of a protein that functions abnormally, or not at all, or to changes in the amount of protein that is produced – including the complete failure of a gene to produce a protein.

Normal cells use epigenetic modifications to regulate gene expression – to control which genes are turned on and off. Patterns of gene expression are crucial to determining the structure of all cells, and how they behave. Control over the pattern of gene expression enables the capabilities of cells to change over time during early development and allows cells to specialise. Although all healthy cells within an organism carry the same genetic code in their DNA, specialised cells have a unique appearance and set of capabilities because they have a particular set of functioning genes, controlled by epigenetic influences.

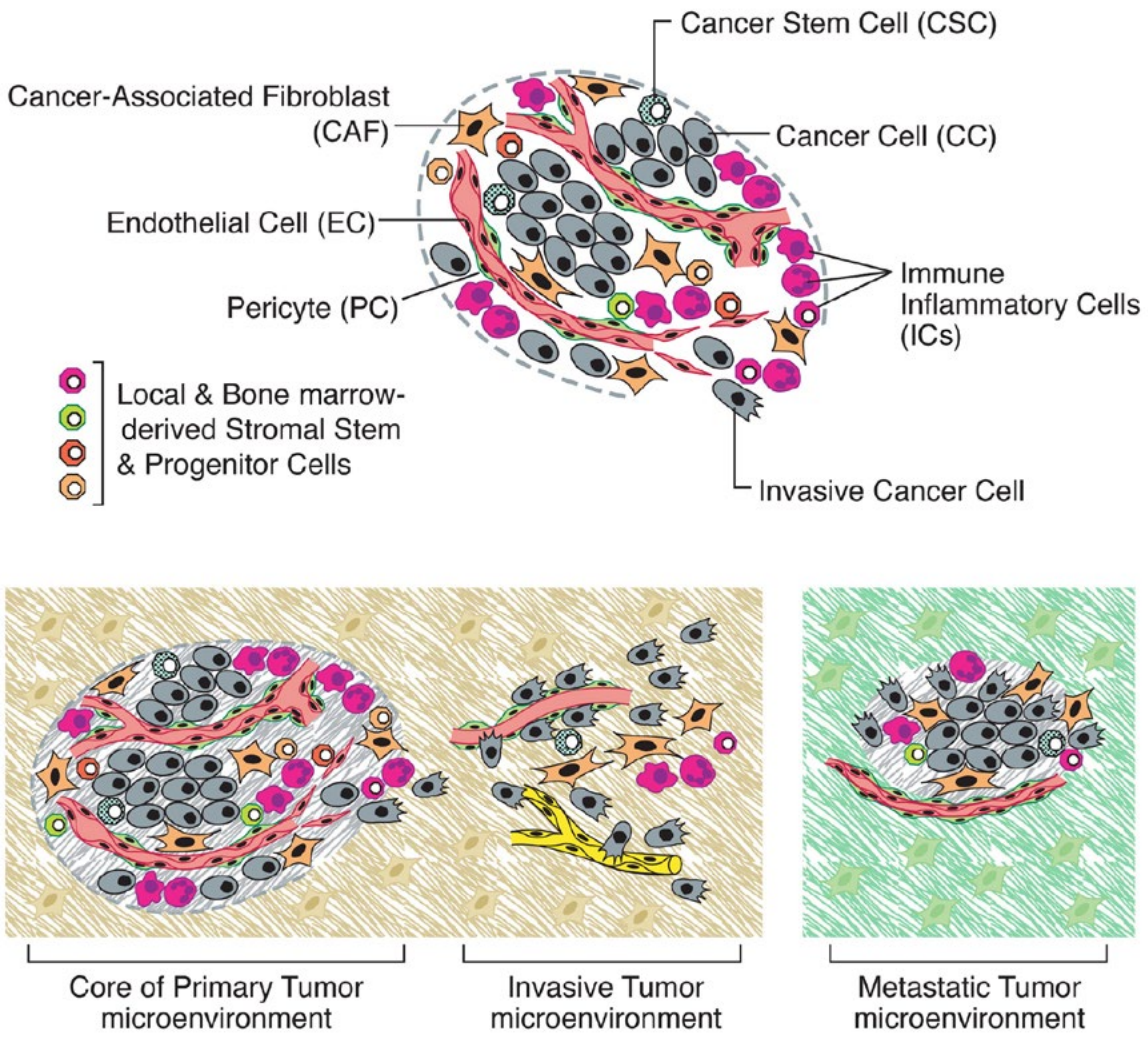
Both the genetic and epigenetic changes that cancer cells accumulate can alter gene expression (see below) in ways that enable the cells to acquire the capabilities known as the hallmarks of cancer.



From: Cell 144, Hanahan D and Weinberg RA, Hallmarks of cancer: the next generation, 646–74, Copyright (2011), with permission from Elsevier.

Please note: this figure updated from what may appear in some printed versions

Box 5: Cells of the tumour microenvironment



Most solid tumours contain a range of distinct cell types and subtypes that collectively enable tumour growth and progression [13].

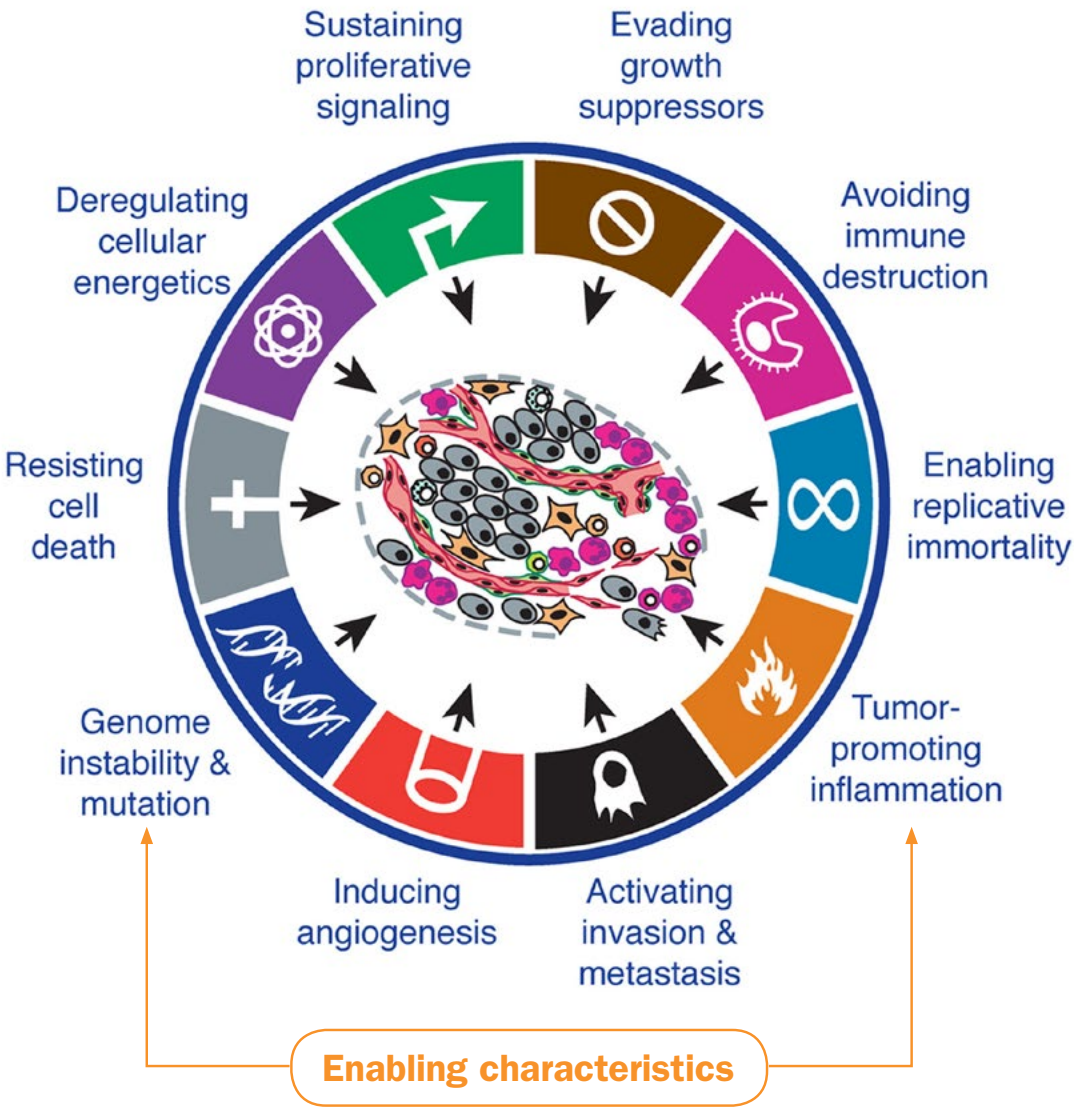
The abundance, spatial organisation and functional characteristics of these multiple cell types, and the make-up of the extracellular matrix, change during progression to create a succession of different tumour microenvironments. Thus, the core of the primary tumour microenvironment differs from microenvironments seen in tumours that are invading normal tissue and in metastatic tumours that are colonising distant tissues. The premalignant stages in tumorigenesis (not shown in the figure) also have distinctive microenvironments.

The normal cells that surround the primary and metastatic tumour sites probably also affect the character of the various tumour microenvironments.

Although a bewildering variety of possible genetic changes can combine to cause cancer, the range of abnormal capabilities that cancer cells share is much narrower. These capabilities are known as the 'hallmarks of cancer' (see **Figures 1** and **2**).

Sometimes one or more of the genetic factors that contributes to the development of cancer is inherited. Such familial cancers are uncommon (playing a role in 5 to 10 per cent of all cancers) [14], but it is important to identify them so that personalised preventive strategies can be offered to carriers and their families.

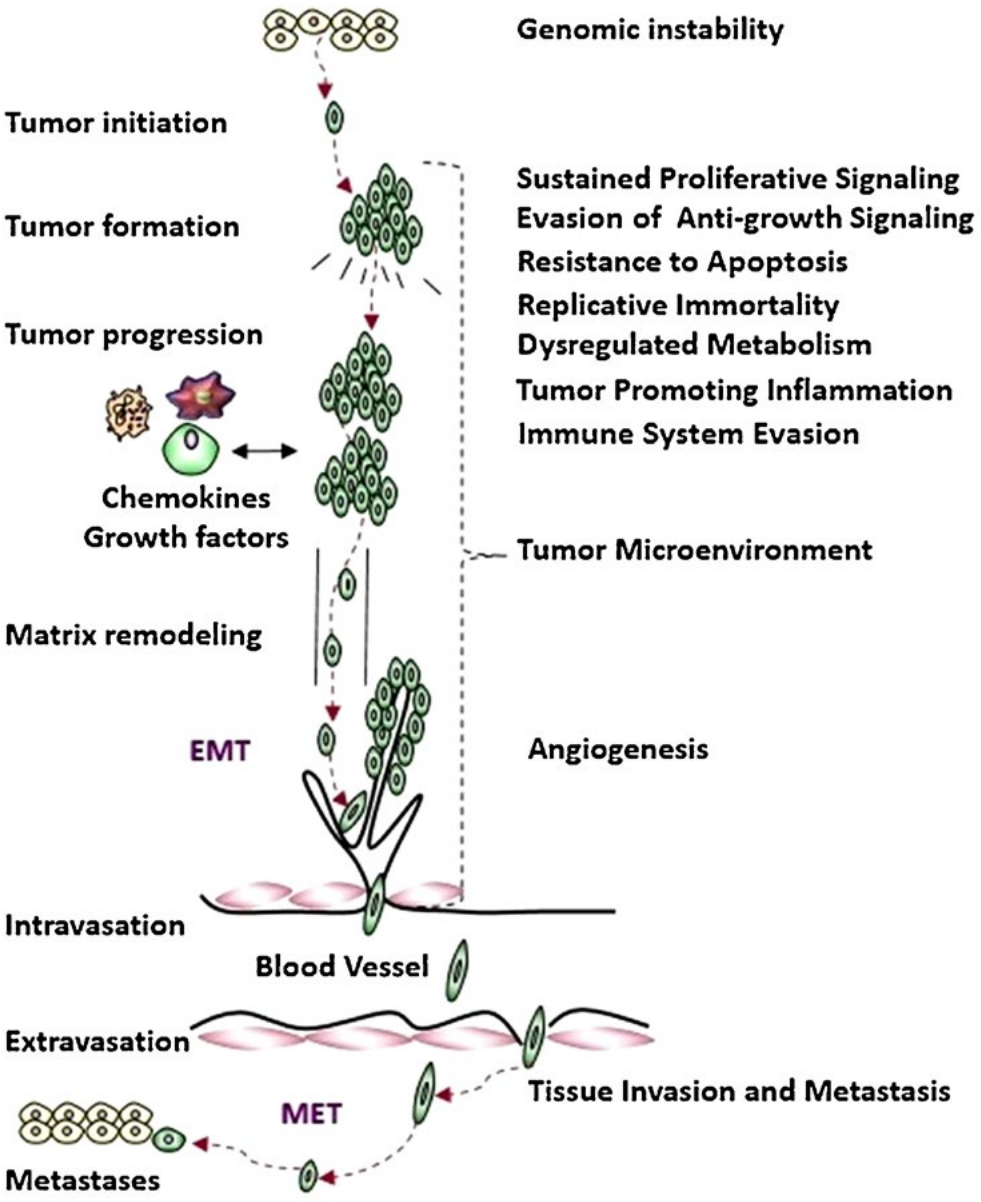
Figure 1: Hallmarks of cancer and two enabling characteristics



Adapted from: Cell 144, Hanahan D and Weinberg RA, Hallmarks of cancer: the next generation, 646–74, Copyright (2011), with permission from Elsevier.

Despite the multitude of pathways through which genetic damage can lead to the development of cancer, almost all solid tumours can be characterised by a relatively small number of phenotypic functional abnormalities. These eight hallmarks of cancer are facilitated by two enabling characteristics, genome instability and mutation, and tumour-promoting inflammation.

Figure 2: Stages of cancer development and the hallmarks of cancer



From: Block KI, Gyllenhaal C, Lowe L, *et al*. Designing a broad-spectrum integrative approach for cancer prevention and treatment. *Semin Cancer Biol* 2015; 35 Suppl: S276-s304. Licenced under CC BY 4.0.

The hallmarks of cancer represented on the right are functional abnormalities characteristic of cancer cells, which can be related to the pathophysiological stages of cancer development, represented on the left.

1.1.2 The rogue capabilities of cancer involve dysregulated activities of normal cells

The rogue capabilities of cancer cells, which can be harmful to an organism, are not all unique to cancer. They are actually beneficial to some normal cells at certain times.

As an organism develops from a fertilised egg during embryonic and fetal life, its cells display a range of behaviours that are appropriate to each stage of development, but which tend to lie dormant at other times. These include capabilities that are typical of cancer cells, such

as rapid cell division and invasion of surrounding tissues. Inappropriate and untimely activation of such capabilities in cells of an adult organism can mean those cells behave in the way that defines cancer. This can happen if the genetic changes that accumulate in cancer cells affect which genes are turned on or off (see **Box 4**).

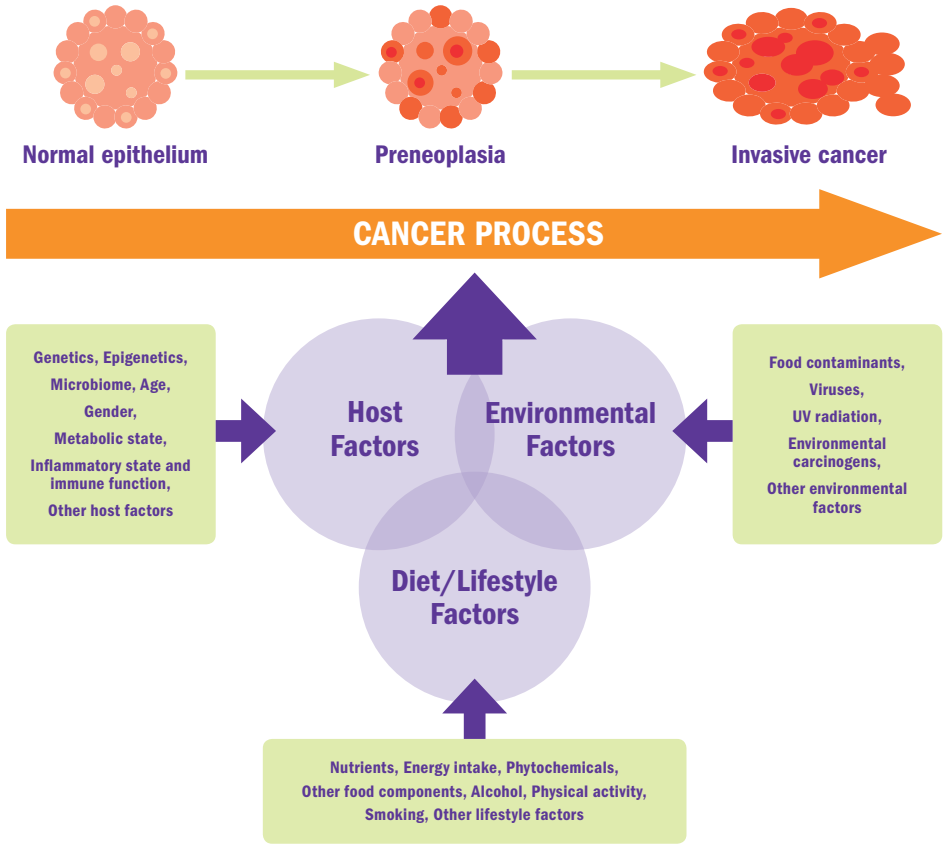
One way of thinking about cancer, therefore, is that it is the inappropriate and abnormal resurrection of capabilities needed by cells during normal development after fertilisation.

1.1.3 Almost all cells are vulnerable to the genetic damage that causes cancer

Almost all cells in an organism are vulnerable to damage to their DNA (see **Figure 3**).

For example, mutations can happen during cell division. Throughout life, an organism's cells are constantly growing and dividing via a highly regulated process called the cell cycle. This allows tissues to grow and stay healthy. Before a cell divides, it must replicate its DNA

Figure 3: Diet, nutrition and physical activity, other environmental exposures and host factors interact to affect the cancer process



The process by which normal cells transform into invasive cancer cells and progress to clinically significant disease typically spans many years. The cancer process is the result of a complex interaction involving diet, nutrition and physical activity, and other lifestyle and environmental factors, with host factors that are related both to inheritance and to prior experience, possibly through epigenetic change. Such host factors influence susceptibility to cancer development, in particular related to the passage of time. This allows both opportunity to accumulate genetic damage, as well as impairment of function, for example, DNA repair processes with ageing. The interaction between the host metabolic state and dietary, nutritional, physical activity and other environmental exposures over the whole life course is critical to protection from or susceptibility to cancer development.

(and therefore its genetic code), so that each of its two daughter cells has identical DNA to the parent cell. DNA replication is a complex process and is vulnerable to the introduction of errors in the DNA sequence.

DNA can be damaged at other times too. Cells are constantly exposed to factors that can damage DNA, either agents from the environment outside the body (exogenous), such as radiation or chemicals in cigarette smoke, or agents generated by processes that occur within the body (endogenous), such as free radicals or other by-products of metabolism. A substance or agent that is capable of causing cancer is known as a carcinogen, although not all carcinogens damage DNA directly.

Ageing allows increasing opportunity for cells to accumulate DNA damage. Ageing is also often accompanied by reduced capacity in many metabolic and physiological functions, including protection against DNA damage.

1.1.4 Cells can protect themselves against acquiring DNA damage and the hallmarks of cancer

Cells have evolved a range of mechanisms to prevent the accumulation of DNA damage, which protects them against acquiring the hallmarks of cancer. These mechanisms include:

- **Eliminating or detoxifying external agents that can cause DNA damage –** Cells can be exposed to a multitude of substances and agents both natural and anthropogenic that have the potential to damage DNA, disrupt normal cell function and contribute to carcinogenesis [15]. Humans have evolved various physiological mechanisms that protect against the adverse effects of some of these carcinogens. For example, a family of enzymes termed 'phase I and phase II metabolising enzymes' are involved in a process that ultimately quenches, or neutralises, reactive agents that can damage DNA so they can be excreted in bile or urine [16].

- **Repairing DNA damage so it is not transmitted to daughter cells –** Cells have a number of processes that can detect and repair particular types of DNA damage. For example, normal progression through the cell cycle is monitored at checkpoints that sense errors in DNA replication. Activation of these checkpoints stops the cell cycle, allowing cells to repair any defects and prevent their transmission to daughter cells [17].

- **Ensuring cells with damaged DNA do not survive –** If DNA repair is unsuccessful and normal cell function is compromised, damaged cells undergo a process called apoptosis, which means the cells effectively self-destruct [18]. This protects the tissues from accumulating cells with damaged DNA.

1.1.5 The protective mechanisms of cells sometimes fail, increasing the chances that cancer will develop

The mechanisms that protect cells against accumulating DNA damage and the hallmarks of cancer are not perfect and may be compromised by several factors that can increase the risk of cancer, such as:

- **Inherited genetic defects –** A small proportion of cancers (<10 per cent) are linked to specific mutations inherited from an individual's parents (germ-line mutations) [14] and therefore present in every cell in the body that has a nucleus. The inheritance of a cancer-linked germ line mutation does not

mean that a person will definitely go on to develop cancer, but it does confer a higher risk of developing cancer compared with the general population.

- **High levels of exposure to external carcinogens –** The physiological mechanisms that protect humans against carcinogens may be overwhelmed by high levels of exposure and may not work as well to protect against unaccustomed types of carcinogens that have appeared more recently, such as industrial pollution.

- **Endogenous factors that compromise DNA integrity –** Excessive production of reactive oxygen and nitrogen species (ROS/RNS) by neutrophils and macrophages, such as occurs with chronic inflammation, can damage nuclear and mitochondrial DNA [19]. Concomitant ROS/RNS damage to key proteins such as DNA polymerases and multiple DNA repair enzymes regulating DNA integrity also contribute to cancer susceptibility.

- **Reduced effectiveness of endogenous protective systems –** Defects in DNA surveillance and repair mechanisms as well as antioxidant defence systems can lead to genomic instability [20], meaning cells accumulate deleterious DNA mutations more rapidly, giving them a predisposition to cancer and its progression. This genetic instability provides a way for a previously healthy cell to accumulate sufficient mutations to become malignant [21].

1.1.6 Inappropriate nutrition and levels of physical activity are conducive to cancer development

Diet, nutrition and physical activity are essential aspects of human existence. Imbalanced and inappropriate levels of these factors can disturb normal homeostasis and reduce resilience to external challenges. This may manifest in many ways, for instance as susceptibility to infections, to cardiometabolic disease or to cancer.

Diet, nutrition and physical activity may influence cancer risk in a range of different ways. Some foods and drinks may be vectors for specific substances that act as carcinogens at particular sites. By contrast, obesity and sedentary ways of life may not act through single discrete pathways – instead, they may alter the systemic metabolic milieu of the body in ways that give rise to cellular microenvironments that are conducive to cancer development at a number of sites.

There is accumulating evidence on how diet, nutrition and physical activity can have an impact on the biological processes that underpin the development and progression of cancer – and influence whether cells acquire the phenotypic changes in cellular structure and function that are characterised as the hallmarks of cancer (see **Figure 4**). For example:

- Inappropriate nutrition at the whole-body level is reflected in a disordered nutritional microenvironment at the cellular and molecular levels. This can create an environment that is conducive to the accumulation of DNA damage and therefore to cancer development.
- Obesity is associated with inflammatory mediators, and metabolic and endocrine abnormalities, that promote cell growth and exert anti-apoptotic effects, meaning cancer cells do not self-destruct even following severe DNA damage.
- Nutritional factors may influence mechanisms involved in DNA repair.
- Dietary compounds may influence pathways by which carcinogens are metabolised.

- Diet may influence epigenetic changes in cells.
- Drinking alcohol can increase the production of metabolites that are genotoxic and carcinogenic [22].
- Reduced functional capacity, which occurs with inappropriate nutrition (and with ageing), reduces resilience to endogenous or external stresses.
- Physical activity has been shown to promote healthy immune and hormonal systems.

The growing body of evidence on such biological processes adds weight to evidence on the effects of diet, nutrition and physical activity on cancer risk measured at the level of the whole body or indeed in whole populations in clinical or epidemiological studies.

1.2 Body fatness and the hallmarks of cancer

This section focuses on links between body fatness and some of the hallmarks of cancer (see **Figure 4**). While there are links between the hallmarks and other exposures studied in the Continuous Update Project (CUP) too, body fatness has been chosen as the example here because the evidence that greater body fatness is a cause of many cancers is particularly strong, and has grown stronger over the last decade (see also the Exposures: Body fatness and weight gain[1] part of the Third Expert Report). What is more, rates of overweight and obesity, in children as well as in adults, have been rising in most countries [23].

The accumulating results of the CUP increasingly point to the importance of the systemic metabolic milieu of the body – as reflected in anthropometric measures such as body fatness – as being a critical determinant of cancer susceptibility (see **Section 6.2: Assessing and interpreting evidence: fine-tuning the approach** in this Summary).

Maintaining a healthy weight throughout life is one of the most important ways to protect against cancer. It also protects against a number of other common non-communicable diseases (NCDs); see the 'Be a healthy weight' Recommendation in **Section 5.1** and in the more detailed Recommendations and public health and policy implications[2] part of the Third Expert Report.

1.2.1 Sustained proliferative signalling

Many of the metabolic and endocrine abnormalities associated with obesity, such as elevated levels of fasting insulin and oestradiol, as well as inflammatory mediators associated with obesity, exert proliferative effects. Therefore, in the obese state, there is a general up-regulation of cell growth.

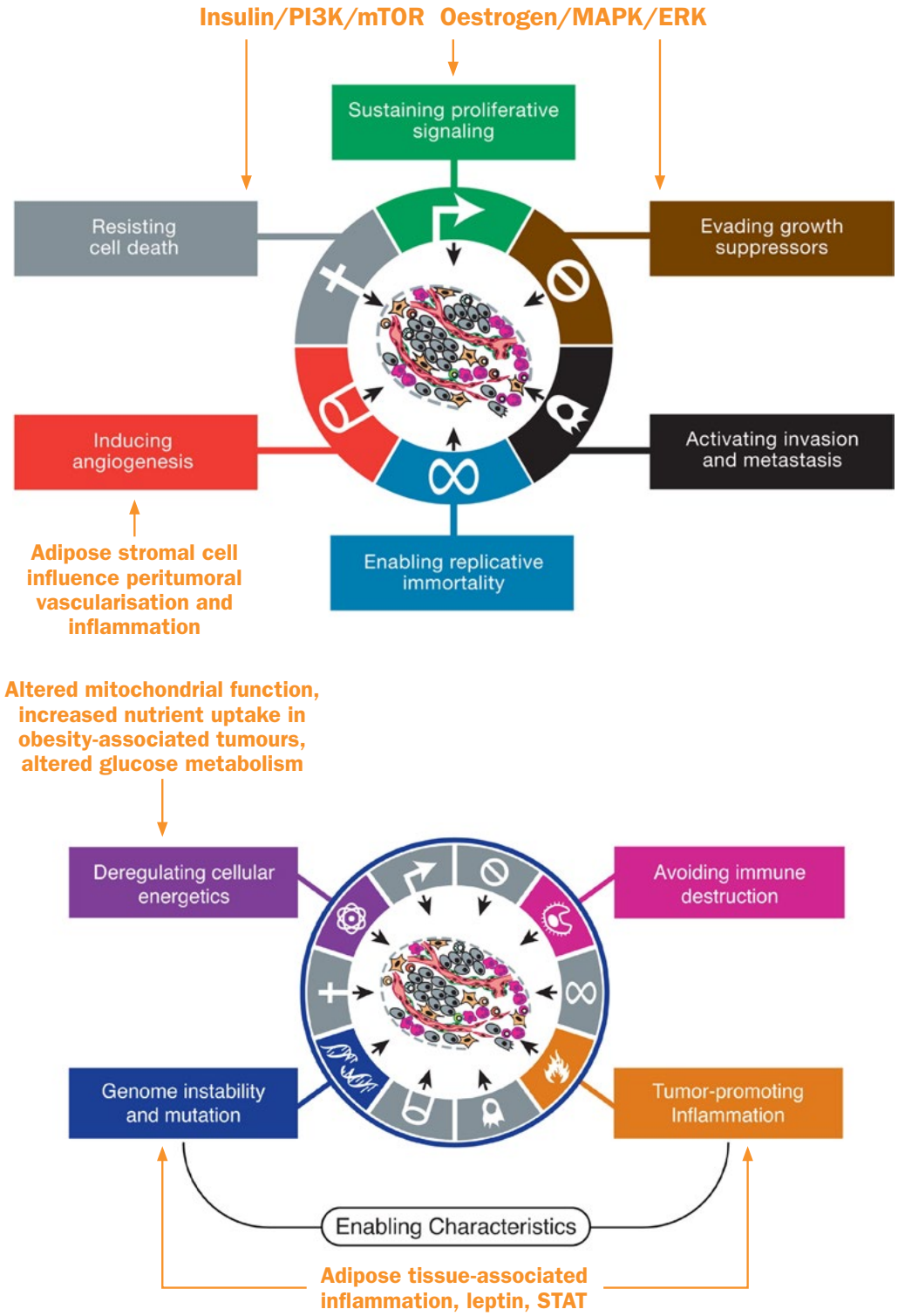
Unlike most healthy cells, cancer cells gradually evolve to become less dependent upon hormones and growth factors for continued growth and replication. Cancer cells may acquire this ability by, for example, producing growth-promoting signals themselves or by permanently activating the growth and survival pathways that normally respond to growth factors, via mutations that lock in these signals.

1.2.2 Resisting cell death

Normal cells 'self-destruct' under certain conditions, a process known as apoptosis. This happens, for example, when a cell's DNA is damaged beyond repair. In contrast, cancer

[1] The Exposures: Body fatness and weight gain part of the Third Expert Report is available online at wcrf.org/body-fatness
[2] The more detailed Recommendations and public health and policy implications part of the Third Expert Report is available online at wcrf.org/cancer-prevention-recommendations

Figure 4: Obesity and the hallmarks of cancer



Adapted from: Cell 144, Hanahan D and Weinberg RA, Hallmarks of cancer: the next generation, 646–74, Copyright (2011), with permission from Elsevier.

Several of the cancer hallmarks, and both enabling characteristics, can be affected by factors relating to diet, nutrition and physical activity. Obesity illustrates the wide range of cellular and molecular processes that may be affected to promote cancer development and progression.

Abbreviations: ERK, extracellular signal-regulated kinases; MAPK, mitogen-activated protein kinase; mTOR, mechanistic/mammalian target of rapamycin; PI3K, phosphoinositide 3-kinase; STAT, signal transducer and activator of transcription.

cells can downregulate apoptosis and survive even after severe DNA damage.

Many of the metabolic and endocrine abnormalities associated with obesity, such as elevated levels of fasting insulin and oestradiol, as well as inflammatory mediators associated with obesity, exert anti-apoptotic effects. Therefore, in the obese state, there is a suppression of apoptosis.

1.2.3 Activating invasion and metastasis

Cancer cells can infiltrate the local tumour microenvironment (invasion) and spread (metastasise) to distant organs via the bloodstream or lymphatic system.

Certain tissues are particularly prone to acting as colonisation sites for metastatic tissue, such as the liver, bones, brain and lungs. This suggests that the specific microenvironment in these tissues is more favourable for the support of tumours than that of other tissues [24]. Body fatness is an important determinant of the tissue microenvironment. Obesity is also linked with metabolic reprogramming in cancer cells so that they are more likely to metastasise [25].

1.2.4 Inducing angiogenesis

Angiogenesis is the term for the growth and establishment of a vascular network. As a tumour develops, relying on the local vascular supply alone causes local hypoxia. This activates genes that lead to the expression of growth factors, such as vascular endothelial growth factor (VEGF), thereby stimulating the development of cancer-associated vascular networks, which are needed to support tumour growth.

Adipose stromal cells may influence tumour vascularisation with associated increases in the proliferative activity of tumour cells.

1.2.5 Genome instability and mutation

Genomic instability is an increased tendency of the genome to acquire mutations because of dysfunction in the process of maintaining the genome. It can be thought of as an underlying enabling characteristic, which expedites cells' acquisition of the other hallmarks of cancer [13].

Human studies have linked the obese phenotype with genomic instability in colorectal and endometrial cancer in women [26, 27]. Visceral obesity is also associated with genomic instability events, both *in vitro* and *in vivo* in oesophageal adenocarcinoma [28].

1.2.6 Tumour-promoting inflammation

Tumour-promoting inflammation can also be thought of as an underlying enabling characteristic, which can inadvertently contribute to cells' acquisition of multiple other hallmark capabilities [13].

Chronic inflammation has long been recognised as a feature of cancer. Several inflammatory conditions are established precursors for specific cancers, including gastritis for gastric cancer, inflammatory bowel disease for colon cancer and pancreatitis for pancreatic cancer. Inflammation is also well-established in the pathogenesis of ovarian cancer.

Chronic inflammation has been implicated in the link between nutrition and cancer in many epidemiological and preclinical studies. In particular, obesity is now recognised as a chronic inflammatory state that predisposes to cancer. Complex interactions between cellular, molecular and metabolic factors underlie the nutrition-inflammation-cancer triad. For example, obesity is associated with elevated secretion of several pro-inflammatory cytokines and with C-reactive protein (an inflammation marker that is elevated with obesity, is related to cancer risk and reduces with weight loss) [29, 30].

1.3 Dietary exposures and the hallmarks of cancer

There is evidence that other exposures, in addition to body fatness, increase or decrease the risk of cancer at multiple cancer sites (see **Section 3: The evidence for cancer risk** and **Section 6.2: Assessing and interpreting evidence: fine-tuning the approach** in this Summary). This section provides examples of how dietary exposures might influence cancer susceptibility. These examples, and others, are summarised in **Table 2** and **Figure 5**.

1.3.1 Vegetables and fruit

Vegetables and fruit form a diverse and complex food group. Their consumption provides the host with many micronutrients, as well as thousands of phytochemicals, which are not nutrients but may have bioactivity in humans (see also Section 3 in the Exposures: Wholegrains, vegetables and fruit[1] part of the Third Expert Report). Phytochemicals that have demonstrated anti-cancer effects in cell and rodent studies include dietary fibre, carotenoids, dithiolthiones, isothiocyanates, flavonoids and phenols.

Vegetables and fruit are also a rich source of various nutrients that can impact cancer risk, such as vitamins C and E, selenium and folate. A substantial body of experimental data links many of these compounds with anti-tumorigenic effects in various cells in both animal and in vitro models [31].

See also the mechanisms for vegetables and fruit in Appendix 2 of the Exposures: Wholegrains, vegetables and fruit[1] part of the Third Expert Report.

1.3.2 Red and processed meat

Examples of biological mechanisms thought to underlie the association of red and processed meat with an increased risk of cancer include:

- Cooking meats at high temperatures results in the formation of heterocyclic amines (HCAs) and polycyclic aromatic hydrocarbons (PAHs), which have mutagenic potential through the formation of DNA adducts and have been linked to cancer development in experimental studies.
- Haem iron intake has been associated with an increased risk of colorectal tumours harbouring transitions from guanosine to adenine in the *KRAS* and *APC* genes, which suggests that alkylating DNA-damaging mechanisms are involved [32].
- The high salt content of processed meat may result in damage to the stomach mucosal lining, leading to inflammation, atrophy and *Helicobacter pylori* colonisation.

See also the mechanisms for red and processed meat in Appendix 2 of the Exposures: Meat, fish and dairy products[2] and Exposures: Preservation and processing of foods[3] parts of the Third Expert Report.

1.3.3 Alcoholic drinks

The diverse mechanisms by which alcohol consumption leads to cancer include:

- Acetaldehyde, a toxic metabolite of ethanol oxidation, can be carcinogenic to some cell types (e.g. colonocytes) [33], due to conversion of ethanol to acetaldehyde by colonic bacteria.
- Higher ethanol consumption can induce oxidative stress through increased production of reactive oxygen species, which are genotoxic and carcinogenic [22].

[1] The Exposures: Wholegrains, vegetables and fruit part of the Third Expert Report is available online at wcrf.org/wholegrains-veg-fruit
[2] The Exposures: Meat, fish and dairy products part of the Third Expert Report is available online at wcrf.org/meat-fish-dairy
[3] The Exposures: Preservation and processing of foods part of the Third Expert Report is available online at wcrf.org/preservation-processing

- Alcohol may also act as a solvent for cellular penetration of dietary or environmental (e.g. tobacco) carcinogen, or interfere with retinoid and one-carbon metabolism and DNA repair mechanisms [34].
- Alcohol has been linked to changes in hormone metabolism and, for example, is associated with increased levels of oestradiol [35, 36].

See also alcohol mechanisms in Appendix 2 of the Exposures: Alcoholic drinks[1] part of the Third Expert Report.

1.4 Physical activity and height and the hallmarks of cancer

There is strong evidence that physical activity and height both affect the risk of cancer at multiple sites (see **Section 3: The evidence for cancer risk** in this Summary). The information below gives examples of the biological mechanisms that may be involved.

1.4.1 Physical activity

Physical activity has a beneficial effect on cancer risk, likely through multiple mechanisms such as reductions in circulating oestrogen levels, insulin resistance and inflammation – all of which have been linked to cancer development at various anatomical sites when increased. Physical activity also reduces body fatness, in particular visceral fat, and therefore may have an additional indirect impact (see **Figure 5**). Evidence on mechanisms includes the following:

- Physical activity improves insulin sensitivity and reduces fasting insulin levels, which may decrease the risk of breast cancer [37, 38]. It may also reduce circulating oestrogen levels) [39, 40].
- Physical activity has been shown to have immunomodulatory effects, enhancing innate and acquired immunity, and promoting tumour surveillance [38, 41].
- Studies have also shown that aerobic exercise can decrease oxidative stress and enhance DNA repair mechanisms, decreasing carcinogenesis [41].

See also physical activity mechanisms in Appendix 2 of the Exposures: Physical activity[2] part of the Third Expert Report.

1.4.2 Height

Mechanisms hypothesised to underlie the association of greater adult attained height with increased cancer risk include the following:

- Taller people generally have higher circulating levels of IGF-I during adolescence and elevated signalling through the insulin-IGF axis [42, 43], which lead to activation of the phosphatidyl-3-kinase-mTOR and MAPK pathways, causing cellular proliferation, suppressed apoptosis and angiogenesis.
- Taller people may have more stem cells and thus there is greater opportunity for mutations leading to cancer development [44].
- Site-specific mechanisms may also be at play. For example, for colorectal cancer taller adults have longer intestines with a greater number of cells at risk; therefore, there may be greater potential for exposure to mutagenic or cancer-promoting agents.

See also height mechanisms in Appendix 2 of the Exposures: Height and birthweight[3] part of the Third Expert Report.

[1] The Exposures: Alcoholic drinks part of the Third Expert Report is available online at wcrf.org/alcoholic-drinks
[2] The Exposures: Physical activity part of the Third Expert Report is available online at wcrf.org/physical-activity
[3] The Exposures: Height and birthweight part of the Third Expert Report is available online at wcrf.org/height-birthweight

1.5 Summary

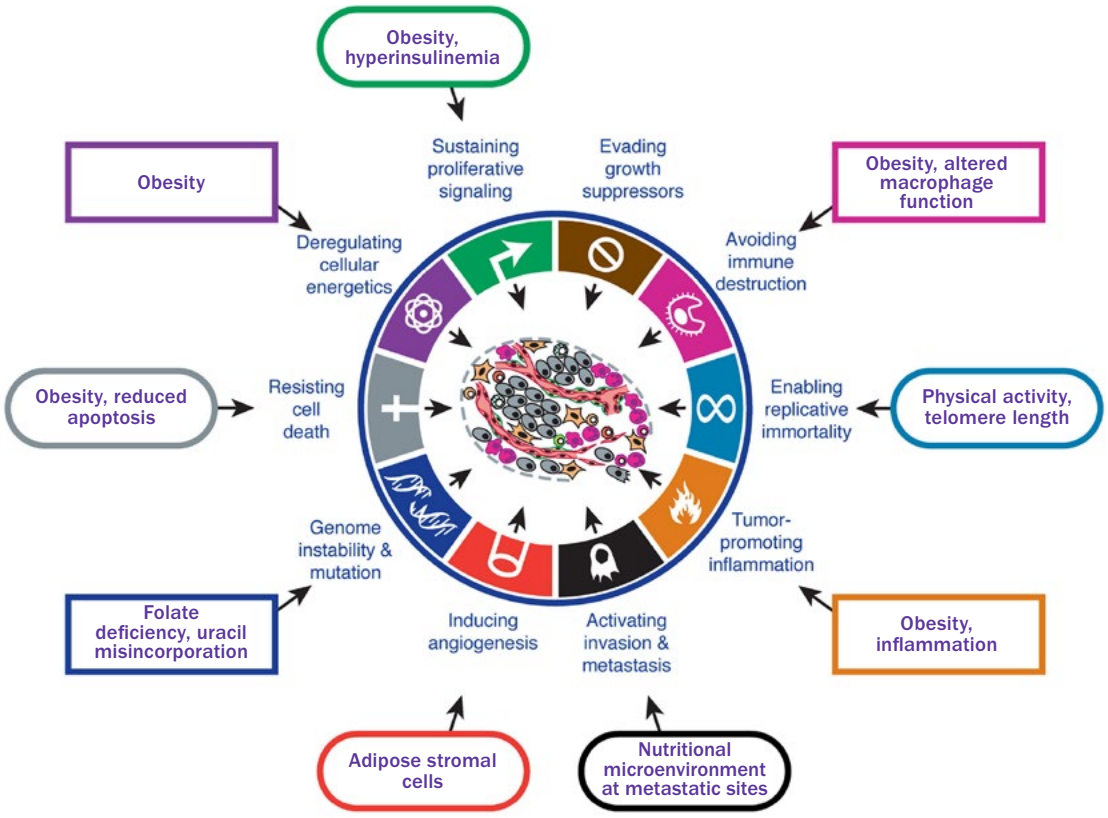
Evidence is growing on how diet, nutrition, physical activity and height can influence the biological processes that underpin the development and progression of cancer.

Some of the general biological mechanisms that may influence cancer risk by linking specific exposures to discrete hallmarks of cancer are summarised in **Figure 5** and **Table 2**. The columns in the table show the potential physiologic or metabolic impact of each exposure at the systemic level, and the molecular or cellular pathways that may be affected, which in turn may lead to one or more of the phenotypic changes that characterise cancer (hallmarks).

Further information on plausible biological mechanisms is available in the more detailed Exposure sections[1], CUP cancer reports[2] and The cancer process[3] part of the Third Expert Report, which are all available online.

Evidence on plausible biological mechanisms forms a vital part of the overall body of evidence that is taken into account in the CUP when making judgements on whether an exposure causes or protects against cancer; see **Section 2: Judging the evidence** of this Summary.

Figure 5: Nutrition, physical activity and the hallmarks of cancer



Adapted from: Cell 144, Hanahan D and Weinberg RA, Hallmarks of cancer: the next generation, 646–74, Copyright (2011), with permission from Elsevier.

A wide range of factors related to diet, nutrition and physical activity can influence the processes represented by the hallmarks of cancer.

[1] The Exposure sections of the Third Expert Report are available online at wcrf.org/exposures
[2] CUP cancer reports of the Third Expert Report are available online at wcrf.org/cancers
[3] The more detailed The cancer process part of the Third Expert Report is available online at wcrf.org/cancer-process

Table 2: Potential impact of diet, nutrition, physical activity and height in increasing susceptibility to cancer

Exposure	Systemic impact	Cell function	Hallmarks possibly affected
Greater body fatness	Hyperinsulinemia	mTOR/PI3K/AKT, MAPK	Reduced apoptosis; increased proliferation, genome instability
	Increased oestradiol	MAPK/ERK/PI3K	Increased proliferation in ER+ tissues; genome instability
	Inflammation	STAT3/NF-κB	Reduced apoptosis, increased cell division, altered macrophage function, etc.; genome instability
		E.g. WNT, P53	E.g. cellular energetics, etc.
Lower fruit and vegetable intake	Folate deficiency	DNA uracil misincorporation	Genome instability
	Low dietary fibre intake	Low butyrate	Reduced apoptosis; increased proliferation
	Low levels of carotenoids, vitamin A, C, E	Oxidative stress, inflammation	Increased inflammation, genomic instability, reduced apoptosis; increased proliferation
Greater intake of red and processed meat	Elevated exposure to nitrites; endogenous N-nitroso compound formation	DNA adduct formation -> mutations in p53, KRAS, etc.	Reduced apoptosis; increased proliferation; genomic instability
		Oxidative stress, inflammation	Increased inflammation, genomic instability
Greater intake of dairy foods	Higher IGF-I	mTOR/PI3K/AKT, MAPK	Reduced apoptosis; increased proliferation
Greater alcohol intake	Elevated acetaldehyde	Oxidative stress, lipid peroxidation	Increased inflammation, genomic instability
	Increased oestradiol	MAPK/ERK/PI3K	Increased proliferation in ER+ tissues
	Inflammation	STAT3/NF-κB	Reduced apoptosis, increased cell division, altered macrophage function, etc.
	Folate deficiency; interference with 1-carbon metabolism	DNA uracil misincorporation	Genome instability
Greater physical activity	Reduction in insulin	mTOR/PI3K/AKT, MAPK	Increased apoptosis; reduced proliferation, less genome instability
	Reduction in oestradiol and testosterone	MAPK/ERK/PI3K	Reduced proliferation in ER+ tissues; reduced genome instability
	Reduced inflammation (long term); improved immune function	STAT3/NF-κB	Increased apoptosis, increased cell division, altered macrophage function etc; reduced genome instability
		E.g. WNT, P53	E.g. cellular energetics, etc.
Greater height	Higher IGF-I	mTOR/PI3K/AKT, MAPK	Reduced apoptosis; increased proliferation

Abbreviations: AKT, also known as protein kinase B; DNA, deoxyribonucleic acid; ER+, oestrogen receptor positive; ERK, extracellular signal-regulated kinases; IGF-I, insulin-like growth factor 1; KRAS, please see glossary; MAPK, mitogen-activated protein kinase; mTOR, mechanistic/mammalian target of rapamycin; NF-kB, nuclear factor kappa-light-chain-enhancer of activated B cells; P53, tumour protein p53; PI3K, phosphoinositide 3-kinase; STAT3, signal transducer and activator of transcription 3; WNT, Wingless-related integration site.

Judging the evidence

2

For further information, see the more detailed **Judging the evidence** part of the Third Expert Report available online at **wcrf.org/judging-evidence**

2.1 The aim

This Third Expert Report brings together all of the findings of the Continuous Update Project (CUP) – an ongoing programme to analyse global research on how diet, nutrition and physical activity affect the risk of developing cancer and influence survival after a diagnosis. Thus, the report provides a comprehensive analysis, using the most meticulous of methods, of the worldwide body of evidence.

The aim when judging evidence is to identify, with sufficient confidence to support a recommendation, what causes cancer, what protects against cancer and what is unlikely to have an effect. This work also reveals where evidence is inadequate and further research is needed.

Judgements are used to update the Cancer Prevention Recommendations (see **Section 5.1: Recommendations for Cancer Prevention** in this Summary) to give people the best possible advice on cancer prevention, helping them to make healthy choices in their daily lives.

Much of the human evidence on diet, nutrition and physical activity is observational, though it is reinforced by findings of extensive laboratory investigations. There is no perfect way to establish whether observed associations between these exposures and cancer are definitely causal. However, the CUP Panel believes the rigorous, integrated and systematic approach enables them to make sound judgements and reliable recommendations.

Methods used are explained and displayed transparently (as summarised here and described in more detail in the full online version of Judging the evidence[1]), so they can be readily accessed and challenged as science develops.

2.2 The approach – in summary

- A team at Imperial College London conducts systematic literature reviews (SLRs) – gathering and presenting the best-available, current, scientific evidence from around the world.
  - There are 18 SLRs (17 on different cancers and one on breast cancer survivors), as well as a review of evidence on energy balance and body fatness (the determinants of weight gain, overweight and obesity conducted by WCRF/AICR).
  - The SLRs are peer reviewed by external peer reviewers.
- The International Agency for Research on Cancer (IARC) provides expert reviews of the main hypotheses-related mechanisms to support the epidemiological evidence.
  - The focus is on possible ways in which the lifestyle factors studied in the CUP may cause or protect from cancer at levels of exposure that are typical in humans.
- The CUP Panel evaluates and interprets the evidence, making judgements on the strength of the evidence and, where possible, the likelihood that the exposures studied increase, decrease or have no effect on the risk of cancer.
- The Panel makes recommendations for the public based on its judgements.
- The WCRF/AICR Secretariat, responsible for day-to-day management of the CUP, supports the work of the Panel.

The CUP Panel comprises internationally renowned, independent experts in a variety of disciplines from around the world. As well as their role in judging evidence and making

[1] The more detailed Judging the evidence part of the Third Expert Report is available online at wcrf.org/judging-evidence

recommendations, the members of the Panel also provide expertise and advice on maintaining a rigorous, independent process (see **Box 2**).

2.3 Gathering and presenting the evidence

2.3.1 Systematic literature reviews

SLRs are conducted according to a common methodology, first used for the 2007 Second Expert Report, which defines how to search for evidence, select which evidence to use, and assess, analyse and display the evidence. The approach is objective, reproducible, openly documented and subject to peer review at critical stages.

2.3.1.1 Evidence considered in systematic literature reviews

The SLRs are updates of those completed for the 2007 Second Expert Report.

When possible, SLRs focus on evidence from randomised controlled trials and cohort studies.

- A *randomised clinical trial* (RCT) is an experiment in which participants are randomly assigned to groups that receive, or do not receive, an experimental intervention (often called intervention and control groups). RCTs are considered the gold standard when testing the efficacy of drugs and other medical treatments, especially when 'double-blind', meaning neither participants nor investigators know which group each participant has been assigned to. However, few RCTs investigate the effect of diet, nutrition and physical activity on the risk of cancer incidence because of feasibility and limitations, for example, trial duration and resources.

- In prospective *cohort studies* (usually simply called cohort studies), the diet, body fatness and/or physical activity levels of a large group (cohort) of healthy people are assessed, and the group is followed over a period of time to identify relevant outcomes (cancer, in the case of a healthy cohort or death in the case of a survivors cohort). Comparisons are then made between people with the relevant outcome and those without it.

  Cohort studies are the most common studies reviewed in the CUP. The main advantages of these studies are that measurements can be taken before a diagnosis of cancer, follow-up may last decades and multiple types of cancer can be examined in one cohort. However, because of their observational nature, it is impossible to fully exclude or adjust for confounding factors, which can make interpretation of the causality of associations difficult.

When there are no, or few, RCTs or cohort studies, evidence from case-control studies is also taken into account:

- In *case-control studies*, people diagnosed with a specific type of cancer ('cases') are compared with otherwise similar people who have not been diagnosed with cancer ('controls'). The control group is a sample of the population from which the cases arose and provides an estimate of how the exposures being studied are distributed in that population.

  Case-control studies are not routinely reviewed for the CUP because such studies related to diet and physical activity may be particularly prone to recall and other biases.

Cohort and case-control studies are examples of *epidemiological research*, which describes and seeks to explain the incidence and distribution of health and disease within human populations and does not involve deliberate intervention.

In epidemiological studies, 'exposures' are factors that may or may not influence the risk of disease, such as people's diet, nutritional state, circumstances or behaviour. The exposures studied include foods and drinks, and their constituents and contaminants, dietary patterns, supplements, physical activity, body fatness, weight gain, height and birthweight. The CUP analyses of epidemiological data reveal associations between these exposures and the risk of cancer, which may or may not be causal.

Other types of studies that may be considered in the CUP include descriptive studies, migrant studies and ecological studies. For further information, see the more detailed Judging the evidence[1] part of the Third Expert Report available online.

2.3.1.2 How evidence is assessed and presented in systematic literature reviews

Owing to widespread interest in the study of diet, nutrition, physical activity and cancer, a large number of studies have been published, which allows meta-analyses to be carried out. Meta-analyses combine the results of several studies that address similar questions, which give them a greater statistical power than the individual studies to detect associations between exposures and the risk of cancer. Increased statistical power also allows subgroup analyses, which help to characterise the association. For example, to evaluate if an association differs by sex, age, body fatness, smoking status, geographical location or cancer subtype.

Where possible, the following types of meta-analyses are conducted and the findings presented visually using plots:

- **Highest versus lowest meta-analyses:** Comparing cancer risk for the highest and the lowest levels of exposure provides information on direction of effect (whether cancer risk is increased, decreased or unchanged at higher levels of exposure than lower levels).
- **Dose–response meta-analyses:** These analyses reveal how the effect on cancer risk changes with the level of exposure, showing both the direction of effect and the shape of the association (see **Box 6**). Considerable weight is placed on linear dose–response meta-analyses, partly because the demonstration of a biological gradient adds weight to evidence that a relationship may be causal. Non-linear dose–response meta-analyses are useful for detecting thresholds and non-linear associations.

2.3.2 Determinants of weight gain, overweight and obesity

As 12 of the 17 cancers reviewed by the CUP are linked to greater body fatness, a review on the determinants of weight gain, overweight and obesity has been undertaken (see the Energy balance and body fatness[2] part of the Third Expert Report). The review aimed to look at how diet, nutrition and physical activity affect weight gain, and the chance of being overweight or obese. Owing to the large amount of published evidence, this was conducted as a review of published reviews.

2.3.3 Experimental evidence on biological mechanisms

Judgements that an exposure causes or protects against cancer require evidence on plausible ways in which that might happen at levels of exposure that are typical in humans. Hypotheses may be based on evidence from human or animal studies, with a preference for human studies.

[1] The more detailed Judging the evidence part of the Third Expert Report is available online at wcrf.org/judging-evidence
[2] The more detailed Energy balance and body fatness part of the Third Expert Report is available online at wcrf.org/energy-balance-body-fatness

Box 6: Interpretation of the evidence

Interpretation of epidemiological evidence is complex. A wide range of general considerations must be taken into account, including the following:

- How relevant are the *patterns and ranges of intake* examined in the existing studies to populations globally?
- What about *classification*? Do the studies classify food and drink consumption, and physical activity, in ways that correspond to patterns globally?
- How accurate are *measurements* of the level of exposure in the study population, such as levels of intake of a food or its dietary constituents?
- Is *terminology* consistent between studies? For some exposures, such as 'processed meat', there are no generally agreed definitions.
- How reliable and complete is the data on *cancer outcomes* – on incidence and mortality, and subtypes?
- Is the *study design* appropriate? The hierarchy of evidence places RCTs at the top, followed by cohort studies, then case control studies, with ecological studies and case reports at the bottom, but there are merits in considering a number of different study designs.
- What is the *shape of the association* between the exposure and the cancer? For example, is it linear, with a uniform increase (or decrease) in risk for rising levels of exposure? Is there a threshold above which an association is found or a plateau where no further increase or decrease in risk is observed? Or does the direction of association (whether risk is increased or decreased) change with the level of exposure?
- Is there high *heterogeneity*, a large variation in the results of the studies, which would lead to less confidence in the overall summary estimate?
- Is the overall evidence limited to a particular geographic area and can results be extrapolated at a global scale?
- Do studies take into account the possibilities of *confounding*, *effect modification* and *reporting bias*?
    - A confounding factor is a variable that is associated with the exposure being studied, and is also a risk factor for the disease (in the case of the CUP, cancer), but is not on the causal pathway from the exposure to the disease. It is essential to adjust for confounding factors to try to minimise distortion of results, as they can account for part or all of an observed association between an exposure and a disease.
    - Effect modification occurs when the magnitude of the effect of an exposure changes depending on the level of another variable (the effect modifier); it means that the effect of an exposure on risk varies depending on a third factor.
    - Reporting bias can introduce systematic errors because of deviation of observed results from their true value in a particular direction. For example, in studies that rely on self-reporting, people tend to over-report consumption of foods and drinks they believe to be healthy and under-report foods and drinks they believe to be unhealthy.

More specific information on issues relating to Interpretation of the evidence is provided in the **Exposure sections**[1] of the Third Expert Report available online.

[1] The Exposure sections of the Third Expert Report are available online at wcrf.org/exposures

Summaries of plausible biological mechanisms – covering the primary hypotheses that currently prevail – are presented in the Exposure sections. These summaries are not currently based on an exhaustive search of the literature, but work to develop a more systematic process for reviewing evidence from experimental studies is continuing.

2.4 Discussing and judging the evidence

2.4.1 Uncertainty in epidemiology

Even though the best available evidence has been used, that evidence does not normally prove, beyond all doubt, whether the exposures – diet, nutrition and physical activity – cause, or protect against, cancer. The exposures themselves are complex and difficult to manipulate in experimental studies. Furthermore, even if a person's way of living does cause cancer, it may take years or decades for that cancer to develop.

Although RCTs have the power to test cause and effect vigorously, controlled manipulation of diet and physical activity in RCTs over the long period of time required to study these exposures is not possible. Much of the data on cancer risk therefore comes from epidemiological studies, and there is normally a degree of uncertainty surrounding whether observed associations in these studies are causal. Best judgement is therefore needed when interpreting and assessing results.

2.4.2 Best judgement and grading criteria

In 1965, Sir Austin Bradford Hill suggested nine characteristics of observational evidence, since used widely, that could be used when judging how likely it is that associations observed in epidemiological studies are causal [45]. Modified grading criteria, which build on Bradford Hill's ideas, are used in the CUP when assessing evidence, drawing conclusions and making recommendations (see the WCRF/AICR grading criteria in Section 8 of the Judging the evidence[1] part of the Third Expert Report).

The WCRF/AICR criteria require a range of factors to be considered. These include the quality of the studies – for example, whether the possibility of confounding, measurement errors and selection bias has been minimised. They also include the number of different study types and cohorts, whether there is any unexplained heterogeneity between results from different studies or populations, whether there is a dose–response relationship, and whether there is evidence of plausible biological mechanisms at typical levels of exposure.

The clearly defined grading criteria provide a systematic way to judge how strong any evidence of causality is. They enable evidence to be categorised as being 'strong' ('convincing', 'probable' or 'substantial effect on risk unlikely') or 'limited' ('limited – suggestive' or 'limited – no conclusion'). Only evidence judged to be strong is usually used as the basis for Recommendations (see **Section 5: Recommendations and public health and policy implications** in this Summary).

Judgements are displayed in the summary matrices. The matrix in **Section 3** presents all of the Panel's judgements from the CUP. The matrix in **Section 5.1.5** presents the strong evidence (judgements of 'probable' or 'convincing') which underpin the 2018 Cancer Prevention Recommendations. Matrices for judgements relating to specific cancer sites can be found in the CUP cancer reports[2]. Matrices for judgements relating to specific exposure groups, for example, alcoholic drinks, can be found in the Exposure sections[3].

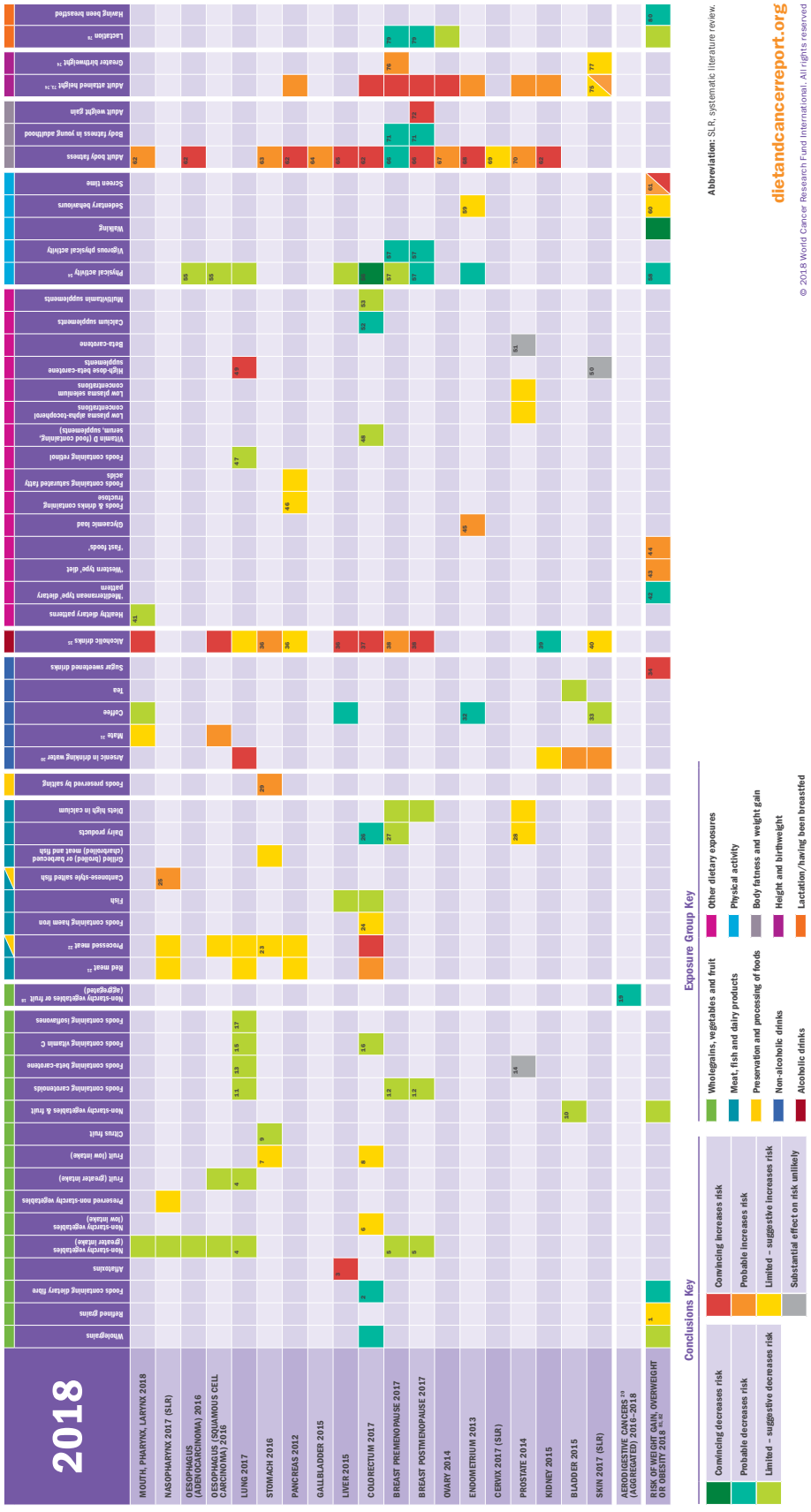
[1] The more detailed Judging the evidence part of the Third Expert Report is available online at wcrf.org/judging-evidence
[2] The CUP cancer reports of the Third Expert Report are available online at wcrf.org/cancers
[3] The Exposure sections of the Third Expert Report are available online at wcrf.org/exposures

The evidence for cancer risk: a summary matrix

3

The Panel's judgements are summarised in this matrix. The evidence is presented by cancer types (in rows) and by exposure (in columns). For breast and oesophageal cancer, two subtypes are presented due to the difference in the nature of the relationship between diet, nutrition physical activity and cancer. The bottom row relates to the outcome of risk of weight gain, overweight and obesity.

Further information can be found in the **CUP cancer reports**, **Exposure sections** and the **Energy balance and body fatness** part of the Third Expert Report available online at **dietandcancerreport.org**



For the full-size version of this summary matrix see the fold-out section inside the back cover of this Summary. See also the online interactive version of this matrix at **wcrf.org/interactivematrix**

Survivors of breast and other cancers

4

For further information, see the more detailed **Survivors of breast and other cancers** part of the Third Expert Report available online at **wcrf.org/cancer-survivors**

4.1 Defining cancer survivors

In recent decades, progress in the early detection and treatment of cancer has led to a dramatic increase in the number of cancer survivors: in 2012, 32.6 million people worldwide were living with a diagnosis of cancer [4]. It is therefore increasingly important that evidence on how diet, nutrition and physical activity influences outcomes in cancer survivors is analysed as part of the Continuous Update Project (CUP).

The term 'cancer survivor' covers people in a wide variety of circumstances beginning at diagnosis, through cancer treatment to the end of life. Using a single term to cover cancer survivors at all of these stages cannot do justice to the diverse nature of cancer and its survivorship.

Each stage of survivorship has its own particular characteristics, and the impact of interventions or exposures, including diet, nutrition and physical activity, varies according to this.

4.2 Findings from the CUP and other sources

The evidence from the CUP (see matrix below) and other sources is persuasive that nutritional factors such as body fatness, as well as physical activity, reliably predict important outcomes for people with breast and other cancers.

However, the evidence that changing these factors after diagnosis will alter the clinical course of cancer is limited, particularly by the quality of published studies and by the

DIET, NUTRITION, PHYSICAL ACTIVITY AND BREAST CANCER SURVIVAL – ALL-CAUSE MORTALITY

		DECREASES RISK		INCREASES RISK	
		Exposure	Timeframe	Exposure	Timeframe
STRONG EVIDENCE	Convincing				
	Probable				
LIMITED EVIDENCE	Limited – suggestive	Physical activity	Before diagnosis	Body fatness	Before diagnosis
			≥12 months after diagnosis		<12 months after diagnosis
		Foods containing fibre	Before diagnosis		≥12 months after 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

challenge of understanding how weight loss and weight gain during the dynamic cancer process affect outcome (for a full review of the evidence see the Survivors of breast and other cancers[1] part of the Third Expert Report available online).

4.3 Nature of the evidence

A major challenge when reviewing the evidence for diet, nutrition, physical activity and cancer survivorship is the scale and heterogeneity of the field. Part of this heterogeneity stems from the different phases of survivorship and the relative priorities of associated endpoints during each phase. Characterisation both of exposure (diet, physical activity, body fatness) and of outcome (such as progression-free survival, disease-specific mortality, co-existing conditions, quality of life or side effects) is complex and imprecise at present. Accurate capture of detailed treatment information is critical to enable adjustment for potential confounders.

As a consequence, the current evidence on breast cancer survivors, as reviewed by the CUP, has a number of limitations, including a lack of evidence from randomised controlled trials. In addition, the quality of most published studies is limited because they do not account for relevant factors such as cancer subtypes, type and intensity of treatment, and other illnesses. These limitations are also likely to apply to the evidence for survivors of other cancers.

4.4 Research gaps on cancer survivors

There are several questions about how diet, nutrition and physical activity affect outcomes in cancer survivors:

- More needs to be known about how these exposures influence responses to or potential adverse effects of therapeutic agents. Given the complexity of cancer care and the unique treatment strategies for specific types or subtypes of cancer, as well as the shortcomings of observational data, especially in the survivor setting, it is important that such evidence is derived from randomised controlled trials (RCTs), which in turn should be based on human observational data and relevant preclinical models.
- For people who have completed therapy, there are few RCTs informing on optimal dietary and physical activity strategies. Many specific cancer treatments have effects on a range of long-term health outcomes, such as cardiac function, bone health, metabolic syndrome and cognition.
- Future studies should focus on dietary and lifestyle interventions that are specifically designed to address pre-defined outcomes.
- Future studies must take account of issues that may be unique to specific cancers, as well as the type of treatment and stage of disease.
- Greater understanding of the underlying biological mechanisms linking diet, nutrition and physical activity to outcomes in cancer survivors is important.

Understanding the different roles that diet, nutrition and physical activity may play at each phase of survivorship, and for each type (and potentially subtype) of cancer, along with the biological mechanisms at play, is a priority (see **Section 7.5** in this Summary).

[1] The more detailed Survivors of breast and other cancers part of the Third Expert Report is available online at wcrf.org/cancer-survivors

4.5 Recommendations for cancer survivors

The available evidence on the effect of diet, nutrition and physical activity on the risk of all-cause mortality in cancer survivors is limited, and the amount and quality of research in this area is insufficient to make firm conclusions.

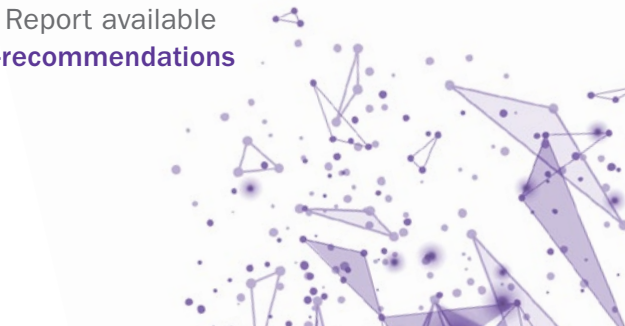
However, the Panel judges that following the Cancer Prevention Recommendations is unlikely to be harmful to cancer survivors who have finished treatment. Therefore, cancer survivors are encouraged, if appropriate to their circumstances and unless otherwise advised by a health professional, to follow the general advice for cancer prevention. For some cancers, especially those diagnosed at early stages (for example, prostate and breast cancer), cardiovascular disease (CVD) will be a more common cause of death than cancer. As the risk of diseases other than cancer are also modified by diet, nutrition and physical activity, following the Cancer Prevention Recommendations is also expected to help reduce the risk of other non-communicable diseases (NCDs). Other organisations also provide guidance on nutrition and physical activity for cancer survivors; this information can be found in the more detailed Survivors of breast and other cancers[1] available online.

[1] The more detailed Survivors of breast and other cancers part of the Third Expert Report is available online at wcrf.org/cancer-survivors

Recommendations and public health and policy implications

5

For further information, see the more detailed **Recommendations and public health and policy implications** part of the Third Expert Report available online at **wcrf.org/cancer-prevention-recommendations**



5.1 Recommendations for Cancer Prevention

The Cancer Prevention Recommendations, presented in this section are one of the most important outputs of the Continuous Update Project (CUP). The Cancer Prevention Recommendations are intended to reduce the incidence of cancer by helping people to maintain a healthy weight and adopt healthy patterns of eating, drinking and physical activity throughout life, and by informing policy action. The Recommendations take the form of a series of general statements to be used by individuals, families, health professionals, communities and policymakers, as well as the media.

A whole-of-government, whole-of-society approach is necessary to create environments for people and communities that are conducive to following the Cancer Prevention Recommendations. For more information, see **Section 5.3: Public health and policy implications** in this Summary.

In addition to the Cancer Prevention Recommendations presented here, the importance of not smoking, and of avoiding other exposure to tobacco, excess sun and long-term infections that can cause cancer, is emphasised.

5.1.1 Making the Cancer Prevention Recommendations

The Panel uses its judgements on the findings of the CUP to make the Cancer Prevention Recommendations. Evidence and judgements from the CUP are summarised in the exposure and cancer parts of the Third Expert Report (see the Exposure sections[1], CUP cancer reports[2] and CUP systematic literature reviews[3] of the Third Expert Report available online).

The risk of other diseases, as well as cancer, is also modified by diet, nutrition and physical activity. This includes diseases related to nutritional deficiencies, cardiovascular diseases (CVDs) and other non-communicable diseases (NCDs). When making the Cancer Prevention Recommendations, other recommendations on the prevention of these diseases made by authoritative international and national organisations from around the world were therefore also taken into account (see Appendix 1 in the more detailed Recommendations and public health and policy implications[4] part of the Third Expert Report available online).

5.1.2 An overall lifestyle

There are individual Recommendations on weight and physical activity and on particular aspects of diet and nutrition. The Recommendations focus on foods and drinks, rather than on nutrients or other bioactive constituents, for a variety of reasons.

It is important to emphasise that the Recommendations are intended to work together and be adopted as a lifestyle package. Individual recommendations are likely to be less effective if followed in isolation. Each has relevance for the others, and there are interactions between the exposures they address. Together, the Recommendations promote an overall way of life – a healthy pattern of diet and physical activity – that is conducive to the prevention of cancer, other NCDs and obesity.

[1] The Exposure sections of the Third Expert Report are available online at wcrf.org/exposures
[2] The CUP cancer reports of the Third Expert Report are available online at wcrf.org/cancers
[3] The CUP systematic literature reviews of the Third Expert Report are available online at wcrf.org/toolkit
[4] The more detailed Recommendations and public health and policy implications part of the Third Expert Report is available online at wcrf.org/cancer-prevention-recommendations

A growing body of evidence shows that the more people adhere to the 2007 Recommendations, the greater the reductions in the risk of specific cancers, of cancer as a whole and of death from any cause [1–3]. Therefore, confidence in the protective effect from following all of the Recommendations is greater than that for any individual Recommendation.

A diet based on the Recommendations is likely to be 'nutrient dense' – containing foods and beverages with a relatively high concentration of vitamins and minerals and other dietary constituents such as dietary fibre, without excessive salt, saturated or trans fats, added sugars or refined starches – thereby promoting good nutritional health and protecting against nutrient deficiency and NCDs.

5.1.3 Realistic and achievable goals

People interested in reducing their risk of cancer, health professionals who advise on preventing cancer and people involved in the development of public health policy need specific, relevant advice that they can act on. People need to know how much of what foods and drinks, what levels of body fatness and how much physical activity are most likely to protect against cancer.

For these reasons, Goals are provided with each Recommendation. The Goals provide specific advice, quantified whenever possible, on how to meet the Recommendations.

Goals are designed to result in real health gains while being achievable for most people. However, even without fully achieving a stated Goal, a change toward the Goal is worthwhile – any change is likely to provide at least some benefit.

When quantifying the Goals, evidence from the CUP was taken into account, as well as recommendations in other reports (on other NCDs, for example) on levels of body fatness and physical activity, and of intake of foods and drinks. To minimise confusion, existing quantified guidance has sometimes been selected from these other reports if consistent with the evidence on cancer prevention.

5.1.4 Relevant worldwide

The Recommendations have been designed to be culturally relevant throughout the world. Most of the available evidence comes from high-income countries, yet cancer is a problem worldwide. The Recommendations are therefore designed to be achievable in and appropriate to the very different circumstances and cultures that exist throughout the world.

Some evidence from the CUP is strong enough to support recommendations but is not suitable for inclusion in a set of global recommendations for a variety of reasons. These examples are discussed in **Section 5.2: Regional and special circumstances** and in the full version of Recommendations and public health and policy implications[1] available online.

[1] The more detailed Recommendations and public health and policy implications part of the Third Expert Report is available online at wcrf.org/cancer-prevention-recommendations

5.1.5 Diet, nutrition, physical activity and cancer – an overview of the Panel's judgements

The matrix presented here summarises all the strong evidence judgements on links between diet, nutrition and physical activity, and the risk of cancer or weight gain, overweight or obesity.

The rows correspond to the cancer types (with cancer as the outcome) and to energy balance and body fatness (with weight gain, overweight and obesity as the outcome). The columns correspond to the exposures. Colours show the strength of the evidence (whether 'convincing', 'probable' or 'substantial effect on risk unlikely') and the direction of the effect (whether there is an increase, a decrease or no effect on the risk of cancer), as explained in the key.

Judgements of 'convincing' and 'probable' are normally strong enough to support a Recommendation, while judgements of 'limited – suggestive' generally are not. Each conclusion on the likely causal relationship between an exposure and outcome forms a part of the overall body of evidence that is considered during the process of making Cancer Prevention Recommendations. Any single conclusion does not represent a Recommendation in its own right. The 2018 Cancer Prevention Recommendations are based on a synthesis of all these separate conclusions, as well as other relevant evidence.

5.1.6 Introducing the Recommendations

There are 10 Cancer Prevention Recommendations. Each Recommendation is intended to be one in a comprehensive package of behaviours that, when taken together, promote a healthy pattern of diet and physical activity conducive to the prevention of cancer, other NCDs and obesity.

Evidence that greater body fatness is a cause of many cancers is particularly strong; hence the following Recommendation is presented first:

- **Be a healthy weight**

The following two Recommendations promote positive changes that can be made to reduce both the risk of cancer and the risk of weight gain, overweight and obesity (which themselves are associated with an increased risk of cancer):

- **Be physically active**
- **Eat a diet rich in wholegrains, vegetables, fruit and beans**

The next four Recommendations focus on what to limit to reduce the risk of cancer, or of weight gain, overweight and obesity, and are listed in order by foods and drinks:

- **Limit consumption of 'fast foods' and other processed foods high in fat, starches or sugars**
- **Limit consumption of red and processed meat**
- **Limit consumption of sugar sweetened drinks**
- **Limit alcohol consumption**

The next Recommendation relates to supplements:

- **Do not use supplements for cancer prevention**

Two special Recommendations aimed at specific groups of people follow:

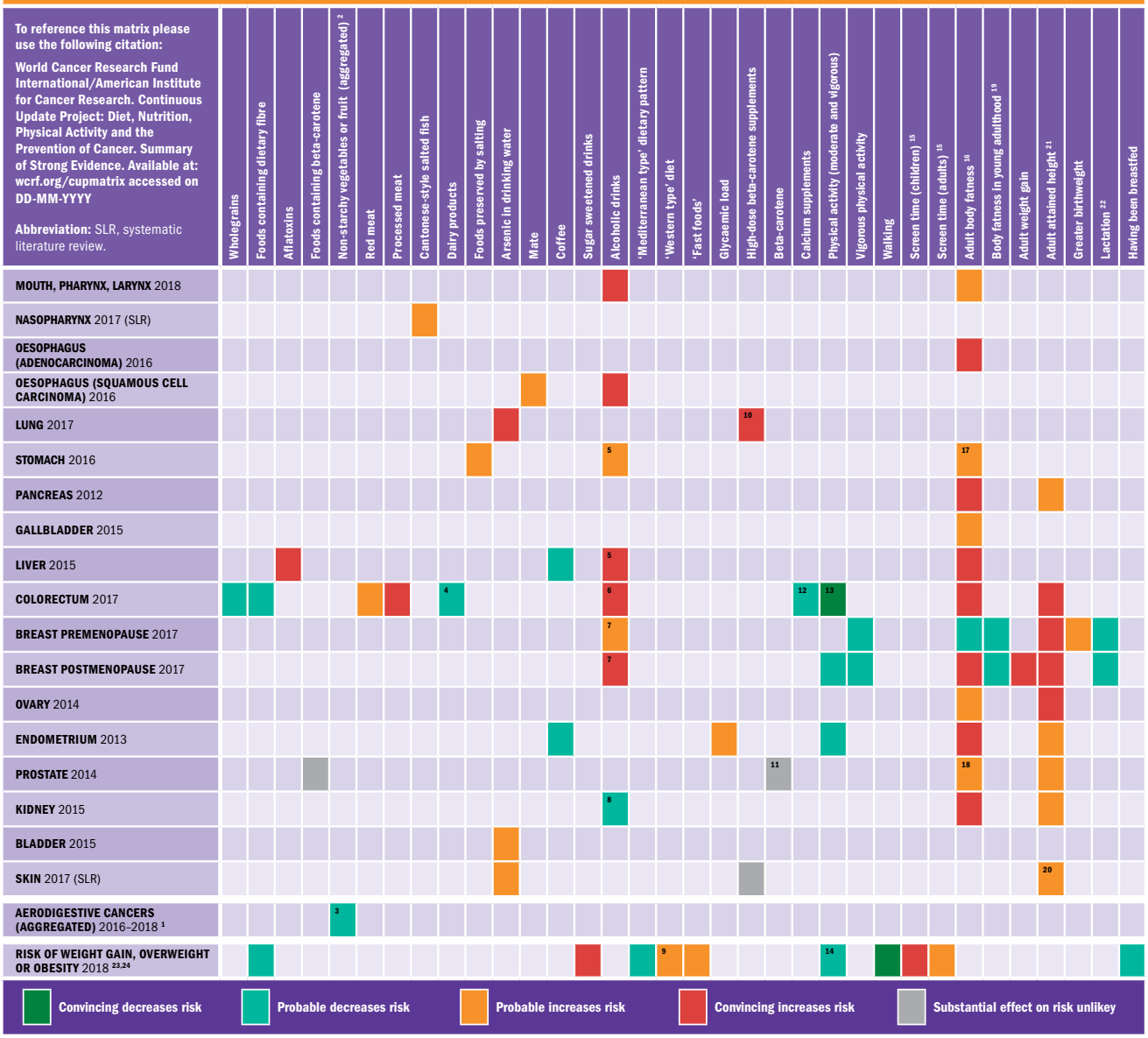
- **For mothers: breastfeed your baby, if you can**
- **After a cancer diagnosis: follow our Recommendations, if you can**

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

To reference this matrix please use the following citation:

World Cancer Research Fund International/American Institute for Cancer Research. Continuous Update Project: Diet, Nutrition, Physical Activity and the Prevention of Cancer. Summary of Strong Evidence. Available at: wcrf.org/cupmatrix accessed on DD-MM-YYYY

Abbreviation: SLR, systematic literature review.



1 Includes mouth, pharynx and larynx, nasopharynx, oesophagus (squamous cell carcinoma and adenocarcinoma), lung, stomach and colorectal cancers.
2 Aggregated exposure which contains evidence for non-starchy vegetables, fruit and citrus fruit.
3 The Panel notes that while the evidence for links between individual cancers and non-starchy vegetables or fruits is limited, the pattern of association is consistent and in the same direction, and overall the evidence is more persuasive of a protective effect.
4 Includes evidence on total dairy, milk, cheese and dietary calcium intakes.
5 Stomach and liver: Based on intakes above approximately 45 grams of ethanol per day (about 3 drinks).
6 Based on intakes above approximately 30 grams of ethanol per day (about 2 drinks per day).
7 No threshold level of intake was identified.
8 Based on intakes up to 30 grams of ethanol per day (about 2 drinks per day). There is insufficient evidence for intake greater than 30 grams per day.
9 Such diets are characterised by high intakes of free sugars, meat and dietary fat; the overall conclusion includes all these factors.
10 Evidence is from studies of high-dose supplements in smokers.
11 Includes both foods naturally containing the constituent and foods which have the constituent added and includes studies using supplements.
12 Evidence derived from studies of supplements at dose >200 milligrams per day.
13 Colon cancer only.
14 Aerobic physical activity only.
15 Screen time is a marker of sedentary behaviour.
16 Body fatness is marked by body mass index (BMI) and where possible waist circumference and waist-hip ratio.
17 Stomach cardia cancer only.
18 Advanced prostate cancer only.
19 Young women aged about 18 to 30 years; body fatness is marked by BMI.
20 Malignant melanoma only.
21 Adult attained height is unlikely to directly influence the risk of cancer. It is a marker for genetic, environmental, hormonal and nutritional factors affecting growth during the period from preconception to completion of growth in length.
22 Evidence relates to effects on the mother who is breastfeeding and not to effects on the child who is being breastfed. Relates to overall breast cancer (unspecified).
23 The factors identified as increasing or decreasing risk of weight gain, overweight or obesity do so by promoting positive energy balance (increased risk) or appropriate energy balance (decreased risk), through a complex interplay of physiological, psychological and social influences.
24 Evidence comes mostly from studies of adults but, unless there is evidence to the contrary, also apply to children (aged 5 years and over).

RECOMMENDATION

Be a healthy weight

Keep your weight within the healthy range[1] and avoid weight gain in adult life

GOAL Ensure that body weight during childhood and adolescence projects towards the lower end of the healthy adult BMI range

GOAL Keep your weight as low as you can within the healthy range throughout life

GOAL Avoid weight gain (measured as body weight or waist circumference)[2] throughout adulthood

[1] The healthy (or, as defined by WHO, 'normal') range of BMI for adults is 18.5–24.9 kg/m^2 [46]. Different reference ranges have been proposed for Asian populations [46]. Where these ranges differ from the WHO definition, they are to be used as the guide. Further research is required to establish appropriate thresholds in other ethnic groups. The healthy range for BMI during childhood varies with age [47].

[2] WHO recommends keeping waist circumference below 94 cm (37 inches) in men and 80 cm (31.5 inches) in women (based on data from European people). These values are roughly equivalent to a BMI of around 25 kg/m^2 [48]. For Asian populations, cut-offs for waist circumferences of 90 cm (35.4 inches) for men and 80 cm (31.5 inches) for women have been proposed [48]. Further research is required to establish appropriate waist circumference values for other ethnic groups.

Overweight and obesity, generally assessed by various anthropometric measures including body mass index (BMI) and waist circumference, are now more prevalent than ever. In 2016, an estimated 1.97 billion adults and over 338 million children and adolescents were categorised as overweight or obese globally [23]. The increase in the proportion of adults categorised as obese has been observed both in low- and middle-income countries and in high-income countries.

Goals

GOAL **Ensure that body weight during childhood and adolescence projects towards the lower end of the healthy adult BMI range**

GOAL **Keep your weight as low as you can within the healthy range throughout life**

These two related Goals emphasise the importance of preventing excess weight gain, overweight and obesity, beginning in childhood.

GOAL **Avoid weight gain (measured as body weight or waist circumference) throughout adulthood**

As there may be adverse effects specifically from gaining weight during adulthood, it is best to maintain weight within the healthy range throughout adult life.

This overall Recommendation is best achieved by maintaining energy balance throughout life by following four of the other Recommendations:

- being physically active
- eating a diet rich in wholegrains, vegetables, fruit and beans
- limiting consumption of 'fast foods' and other processed foods high in fat, starches or sugars
- limiting consumption of sugar sweetened drinks.

Justification

This recommendation was made for several reasons:

- There is **strong evidence** from the CUP (see matrices in **Sections 3** and **5.1.5**):
  - Greater body fatness is a cause of many cancers. This evidence has become stronger over the last decade.
  - For some cancers the increase in risk is seen with increasing body fatness even within the so-called 'healthy' range. Nevertheless, most benefit is to be gained by avoiding overweight and obesity.
- The International Agency for Research on Cancer (IARC) reviewed evidence for three additional cancers and concluded that greater body fatness is a cause of thyroid cancer, multiple myeloma and meningioma [49].
- Overweight and obesity in childhood and early life are liable to be carried through to adulthood.

Implications for other diseases

It is well established that greater body fatness has a causal role in the development of several other disorders and diseases, such as type 2 diabetes, dyslipidaemia, hypertension, stroke and coronary heart disease, as well as digestive and musculoskeletal disorders [50–54]. People with obesity often develop several of these disorders or diseases, leading to multiple comorbidities (see Appendix 1 in the more detailed Recommendations and public health and policy implications[1] part of the Third Expert Report available online).

Public health and policy implications

A comprehensive package of policies is needed to enable people to achieve and maintain a healthy weight, including policies that influence the food environment, food system, built environment and behaviour change communication across the life course. These policies can also help contribute to a sustainable ecological environment. Policymakers are encouraged to frame specific goals and actions according to their national context.

For further information on the evidence, analyses and judgements that led to this Recommendation, see the following parts of the Third Expert Report available online:

Recommendations and public health and policy implications (wcrf.org/cancer-prevention-recommendations)

Exposures: Body fatness and weight gain (wcrf.org/body-fatness)

Energy balance and body fatness (wcrf.org/energy-balance-body-fatness)

CUP cancer reports (wcrf.org/cancers)

CUP systematic literature reviews (wcrf.org/toolkit)

[1] The more detailed Recommendations and public health and policy implications part of the Third Expert Report is available online at wcrf.org/cancer-prevention-recommendations

RECOMMENDATION

Be physically active

Be physically active as part of everyday life – walk more and sit less

GOAL Be at least moderately physically active[1], and follow or exceed national guidelines

GOAL Limit sedentary habits

[1] Moderate physical activity increases heart rate to about 60 to 75 per cent of its maximum.

In most parts of the world, levels of physical activity are insufficient for optimal health [64]. Sedentary ways of life have become common in high-income countries since the second half of the 20th century and have subsequently also become widespread in most populations around the world [65].

Goals

GOAL **Be at least moderately physically active, and follow or exceed national guidelines**

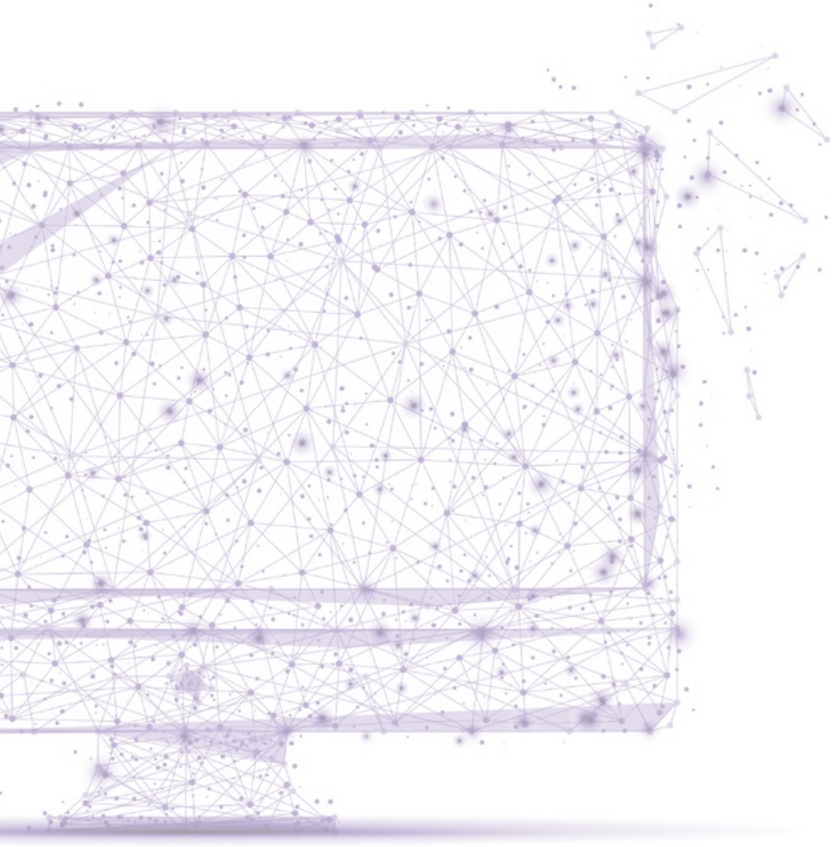
Establish a daily habit of being physically active throughout life, including when older. People whose work is sedentary need to take special care to build some physical activity into everyday life.

WHO advises adults to be active daily, taking part throughout each week in at least 150 minutes of moderate-intensity, aerobic physical activity or at least 75 minutes of vigorous, aerobic physical activity (or a combination) [55]. This represents a minimum amount of physical activity for cardiometabolic health.

For cancer prevention, it is likely that the greater the amount of physical activity, the greater the benefit. To have a significant impact on weight control, higher levels of activity are required (45–60 minutes of moderate-intensity physical activity per day) [56].

Children and young people aged 5 to 17 are advised to accumulate at least 60 minutes of moderate- to vigorous-intensity physical activity daily. Being physically active for longer than 60 minutes provides additional health benefits [57].

Activities that are moderate in intensity include walking, cycling, household chores, gardening and certain occupations, as well as recreational activities such as swimming and dancing. Vigorous activities include running, fast swimming, fast cycling, aerobics and some team sports.



GOAL

Limit sedentary habits

Both adults and children are advised to minimise the amount of time spent being sedentary for extended periods.

For adults, many occupations involve prolonged periods of sitting.

For both adults and children, watching screens (including when working) on devices such as televisions, computers, smartphones and video games is a form of sedentary behaviour. In some countries, children commonly spend more than three hours a day on such devices, during which they are also often exposed to heavy marketing of highly processed foods and drinks high in fat, refined starches or sugars [58, 59]. Screen time may also be associated with consumption of energy dense snacks and drinks [60–63].

Justification

This recommendation was made for several reasons:

- There is **strong evidence** from the CUP (see matrices in **Sections 3** and **5.1.5**):
  - Physical activity helps protect against several cancers.
  - Physical activity, including walking, helps protect against weight gain, overweight and obesity.
  - Greater screen time is a cause of weight gain, overweight and obesity.
  - Greater body fatness is a cause of many cancers.
- A lack of physical activity and sedentary lifestyles are both globally widespread.
  - In most parts of the world, levels of physical activity are insufficient for optimal health [64].
  - Sedentary ways of life have become common in high-income countries since the second half of the 20th century and have subsequently also become widespread in most populations around the world [65].

Implications for other diseases

Regular physical activity of at least moderate intensity decreases the risk of all-cause mortality [66], coronary heart disease [67], high blood pressure [68], stroke [69], type 2 diabetes [67], metabolic syndrome [70] and depression [71].

Regular weight-bearing and muscle-strengthening exercise has documented health benefits, including promoting bone health and reducing blood pressure [72].

Greater body fatness is a common risk factor for many other diseases and disorders, including cardiovascular disease (CVD) and type 2 diabetes (see the Recommendation 'be a healthy weight').

For further information on the implications for other diseases see Appendix 1 in the more detailed Recommendations and public health and policy implications[1] part of the Third Expert Report available online.

Public health and policy implications

A comprehensive package of policies is needed to promote and support physical activity, including policies that influence the food environment, food system, built environment and behaviour change communication across the life course. These policies can also help contribute to a sustainable ecological environment. Policymakers are encouraged to frame specific goals and actions according to their national context.

For further information on the evidence, analyses and judgements that led to this Recommendation, see the following parts of the Third Expert Report available online:

Recommendations and public health and policy implications (wcrf.org/cancer-prevention-recommendations)

Exposures: Physical activity (wcrf.org/physical-activity)

Energy balance and body fatness (wcrf.org/energy-balance-body-fatness)

CUP cancer reports (wcrf.org/cancers)

CUP systematic literature reviews (wcrf.org/toolkit)

[1] The more detailed Recommendations and public health and policy implications part of the Third Expert Report is available online at wcrf.org/cancer-prevention-recommendations

RECOMMENDATION

Eat a diet rich in wholegrains, vegetables, fruit and beans

Make wholegrains, vegetables, fruit, and pulses (legumes) such as beans and lentils a major part of your usual daily diet

- GOAL Consume a diet that provides at least 30 grams per day of fibre[1] from food sources
- GOAL Include in most meals foods containing wholegrains, non-starchy vegetables, fruit and pulses (legumes) such as beans and lentils
- GOAL Eat a diet high in all types of plant foods including at least five portions or servings (at least 400 grams or 15 ounces in total) of a variety of non-starchy vegetables and fruit every day
- GOAL If you eat starchy roots and tubers as staple foods, eat non-starchy vegetables, fruit and pulses (legumes) regularly too if possible

[1] Measured by the AOAC method.

Relatively unprocessed foods of plant origin are rich in nutrients and dietary fibre. Higher consumption of these foods instead of processed foods high in fat, refined starches and sugars[1] would provide a diet that is higher in essential nutrients and more effective for regulating energy intake relative to energy expenditure. This could protect against weight gain, overweight and obesity and therefore protect against obesity-related cancers. Wholegrains, non-starchy vegetables, fruit and beans are a consistent feature of diets associated with lower risk of cancer and other non-communicable diseases (NCDs), as well as obesity [73].

Goals

- GOAL Consume a diet that provides at least 30 grams per day of fibre from food sources
- GOAL Include in most meals foods containing wholegrains, non-starchy vegetables, fruit and pulses (legumes) such as beans and lentils
- GOAL Eat a diet high in all types of plant foods including at least five portions or servings (at least 400 grams or 15 ounces in total) of a variety of non-starchy vegetables and fruit every day

[1] Processed foods high in refined starches include products made from white flour such as bread, pasta and pizza; and processed foods that are high in fat, starches or sugars include cakes, pastries, biscuits (cookies), other bakery foods and confectionery (candy).

The goal for fibre intake can be met by eating a range of foods of plant origin, including wholegrains and non-starchy vegetables and fruit of different colours (for example, red, green, yellow, white, purple and orange).

Examples of wholegrains include brown rice, wheats, oats, barley and rye.

Examples of non-starchy vegetables include green leafy vegetables, broccoli, okra, aubergine (eggplant) and bok choy, but not, for instance, potatoes, yams or cassava.

For the purposes of this Recommendation, non-starchy roots and tubers such as carrots, artichokes, celeriac (celery root), swede (rutabaga) and turnips are considered to be non-starchy vegetables.

One portion of non-starchy vegetables or fruit is approximately 80 grams or 3 ounces. If consuming the recommended amount of vegetables and fruit, consumption would be at least 400 grams or 15 ounces per day.

GOAL **If you eat starchy roots and tubers as staple foods, eat non-starchy vegetables, fruit and pulses (legumes) regularly too if possible**

In many parts of the world, traditional food systems are based on roots or tubers such as cassava, sweet potatoes, yams and taro. Where appropriate, it is advisable to protect traditional food systems – in addition to their cultural value, and their suitability to local climate and terrain, they are often nutritionally superior to the diets that tend to displace them. However, monotonous traditional diets, especially those that contain only small amounts of non-starchy vegetables, fruit and pulses (legumes), are likely to be low in essential micronutrients and thereby increase susceptibility to some cancers.

Wholegrains, non-starchy vegetables, fruit and pulses (legumes) all contain substantial amounts of fibre and a variety of micronutrients, and are low or relatively low in energy density. For cancer prevention, it is best if these, and not foods of animal origin, are the basis for a usual daily diet.

Justification

This recommendation was made for several reasons:

- There is **strong evidence** from the CUP (see matrices in **Sections 3** and **5.1.5**):
  - Consuming wholegrains helps protect against colorectal cancer.
  - Consuming dietary fibre helps protect against colorectal cancer and weight gain, overweight and obesity.
  - Greater body fatness is a cause of many cancers.
  - Although the evidence for links between individual cancers and consumption of non-starchy vegetables or fruit is limited, the pattern of association and the direction of effect are both consistent. Overall the evidence is more persuasive of a protective effect and that greater consumption of non-starchy vegetables and or fruit helps protects against a number of aerodigestive cancers and some other cancers.
- There is **some evidence** from the CUP (see matrix in **Section 3**) to suggest:
  - Consuming fruit and vegetables might decrease the likelihood of many cancers.
  - Consuming fruit and vegetables might decrease the likelihood of weight gain, overweight and obesity.

- People who eat no or low levels of vegetables and fruit, who increase their consumption, may benefit most from following this Recommendation

- Wholegrains, non-starchy vegetables, fruit and beans are a consistent feature of diets associated with lower risk of cancer and other NCDs, as well as obesity [73].

- Relatively unprocessed foods of plant origin are rich in nutrients and dietary fibre. Higher consumption of these foods instead of processed foods high in fat, refined starches and sugars would mean the diet is higher in essential nutrients and more effective for regulating energy intake relative to energy expenditure.

Implications for other diseases

The Goals and Recommendation on wholegrains, vegetables, fruit and beans are based on evidence on cancer, but are supported by evidence on cardiovascular disease and type 2 diabetes [67, 74, 75]. Many other, broadly similar recommendations have been issued by a range of authoritative international and national organisations (see Appendix 1 in the more detailed Recommendations and public health and policy implications[1] part of the Third Expert Report available online).

Greater body fatness is a common risk factor for many other diseases and disorders, including cardiovascular diseases (CVDs) and type 2 diabetes (see the Recommendation 'Be a healthy weight' and Appendix 1 in Recommendations and public health and policy implications[1]).

Public health and policy implications

A comprehensive package of policies is needed to promote and support physical activity, including policies that influence the food environment, food system and behaviour change communication across the life course. These policies can also help contribute to a sustainable ecological environment. Policymakers are encouraged to frame specific goals and actions according to their national context.

For further information on the evidence, analyses and judgements that led to this Recommendation, see the following parts of the Third Expert Report available online:

Recommendations and public health and policy implications (wcrf.org/cancer-prevention-recommendations)

Exposures: Body fatness and weight gain (wcrf.org/body-fatness)

Exposures: Wholegrains, vegetables and fruit (wcrf.org/wholegrains-veg-fruit)

Energy balance and body fatness (wcrf.org/energy-balance-body-fatness)

CUP cancer reports (wcrf.org/cancers)

CUP systematic literature reviews (wcrf.org/toolkit)

[1] The more detailed Recommendations and public health and policy implications part of the Third Expert Report is available online at wcrf.org/cancer-prevention-recommendations

RECOMMENDATION

Limit consumption of 'fast foods' and other processed foods high in fat, starches or sugars

Limiting these foods helps control calorie intake and maintain a healthy weight

GOAL **Limit consumption of processed foods high in fat, starches or sugars – including 'fast foods'[1]; many pre-prepared dishes, snacks, bakery foods and desserts; and confectionery (candy)**

[1] 'Fast foods' are readily available convenience foods that tend to be energy dense and are often consumed frequently and in large portions.

Overweight and obesity are at the highest levels ever seen globally. Processed foods high in fat, starches or sugars embody a cluster of characteristics that encourage excess energy consumption, for example, by being highly palatable, high in energy, affordable, easy to access and convenient to store.

Goal

GOAL **Limit consumption of processed foods high in fat, starches or sugars – including 'fast foods'; many pre-prepared dishes, snacks, bakery foods and desserts; and confectionery (candy)**

This Recommendation does not imply that all foods high in fat need to be avoided. Some, such as certain oils of plant origin, nuts and seeds, are important sources of nutrients. Their consumption has not been linked with weight gain and by their nature they tend to be consumed in smaller portions.

Justification

This recommendation was made for several reasons:

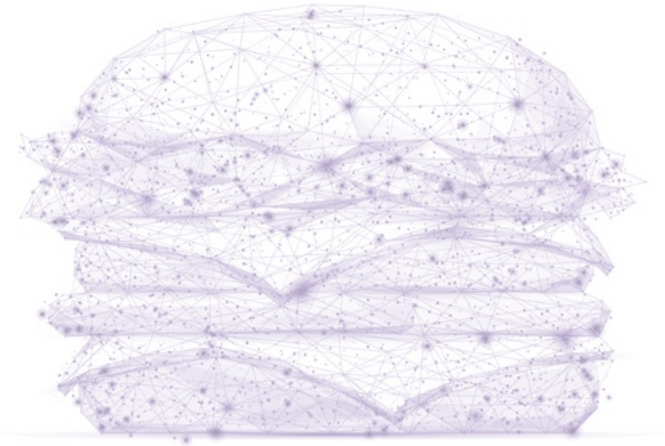
- There is **strong evidence** from the CUP (see matrices in **Sections 3** and **5.1.5**):
  - Consuming 'fast foods' (readily available convenience foods that tend to be energy dense and are often consumed frequently and in large portions) is a cause of weight gain, overweight and obesity.
  - Consuming a 'Western type' diet (characterised by a high amount of free sugars, meat and fat) is a cause of weight gain, overweight and obesity.
  - Glycaemic load (the increase in blood glucose (and insulin) after consumption of food) is a cause of endometrial cancer.
  - Greater body fatness is a cause of many cancers.

- The increasing availability, affordability and acceptability of 'fast foods' and other processed foods high in fat, starches or sugars (which are highly palatable, high in energy and convenient to store) is contributing to rising rates of overweight and obesity worldwide [76].

Implications for other diseases

Limited intake of processed foods high in fat, starches or sugars is recommended by many other organisations to reduce the risk of several non-communicable diseases (NCDs) [77].

Limiting intake of 'fast foods' and other processed foods high in fat, starches or sugars reduces the risk of weight gain, overweight and obesity. Greater body fatness is a common risk factor for many other diseases and disorders, including cardiovascular diseases (CVDs) and type 2 diabetes (see the Recommendation 'Be a healthy weight' and Appendix 1 in the more detailed Recommendations and public health and policy implications[1] part of the Third Expert Report available online).



Public health and policy implications

A comprehensive package of policies is needed to limit the availability, affordability and acceptability of 'fast foods' and other processed foods, including policies that restrict marketing of such foods, especially to children. Policies are needed that influence the food environment, food system and behaviour change communication across the life course. These policies can also help contribute to a sustainable ecological environment. Policymakers are encouraged to frame specific goals and actions according to their national context.

For further information on the evidence, analyses and judgements that led to this Recommendation, see the following parts of the Third Expert Report available online:

Recommendations and public health and policy implications (wcrf.org/cancer-prevention-recommendations)

Exposures: Body fatness and weight gain (wcrf.org/body-fatness)

Energy balance and body fatness (wcrf.org/energy-balance-body-fatness)

CUP cancer reports (wcrf.org/cancers)

CUP systematic literature reviews (wcrf.org/toolkit)

[1] The more detailed Recommendations and public health and policy implications part of the Third Expert Report is available online at wcrf.org/cancer-prevention-recommendations

RECOMMENDATION

Limit consumption of red and processed meat

Eat no more than moderate amounts of red meat[1], such as beef, pork and lamb. Eat little, if any, processed meat[2]

GOAL If you eat red meat, limit consumption to no more than about three portions per week. Three portions is equivalent to about 350 to 500 grams (about 12 to 18 ounces) cooked weight of red meat.[3] Consume very little, if any, processed meat

[1] The term 'red meat' refers to all types of mammalian muscle meat, such as beef, veal, pork, lamb, mutton, horse and goat.

[2] The term 'processed meat' refers to meat that has been transformed through salting, curing, fermentation, smoking or other processes to enhance flavour or improve preservation.

[3] 500 grams of cooked red meat is roughly equivalent to 700–750 grams of raw meat, but the exact conversion depends on the cut of meat, the proportions of lean meat and fat, and the method and degree of cooking.

An integrated approach to the evidence shows that diets that reduce the risk of cancer and other non-communicable diseases (NCDs) contain no more than modest amounts of red meat and little or no processed meat.

Goal

GOAL If you eat red meat, limit consumption to no more than about three portions per week. Three portions is equivalent to about 350 to 500 grams (about 12 to 18 ounces) cooked weight of red meat. Consume very little, if any, processed meat

The Recommendation is not to completely avoid eating meat; meat can be a valuable source of nutrients, in particular protein, iron, zinc and vitamin B12. However, it is not necessary to consume red meat in order to maintain adequate nutritional status [78]. People who choose to eat meat-free diets can obtain adequate amounts of these nutrients through careful food selection. Protein can be obtained from a mixture of wholegrains (cereals) and pulses (legumes), such as beans and lentils. Iron is present in many plant foods, though it is less bioavailable than that in meat.

Poultry and fish are valuable substitutes for red meat. Eggs and dairy are also valuable sources of protein and micronutrients for people who do eat other foods of animal origin.

High consumers of red meat and processed meat who reduce their intakes are expected to gain the greatest benefit from following this Recommendation.

Opportunities to use refrigeration to preserve fresh meat remain limited in some countries, where processed meat might be an important source of protein and iron.

Justification

This recommendation was made for several reasons:

- There is **strong evidence** from the CUP (see matrices in **Sections 3** and **5.1.5**):
  - Consuming red meat and consuming processed meat are causes of colorectal cancer.

- Red meat is a good source of protein, iron and other micronutrients (although consumption of red meat is not necessary to maintain adequate nutritional status) [78].
  - The amount of red meat specified in the Recommendation was chosen to provide a balance between the advantages of eating red meat (as a source of essential macro- and micronutrients) and the disadvantages (an increased risk of colorectal cancer and other NCDs).

- Processed meat is generally energy dense, can contain high levels of salt, and some of the methods used to create it generate carcinogens.
  - The data on processed meat show that there is no level of intake that can confidently be associated with a lack of risk of colorectal cancer.

Implications for other diseases

Greater consumption of red and processed meat is associated with increased risk of death from cardiovascular disease (CVD) [78] and risk of stroke [79] and type 2 diabetes [80].

Eating patterns that include a low intake of meat, processed meat and processed poultry are associated with reduced risk of CVD in adults [77] and possibly of type 2 diabetes [77].

Meat is an important source of iron but restricting the amount of red meat consumed per person per week to a maximum of 350 to 500 grams would have little effect on the proportion of adults with iron intakes below recommended levels in people eating a mixed diet [82]. If unbalanced, vegetarian diets may increase the risk of iron deficiency.

Public health and policy implications

A comprehensive package of policies is needed to support people to consume diversified diets including limited red meat and little, if any, processed meat, including policies that influence the food environment, food system and behaviour change communication across the life course. Globally, food systems that are directed towards foods of plant rather than animal origin are more likely to contribute to a sustainable ecological environment. Policymakers are encouraged to frame specific goals and actions according to their national context.

For further information on the evidence, analyses and judgements that led to this Recommendation, see the following parts of the Third Expert Report available online:

Recommendations and public health and policy implications (wcrf.org/cancer-prevention-recommendations)

Exposures: Meat, fish and dairy products (wcrf.org/meat-fish-dairy)

CUP cancer reports (wcrf.org/cancers)

CUP systematic literature reviews (wcrf.org/toolkit)

RECOMMENDATION

Limit consumption of sugar sweetened drinks

Drink mostly water and unsweetened drinks

GOAL **Do not consume sugar sweetened drinks**[1]

[1] Sugar sweetened drinks are defined here as liquids that are sweetened by adding free sugars, such as sucrose, high fructose corn syrup and sugars naturally present in honey, syrups, fruit juices and fruit juice concentrate. This includes, among others, sodas, sports drinks, energy drinks, sweetened waters, cordials, barley water, and coffee- and tea-based beverages with sugars or syrups added. This does not include versions of these drinks which are 'sugar free' or sweetened only with artificial sweeteners.

Consumption of sugar sweetened drinks is increasing in many countries worldwide and is contributing to the global increase in obesity, which increases the risk of many cancers.

There is no strong evidence in humans to suggest that artificially sweetened drinks with minimal energy content, such as diet sodas, are a cause of cancer.

Goal

GOAL **Do not consume sugar sweetened drinks**

To maintain adequate hydration, it is best to drink water or unsweetened drinks, such as tea (*Camellia sinensis*) or coffee without added sugar.

Coffee and tea both contain caffeine. For healthy adults, the maximum safe daily intake of caffeine recommended by the European Food Safety Authority [83] is 400 milligrams per day (approximately four cups of brewed coffee). The limit is lower in pregnancy.

Do not consume fruit juices in large quantities, as even with no added sugar they are likely to promote weight gain in a similar way to sugar sweetened drinks. Most national guidelines now recommend limiting intake of fruit juice.

Justification

This recommendation was made for several reasons:

- There is **strong evidence** from the CUP (see matrices in **Sections 3** and **5.1.5**):
  - Consuming sugar sweetened drinks (which provide energy but may not reduce appetite) is a cause of weight gain, overweight and obesity in both children and adults, especially when consumed frequently or in large portions. This effect is compounded at low levels of physical activity.
  - Sugar sweetened drinks do so by promoting excess energy intake relative to energy expenditure.
  - Greater body fatness is a cause of many cancers.

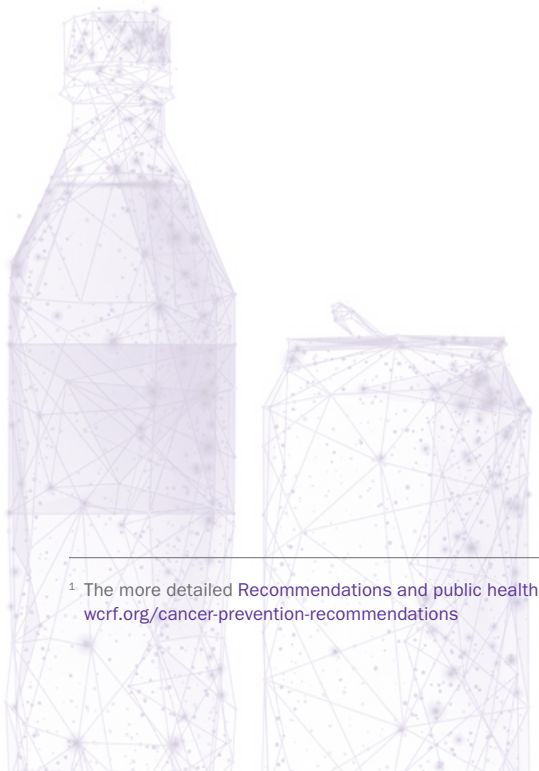
- Consumption of sugar sweetened drinks has rapidly increased in many parts of the world, especially in low- and middle-income countries, contributing to rising rates of overweight and obesity [84]. Although sales of sugar sweetened drinks have decreased in many high-income countries over the same period, total consumption has remained high [84].

Implications for other diseases

Greater body fatness is a common risk factor for many other diseases and disorders, including cardiovascular disease (CVD) and type 2 diabetes (see the Recommendation 'Be a healthy weight' and Appendix 1 in the more detailed Recommendations and public health and policy implications[1] part of the Third Expert Report available online).

Some evidence suggests regular consumption of sugar sweetened drinks increases the risk of type 2 diabetes independently of effects on adiposity [85].

Consumption of sugar sweetened drinks is a cause of dental caries and impaired oral health, particularly in children [86].



Public health and policy implications

A comprehensive package of policies is needed to limit the availability, affordability and acceptability of sugar sweetened drinks, including marketing restrictions and taxes on sugar sweetened drinks, and securing access to clean water (this is of particular relevance to school settings). Policies are needed that influence the food environment, food system and behaviour change communication across the life course. These policies can also help contribute to a sustainable ecological environment. Policymakers are encouraged to frame specific goals and actions according to their national context.

For further information on the evidence, analyses and judgements that led to this Recommendation, see the following parts of the Third Expert Report available online:

Recommendations and public health and policy implications (wcrf.org/cancer-prevention-recommendations)

Exposures: Body fatness and weight gain (wcrf.org/body-fatness)

Energy balance and body fatness (wcrf.org/energy-balance-body-fatness)

CUP cancer reports (wcrf.org/cancers)

CUP systematic literature reviews (wcrf.org/toolkit)

[1] The more detailed Recommendations and public health and policy implications part of the Third Expert Report is available online at wcrf.org/cancer-prevention-recommendations

RECOMMENDATION

Limit alcohol consumption

For cancer prevention, it's best not to drink alcohol

GOAL For cancer prevention, it's best not to drink alcohol

Consuming alcoholic drinks is a cause of many cancers. There is no threshold for the level of consumption below which there is no increase in the risk of at least some cancers.

Goal

GOAL For cancer prevention, it's best not to drink alcohol

If you do consume alcoholic drinks, do not exceed your national guidelines. Children should not consume alcoholic drinks. Do not consume alcoholic drinks if you are pregnant.

Justification

This recommendation was made for several reasons:

- There is **strong evidence** from the CUP (see matrices in **Sections 3** and **5.1.5**):
  - Drinking alcohol is a cause of many cancers.
  - Drinking alcohol helps protect against kidney cancer (at least up to 30 grams or two drinks per day), but this is far outweighed by the increased risk for other cancers.
- Evidence from the CUP also shows:
  - Even small amounts of alcoholic drinks can increase the risk of some cancers – there is no level of consumption below which there is no increase in the risk of at least some cancers.
  - Alcoholic drinks of all types have a similar impact on cancer risk. This Recommendation therefore covers all types of alcoholic drinks.

Implications for other diseases

Studies suggest some people who consume small amounts of alcohol may have lower risks of coronary heart disease (CHD) and early death than non-drinkers, but only at low levels of consumption (about one unit a day) [87].

Heavy alcohol use is overwhelmingly detrimentally related to many cardiovascular diseases (CVDs), including hypertensive disease, haemorrhagic stroke and atrial fibrillation [88]. Alcohol consumption is associated with various kinds of liver disease – with fatty liver, alcoholic hepatitis and cirrhosis being the most common – and with an increased risk of pancreatitis [88] (see Appendix 1 in the more detailed Recommendations and public health and policy implications[1] part of the Third Expert Report available online).

Despite the uncertainties about the effects of moderate alcohol consumption on non-cancer outcomes, drinking alcohol is not recommended for any health benefit.

Public health and policy implications

A comprehensive package of policies is needed to reduce alcohol consumption at a population level, including policies that influence the availability, affordability and marketing of alcoholic drinks. Policymakers are encouraged to frame specific goals and actions according to their national context.

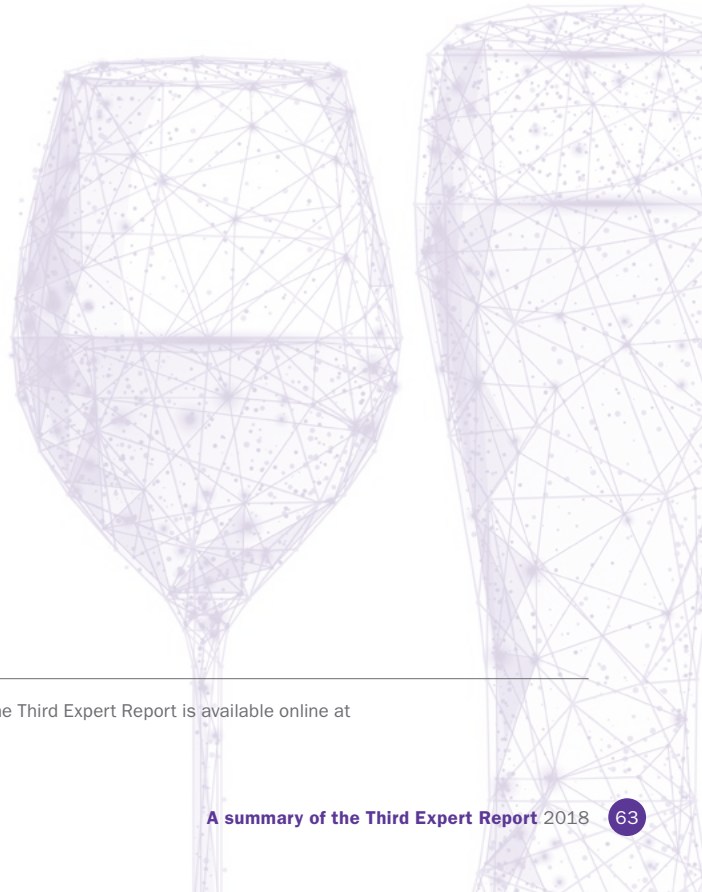
For further information on the evidence, analyses and judgements that led to this Recommendation, see the following parts of the Third Expert Report available online:

Recommendations and public health and policy implications (wcrf.org/cancer-prevention-recommendations)

Exposures: Alcoholic drinks (wcrf.org/alcoholic-drinks)

CUP cancer reports (wcrf.org/cancers)

CUP systematic literature reviews (wcrf.org/toolkit)



[1] The more detailed Recommendations and public health and policy implications part of the Third Expert Report is available online at wcrf.org/cancer-prevention-recommendations

RECOMMENDATION

Do not use supplements for cancer prevention

Aim to meet nutritional needs through diet alone

GOAL **High-dose dietary supplements[1] are not recommended for cancer prevention – aim to meet nutritional needs through diet alone**

[1] A dietary supplement is a product intended for ingestion that contains a 'dietary ingredient' intended to achieve levels of consumption of micronutrients or other food components beyond what is usually achievable through diet alone.

For most people consumption of the right food and drink is more likely to protect against cancer than consumption of dietary supplements.

Goal

GOAL **High-dose dietary supplements are not recommended for cancer prevention – aim to meet nutritional needs through diet alone**

This Recommendation applies to all doses and formulations of supplements, unless supplements have been advised by qualified health professional, who can assess individual requirements as well as potential risks and benefits.

In some situations – for example, in preparation for pregnancy or in dietary inadequacy – supplements may be advisable to prevent nutrient or calorie deficiencies. In general though, for otherwise healthy people with secure access to a regular supply of a variety of foods and drinks, nutrient-dense diets can provide adequate intake of nutrients.

Justification

This recommendation was made for several reasons:

- There is **strong evidence** from the CUP (see matrices in **Sections 3** and **5.1.5**):
  - Taking high-dose beta-carotene supplements is a cause of lung cancer in current and former smokers.
  - Trials of other high-dose supplements have not consistently demonstrated the protective effects of micronutrients on cancer risk suggested by observational studies. Although taking calcium supplements helps protect against colorectal cancer, some trials for other cancer sites have shown potential for unexpected adverse effects.
  - Disparity between the beneficial effects of micronutrients from foods observed in long-term dietary data and the lack of beneficial effects observed in short-term supplements trial data can lead to uncertainty as to the effect of dietary supplements on cancer risk.
  - For most people, it is possible to obtain adequate nutrition from a healthy diet that includes the right foods and drinks.

Implications for other diseases

Supplementation may be needed to achieve adequate intake of nutrients in populations or people with nutrient insufficiency. For example, people with dietary anaemia may need iron or folic acid supplementation [89]. To promote bone health, adequate calcium intakes and adequate supply of vitamin D are required; supplementation is sometimes necessary [72] (see Appendix 1 in the more detailed Recommendations and public health and policy implications[1] part of the Third Expert Report available online).

Public health and policy implications

In many parts of the world, nutritional inadequacy is endemic and may increase the risk of non-communicable diseases (NCDs) [90]. In crisis situations it is necessary to supply supplements of nutrients to such populations or to fortify food to ensure at least minimum adequacy of nutritional status.

The best approach is to protect or improve local food systems so that they are nutritionally adequate and promote healthy diets. This also applies in high-income countries, where impoverished communities and families, vulnerable people including those living alone, the elderly, and the chronically ill or infirm, may also be consuming nutritionally inadequate diets. Again, in such cases of immediate need, supplementation is necessary.

Policymakers are advised to maximise the proportion of the population achieving nutritional adequacy without dietary supplements by implementing policies that create a healthy food environment and food system. Policymakers are encouraged to frame specific goals and actions according to their national context.

For further information on the evidence, analyses and judgements that led to this Recommendation, see the following parts of the Third Expert Report available online:

Recommendations and public health and policy implications (wcrf.org/cancer-prevention-recommendations)

Exposures: Other dietary exposures (wcrf.org/other-dietary-exposures)

CUP cancer reports (wcrf.org/cancers)

CUP systematic literature reviews (wcrf.org/toolkit)

[1] The more detailed Recommendations and public health and policy implications part of the Third Expert Report is available online at wcrf.org/cancer-prevention-recommendations

RECOMMENDATION

For mothers: breastfeed your baby, if you can

Breastfeeding is good for both mother and baby

GOAL **This recommendation aligns with the advice of the World Health Organization, which recommends infants are exclusively breastfed[1] for 6 months, and then up to 2 years of age or beyond alongside appropriate complementary foods**

[1] 'Exclusive breastfeeding' is defined as giving a baby only breastmilk (including breastmilk that has been expressed or is from a wet nurse) and nothing else – no other liquids or solid foods, not even water [93]. It does, however, allow the infant to receive oral rehydration solution, drops or syrups consisting of vitamins, minerals, supplements or medicines [93].

Data from the World Health Organization (WHO) show that the percentage of infants who are exclusively breastfed for the first 6 months of life is highest in low-income countries (47 per cent) and lowest in upper-middle-income countries (29 per cent) [91]. The global average prevalence is 36 per cent [92].

Goal

GOAL **This recommendation aligns with the advice of the World Health Organization, which recommends infants are exclusively breastfed for 6 months, and then up to 2 years of age or beyond alongside appropriate complementary foods**

The benefits for both mother and baby are greater the longer the cumulative duration of breastfeeding.

Breastfeeding is recommended with caution or is not advised in some situations, for example, for mothers with HIV/AIDS; see WHO guidance for further information [94].

Justification

This recommendation was made for several reasons:

- There is **strong evidence** from the CUP (see matrices in **Sections 3** and **5.1.5**):
  - Breastfeeding helps protect the mother against breast cancer.
  - Having been breastfed helps protect children against excess weight gain, overweight and obesity.
  - Greater body fatness is a cause of many cancers.
- Excess body fatness during childhood tends to track into adult life (see the more detailed Energy balance and body fatness[1] part of the Third Expert Report available online).
- Excess body fatness during childhood is associated with an earlier menarche in girls, which in turn increases the risk of several cancers.

[1] The more detailed Energy balance and body fatness part of the Third Expert Report is available online at wcrf.org/energy-balance-body-fatness

- Breastfeeding protects the development of the immature immune system and protects against infections in infancy and other childhood diseases.

- Breastfeeding is vital where water supplies are not safe.

- Breastfeeding is important for the development of the bond between mother and child.

- In most countries, only a minority of mothers exclusively breastfeed their babies until 4 months, and an even smaller number until 6 months. Increasing the rate of exclusive breastfeeding is one of WHO's Global Nutrition Targets 2025 [95].

Implications for other diseases

The incidence of infections, as well as mortality rates, during infancy are lower in children who are breastfed [96]. Benefits continue into childhood and adulthood, with lower risks of other diseases, such as asthma [97]. There is some evidence to suggest risk of type 2 diabetes is reduced in adulthood [97].

Mothers who breastfeed have a lower risk of type 2 diabetes [97].

Greater body fatness is a common risk factor for many other diseases and disorders, including cardiovascular diseases (CVDs) and type 2 diabetes.

For further information on the implications for other diseases see Appendix 1 in the more detailed Recommendations and public health and policy implications[1] part of the Third Expert Report available online.

Public health and policy implications

A comprehensive package of policies is needed to promote, protect and support breastfeeding, including making all hospitals supportive of breastfeeding, providing counselling in healthcare settings, implementing maternity protection in the workplace, and regulating marketing of breastmilk substitutes. Policymakers are encouraged to frame specific goals and actions according to their national context.

For further information on the evidence, analyses and judgements that led to this Recommendation, see the following parts of the Third Expert Report available online:

Recommendations and public health and policy implications (wcrf.org/cancer-prevention-recommendations)

Exposures: Lactation (wcrf.org/lactation)

Energy balance and body fatness (wcrf.org/energy-balance-body-fatness)

CUP cancer reports (wcrf.org/cancers)

CUP systematic literature reviews (wcrf.org/toolkit)

[1] The more detailed Recommendations and public health and policy implications part of the Third Expert Report is available online at wcrf.org/cancer-prevention-recommendations

RECOMMENDATION

After a cancer diagnosis: follow our Recommendations, if you can

Check with your health professional what is right for you

GOAL **All cancer survivors[1] should receive nutritional care and guidance on physical activity from trained professionals**

GOAL **Unless otherwise advised, and if you can, all cancer survivors are advised to follow the Cancer Prevention Recommendations as far as possible after the acute stage of treatment**

[1] Cancer survivors are people who have been diagnosed with cancer, including those who have recovered from the disease.

The circumstances of cancer survivors vary greatly. There is increased recognition of the potential importance of diet, nutrition, physical activity and body fatness in cancer survival. People who have been diagnosed with cancer should consult an appropriately trained health professional as soon as possible, who can take each person's circumstances into account.

Goals

GOAL **All cancer survivors should receive nutritional care and guidance on physical activity from trained professionals**

There is increased recognition of the potential importance of diet, nutrition, physical activity and body fatness in cancer survival. Circumstances of cancer survivors vary greatly and people who have been diagnosed with cancer should be given the opportunity, as soon as possible, to consult an appropriately trained health professional who can take each person's circumstances into account.

People who are undergoing treatment for cancer are likely to have special nutritional requirements; as are people after treatment whose ability to consume or metabolise food has been altered by treatment; and people in the later stages of cancer whose immediate need is to arrest or slow down weight loss. The advice of an appropriately trained health professional is essential in all of these situations.

The evidence does not support the use of supplements as a means of improving survival. However, supplements may be specifically advised by an appropriately trained professional for other reasons.

GOAL **Unless otherwise advised, and if you can, all cancer survivors are advised to follow the Cancer Prevention Recommendations as far as possible after the acute stage of treatment**

There is growing evidence that physical activity and other measures that control weight (both features of the Cancer Prevention Recommendations) may help to improve survival and health-related quality of life after a breast cancer diagnosis.

Justification

This recommendation was made for several reasons:

- For breast cancer survivors, there is persuasive evidence that nutritional factors (in particular body fatness) and physical activity reliably predict important outcomes from breast cancer. However, the evidence that changing these factors would alter the clinical course of breast cancer is limited, particularly by the quality of published studies.

- Although research on the effects of diet, nutrition and physical activity and the risk of cancer is growing, only evidence on the effects of these lifestyle factors on survival and future risk of breast cancer has been reviewed. This is currently the best evidence available.

- The current understanding of the biology of cancer and its interactions with diet, nutrition and physical activity supports this Recommendation.

- More people are surviving cancer than ever before, at least partly because of earlier detection and increasing success of treatment for many cancers. As a result, cancer survivors are living long enough to develop new primary cancers or other non-communicable diseases (NCDs). Following the Cancer Prevention Recommendations may improve survival and reduce the risk both of cancer and of other NCDs.

Implications for other diseases

Evidence shows that following a dietary pattern close to the Cancer Prevention Recommendations is likely to help prevent other NCDs [1–3] as well as to help management and control of co-existing NCDs, which can complicate treatment and reduce survival (see Appendix 1 in the more detailed Recommendations and public health and policy implications[1] part of the Third Expert Report available online).

Public health and policy implications

A comprehensive whole-of-government, whole-of-society approach is necessary to create environments for cancer survivors that are conducive to following the Cancer Prevention Recommendations, and future, more specific evidence-based recommendations.

For further information on the evidence, analyses and judgements that led to this Recommendation, see the following parts of the Third Expert Report available online:

Recommendations and public health and policy implications (wcrf.org/cancer-prevention-recommendations)

Survivors of breast and other cancers (wcrf.org/cancer-survivors)

CUP breast cancer survivors report 2014 (wcrf.org/breast-cancer-survivors-report)

Energy balance and body fatness (wcrf.org/energy-balance-body-fatness)

CUP cancer reports (wcrf.org/cancers)

CUP systematic literature reviews (wcrf.org/toolkit)

[1] The more detailed Recommendations and public health and policy implications part of the Third Expert Report is available online at wcrf.org/cancer-prevention-recommendations

5.2 Regional and special circumstances

This section summarises findings of the CUP that were not suitable for inclusion in the global Recommendations even though the evidence is judged to be strong (either 'probable' or 'convincing'). Where appropriate, locally applicable actions are recommended.

For further information, see the more detailed Recommendations and public health and policy implications part of the Third Expert Report available online at wcrf.org/cancer-prevention-recommendations

5.2.1 Issues of public health significance

The following exposures are judged to be causally linked to cancer but are public health issues that people cannot necessarily influence themselves.

Height and birthweight

The Panel's judgements:

- **There is strong evidence** that developmental factors leading to greater growth in length in childhood (marked by adult attained height) are a cause of many cancers.
- **There is strong evidence** that factors that lead to greater birthweight, or its consequences, are a cause of premenopausal breast cancer.

Height and birthweight are not subject to a Recommendation for several reasons:

- To date, growth standards have not taken into account the lifelong risk of NCDs, including cancer, as policies and programmes have focused on the need to provide adequate nutrition to prevent stunting (which remains an important issue for some parts of the world).
- In adulthood there is no way to modify these factors.
- A better understanding of the developmental factors that underpin the association between greater growth and cancer risk is needed.

For further information, see the Exposures: Height and birthweight[1] part of the Third Expert Report available online.

Arsenic in drinking water

Arsenic may contaminate water supplies as a result of agricultural, mining and industrial practices. It can also occur naturally.

The Panel's judgement:

- **There is strong evidence** that consuming arsenic in drinking water is a cause of several cancers.

The International Agency for Research on Cancer (IARC) has judged arsenic and inorganic arsenic compounds to be carcinogenic to humans [98]. Drinking water contaminated with arsenic is also classed separately as a human carcinogen [98].

The joint Food and Agriculture Organization of the United Nations/WHO Expert Committee on Food Additives has set a provisional tolerable weekly intake of 0.015 milligrams of arsenic per kilogram of body weight [99].

For further information, see the Exposures: Non-alcoholic drinks[2] part of the Third Expert Report available online.

[1] The Exposures: Height and birthweight part of the Third Expert Report is available online at wcrf.org/height-birthweight
[2] The Exposures: Non-alcholic drinks part of the Third Expert Report is available online at wcrf.org/non-alcoholic-drinks

Actions:

- Do not use any source of water that may be contaminated with arsenic.
- Authorities should ensure that safe water supplies are available when such contamination occurs.

Aflatoxins

Some foods may become contaminated with aflatoxins, which are produced by some moulds when foods are stored for too long at warm temperatures in a humid environment. Foods that may be affected include cereals, spices, peanuts, pistachios, Brazil nuts, chillies, black pepper, dried fruit and figs.

The Panel's judgement:

- **There is strong evidence** that higher consumption of aflatoxin-contaminated foods is a cause of liver cancer.

For further information, see the Exposures: Wholegrains, vegetables and fruit[1] part of the Third Expert Report available online.

Actions:

- Do not eat mouldy cereals (grains) or pulses (legumes).
- Authorities should ensure that facilities for the safe storage of foods are made available in areas at risk of aflatoxin contamination.

5.2.2 Issues relevant only in specific parts of the world

If foods and drinks are consumed only in particular regions of the world, general actions are recommended for use by relevant local or regional authorities, other policymakers, health professionals and for people.

Mate

Mate, an aqueous infusion prepared from dried leaves of the plant *Ilex paraguariensis*, is traditionally consumed scalding hot following repeated addition of almost boiling water to the infusion.

The Panel's judgement:

- **There is strong evidence** that consuming mate, as drunk in the traditional style in South America, is a cause of oesophageal squamous cell carcinoma.

For further information, see the Exposures: Non-alcoholic drinks[2] part of the Third Expert Report available online.

Actions:

- The Panel recognises that consumption of mate is a traditional practice in parts of South America. However, for cancer prevention, do not consume mate as drunk scalding hot in the traditional style.

Foods preserved by salting

Preserved foods may be eaten more by people who do not have access to refrigeration.

The Panel's judgement:

- **There is strong evidence**, mostly from Asia, that consuming foods preserved by salting (including salt-preserved vegetables, fish and salt-preserved foods in general) is a cause of stomach cancer.

[1] The Exposures: Wholegrains, vegetables and fruit part of the Third Expert Report is available online at wcrf.org/wholegrains-veg-fruit
[2] The Exposures: Non-alcholic drinks part of the Third Expert Report is available online at wcrf.org/non-alcoholic-drinks

For further information, see the Exposures: Preservation and processing of foods[1] part of the Third Expert Report available online.

Actions:

- Do not consume salt-preserved, salted or salty foods.
- Preserve foods without using salt.

Cantonese-style salted fish

Cantonese-style salted fish, which is part of the traditional diet consumed by people living in the Pearl River Delta region in Southern China, is allowed to ferment and is eaten in a decomposed state.

The Panel's judgement:

- **There is strong evidence** that consuming Cantonese-style salted fish is a cause of nasopharyngeal cancer.

For further information, see the Exposures: Meat, fish and dairy products[2] part of the Third Expert Report available online.

Actions:

- Do not consume Cantonese-style salted fish.
- Do not feed fish prepared in this way to children.

5.2.3 Issues of inadequate information

For some exposures, although the Panel judged there to be strong evidence of an effect on cancer risk, some aspects of that evidence, such as the influence of dose, were inadequate to permit a meaningful recommendation.

Coffee

Coffee is one of the main hot drinks consumed worldwide. It contains several bioactive constituents.

The Panel's judgement:

- **There is strong evidence** that consuming coffee helps protect against some cancers.

More research is needed to improve understanding of how the volume and regularity of consumption, type of coffee, and style of preparation and serving (many people add milk and sugar), as well as the underlying potential mechanisms, affect the risk of cancer.

For further information, see the Exposures: Non-alcoholic drinks[3] part of the Third Expert Report available online.

'Mediterranean type' dietary pattern

Many studies have included a measure of adherence to the so-called 'Mediterranean type' dietary pattern, but it is unclear exactly what such a diet comprises. It generally describes a diet rich in fruit, vegetables and unrefined olive oil, with modest amounts of meat and dairy, and some fish and wine. This dietary pattern is traditionally associated with high levels of physical activity.

Currently the populations of most countries around the Mediterranean do not consume such a diet. A dietary and lifestyle pattern conforming to these principles represents one example of an approach to meeting the Recommendations.

For further information, see the Energy balance and body fatness[4] part of the Third Expert Report available online.

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[1] The Exposures: Preservation and processing of foods part of the Third Expert Report is available online at wcrf.org/preservation-processing
[2] The Exposures: Meat, fish and dairy products part of the Third Expert Report is available online at wcrf.org/meat-fish-dairy
[3] The Exposures: Non-alcoholic drinks part of the Third Expert Report is available online at wcrf.org/non-alcoholic-drinks
[4] The Energy balance and body fatness part of the Third Expert Report is available online at wcrf.org/energy-balance-body-fatness

5.2.4 Issues of divergent evidence

For some exposures, although there was strong evidence of increase or decrease in the risk of cancer, there was evidence of an opposite effect on another cancer or other disease, meaning a general recommendation is inappropriate.

Dairy products and calcium

The evidence on dairy products and diets high in calcium is mixed.

The Panel's judgement:

- **There is strong evidence** that **consumption of dairy products, and consumption of calcium supplements, both help to protect against colorectal cancer.**

However, there is also limited but suggestive evidence that consumption of dairy products might increase the risk of prostate cancer. The evidence of potential for harm means no recommendation has been made for dairy products.

For further information, see the Exposures: Meat, fish and dairy products[1] part of the Third Expert Report available online.

5.3 Public health and policy implications

5.3.1 Cancer Prevention Recommendations

The Cancer Prevention Recommendations together constitute a blueprint for reducing cancer risk through changing dietary patterns, reducing alcohol consumption, increasing physical activity and achieving and maintaining a healthy body weight.[2] Together these exposures represent the major modifiable risk factors for cancer after tobacco smoking and other forms of tobacco use [100]; for non-smokers, they are the most important means of helping prevent cancer [101].

The Recommendations provide guidance for people on how to reduce their risk by modifying their choices, and from a policy perspective can be divided into four main areas: *diet*, *physical activity*, *alcohol consumption* and *breastfeeding*, recognising that these exposures also influence body weight.

For further information, see the more detailed Recommendations and public health and policy implications part of the Third Expert Report available online at wcrf.org/cancer-prevention-recommendations

5.3.2 Need for policy action

Although well-informed choices are important in influencing personal risks of cancer and other diseases, many factors, such as the availability of different foods and the accessibility of physical environments for active ways of life, are outside people's direct personal control. In order to effect change at a population level, it is essential to consider the environment within which people make their choices [102].

[1] The Exposures: Meat, fish and dairy products part of the Third Expert Report is available online at wcrf.org/meat-fish-dairy
[2] The Panel emphasises the importance of not smoking, avoiding other exposure to tobacco, avoiding excess exposure of the skin to ultraviolet radiation (for example, sunlight) and preventing long-term infections that can cause cancer.

Environmental, economic and social factors are all important upstream determinants of the behaviours and choices that influence the risk of cancer and other NCDs. These factors – which determine levels of physical activity, for example, and patterns of production and consumption of foods and drinks (and thus body composition) – overlap and operate on global, national and local levels.

These factors are experienced at a personal level through their effects on the availability, affordability, awareness and acceptability of healthy foods, drinks and lifestyles – as well as breastfeeding[1] – relative to unhealthy foods and drinks, alcohol and physical inactivity [103]. They also contribute to health inequalities.

The same preventive strategies that target upstream determinants of cancer risk can often provide benefits across other diet-related NCDs, owing to common underlying risk factors, making a strong case for a coordinated policy approach. It is crucial that governments prioritise disease prevention.

WHO's Global Action Plan for the Prevention and Control of NCDs 2013–2020 [104] was created to strengthen national efforts to address the burden of NCDs. It includes a menu of policy options (updated in 2017 [105]) and nine voluntary global targets, including a 25 per cent relative reduction in premature mortality from NCDs by 2025, but progress towards those targets has been insufficient [106].

5.3.3 Sustainability and health

Sustainable development is also important when considering lifestyle factors that influence the risk of cancer and other NCDs. NCDs pose a major challenge to sustainable development; they are integrated throughout the United Nations' 2030 Agenda for Sustainable Development [107].

Supporting people and communities to follow the Cancer Prevention Recommendations contributes to the global sustainable development agenda by promoting dietary patterns based on foods of plant origin, and helping to reduce premature mortality from cancer and other NCDs. With the world's population projected to reach 8.6 billion by 2030 and 9.8 billion in 2050, finding a way to feed the world sustainably is critical [108]. Transport policies and systems that prioritise walking, cycling and public transport provide opportunities for combined benefits: reducing fossil fuel consumption and traffic congestion, improving air quality and increasing the health benefits associated with being physically active [109].

Vulnerable populations are often hit hardest by the burden of NCDs and impact of climate change; therefore policy responses that promote equity are needed.

5.3.4 Using a policy framework to support action

A whole-of-government, whole-of-society approach is needed to create environments for people and communities that are conducive to following the Cancer Prevention Recommendations (and improving overall health outcomes).

In order to develop an appropriate and coordinated response, a framework-type approach, as illustrated by the NOURISHING framework described below, is useful. Policy frameworks can help policymakers to:

- conceptualise, organise and package policies to address risk factors

[1] Policies are needed to promote, protect and support breastfeeding; however, it is recognised that not all mothers are able to breastfeed.

- plan, develop, implement and evaluate policies
- identify available policy levers and policy options that can be used to create health-enhancing environments
- develop a comprehensive policy approach, which can be adapted to reflect national contexts to achieve system-wide change.

5.3.4.1 The NOURISHING framework

A well-developed example of a framework-type approach is WCRF International's NOURISHING food policy framework (see **Figure 6**). Developed in 2013, the framework formalises a comprehensive package of policies to promote healthy diets and reduce overweight, obesity and diet-related NCDs, including cancer [110]. Together with an accompanying database of implemented policies from around the world (see **Box 7**), it is a tool designed to help policymakers, civil society organisations and researchers (see **Box 8**).

The NOURISHING framework outlines 10 policy areas in which governments need to take action across three domains: *food environment*, *food system* and *behaviour change communication* (see **Figure 6**). Each letter in NOURISHING represents a different policy area.

A comprehensive approach to policy – taking action across all 10 policy areas – is vital.

Box 7: The NOURISHING policy database

The NOURISHING database provides an extensive, regularly updated compendium of policy actions implemented in countries around the world. A structured methodology is followed when compiling and updating the database [111], which includes a process to verify the details and implementation of policy actions with in-country or regional policy experts. wcrf.org/NOURISHING

Box 8: How different groups use NOURISHING

Policymakers:

- **Enable and inform policy development and strategic direction**
- **Identify what action is needed**
- **Select and tailor policy options for different populations**
- **Assess whether an approach is comprehensive**

Civil society organisations:

- **Monitor what governments are doing**
- **Benchmark progress**
- **Hold governments to account**
- **Assist governments**

Researchers:

- **Identify the evidence available for different policies**
- **Identify research gaps**
- **Monitor and evaluate policies**

5.3.4.2 Broader application of the NOURISHING framework

Given the success of the NOURISHING framework, as evidenced by its wide uptake by policymakers, researchers and civil society organisations, WCRF International has used it to inform the development of a new structured policy framework that addresses physical activity, alcohol consumption and breastfeeding, in addition to diet. Common policy levers – broadly, policy measures that influence availability, affordability, awareness and acceptability – can be used to promote healthy diets, physical activity and breastfeeding, and reduce alcohol consumption.

To address the four factors of diet, physical activity, alcohol consumption and breastfeeding, the new WCRF International framework has broadened NOURISHING's three overarching policy domains to *health-enhancing environments*, *systems change* and *behaviour change communication* and modified and expanded NOURISHING's 10 policy areas to 11, to include healthy urban design (see **Figure 7**).

For examples of policy options, and information on how they fit within the broadened framework, see Appendix 2 in the more detailed Recommendations and public health and policy implications[1] part of the Third Expert Report available online.

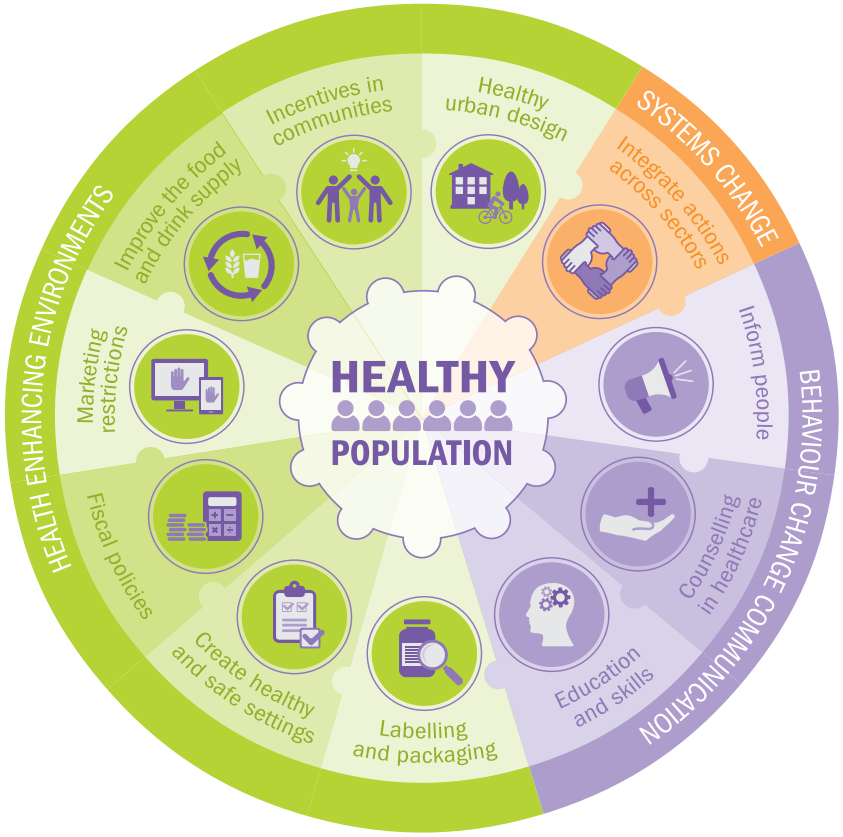
Figure 6: The NOURISHING framework

	POLICY AREA
N	Nutrition label standards and regulations on the use of claims and implied claims on food
O	Offer healthy food 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

The WCRF International NOURISHING framework formalises a comprehensive package of policies to promote healthy diets and reduce overweight, obesity and diet-related non-communicable diseases.

[1] The more detailed Recommendations and public health and policy implications part of the Third Expert Report is available online at wcrf.org/cancer-prevention-recommendations

Figure 7: A new policy framework to address diet, physical activity, breastfeeding and alcohol consumption



A new policy framework that can be used to identify a comprehensive package of actions needed to create environments for people and communities that are conducive to following the Cancer Prevention Recommendations.

5.3.5 Responsibility for health

Securing public health requires the organised efforts of society as a whole.

There are many ways of characterising how society is constructed. One example features four main pillars – multinational and regional bodies, government, private sector and civil society – which can each be segmented further into different groups of policymakers and decision-makers.

These 'actors' operate across different settings, including schools and other educational institutions, workplaces, public institutions, cities, towns and rural communities, media, social media and networks, and homes.

All actors have an opportunity, and often a responsibility, to make decisions with a view to their impact on public health, including cancer prevention, but this does not necessarily happen unless mandated by the highest level of government.

The common feature of successful policy is concerted action led by governments (and through them multinational and regional bodies), with the support of civil society and professional organisations, all working in the public interest. It is important to strive for policy coherence – where policies work together to achieve agreed objectives rather than undermining each other. Governance structures that support the engagement of multiple sectors and stakeholders can help improve policy coherence.

However, the development, adoption and implementation of policies to promote public health are often strongly opposed by industry and other actors (for example, government agencies concerned with trade), who may see such policies as obstructing their interests. Strategic advocacy efforts by civil society and professional organisations working in the public interest can help counter this opposition, as can robust safeguards against conflicts of interest (see **Box 9**).

5.3.6 Monitoring and evaluation of impact and effectiveness

It is critically important to develop a framework for monitoring and evaluating policies, to assess the impact and effectiveness of implemented policies, prior to the implementation of regulatory measures.

Monitoring is an ongoing process that uses the systematic collection of data on specified indicators to assess the extent of progress towards the achievement of a policy's objective. Monitoring compliance, and imposing effective sanctions for violations, is essential to enforcing regulations.

In contrast, evaluation is the systematic assessment of a policy's design, implementation and outcomes, used to draw conclusions about a policy's relevance, effectiveness, cost-effectiveness, efficiency, impact and sustainability. It provides a basis for revising and improving policy over time.

'Real world' implementation of policies can have unintended positive, negative or neutral impacts. As such, it is necessary to monitor and evaluate policies to determine whether they are having the anticipated impact(s) along the pathway of effects and, if not, why, so the policy can be adjusted accordingly.

Lessons learned when developing and implementing a policy, including factors that promoted or obstructed success, can benefit others around the world. However, too few evaluations of implemented policies are being conducted, with most evaluations taking place in high-income countries.

Box 9: Protecting policymaking from conflicts of interest

It is important to consider how the core interests of different actors might conflict with those of health, and whether the way they conduct their activities helps or hinders the promotion of healthy diets, physical activity and breastfeeding, and the reduction of alcohol consumption.

Governments bear responsibility for setting the policy and regulatory framework for promoting health, and for the prevention of cancer and other NCDs. Bodies such as the World Health Organization (WHO) also have responsibility for establishing normative standards in public health; the need to protect WHO from conflicts of interest is well established.

Industry does have a role to play, but this should be restricted to the implementation stage of the policymaking process. It is not the role of industry, in particular the food and beverage industry, to be involved in setting policies (aside from when called upon to give specific feedback), owing to the inherent and unavoidable conflict of interest.

Key questions to consider when engaging with private sector entities include whether core products and services are damaging to health, whether corporate social responsibility practices are independently audited, and whether clear parameters are set for engagement (which define, for example, responsibilities of different actors).

Changes since the 2007 Second Expert Report

6

6.1 An important shift in emphasis to a more holistic focus

The Recommendations in the Third Expert Report are similar to those in the 2007 Second Expert Report. However, they incorporate an important shift in emphasis in the Panel's interpretation of the evidence.

Through the years the Continuous Update Project (CUP), and its predecessors the First and Second Expert Reports [112, 113], have identified many specific foods (such as processed meat) and components of foods (such as dietary fibre) in the human diet that increase or decrease the risk of one or more particular cancers.

However, it appears increasingly unlikely that specific foods, nutrients or other components of foods are themselves important singular factors in causing or protecting against cancer: rather, different patterns of diet and physical activity combine to create a metabolic state that is more, or less, conducive to the acquisition of the genetic and epigenetic alterations that lead to the phenotypical structural and functional alterations in cells described by the hallmarks of cancer (see **Section 1: Diet, nutrition, physical activity and the cancer process** of this Summary).

In humans, as with all organisms, the normal physiological and metabolic state is subject to external and endogenous challenges (stresses). Nutrition is an important component of the body's capacity to withstand these stresses and avoid the development of diseases; in the absence of frank nutritional deficiency, this resilience is not dependent on the singular effect of specific nutrients. A more holistic focus on the determinants of resilience to external and endogenous challenge may be more fruitful than a continuing search for specific dietary factors that may cause or protect against cancer.

Furthermore, studies evaluating the impact of adherence to the Cancer Prevention Recommendations from 2007 have shown that the more people adhere to those recommendations, the greater the reductions in the risk of specific cancers, of cancer as a whole and of death from any cause [1–3].

For all these reasons, therefore, the Panel emphasises the importance of recognising that, while following each individual Recommendation is expected to offer cancer protection benefit, the most benefit is to be gained by treating them as an integrated pattern of behaviours relating to diet and physical activity, and other factors, that can be considered as a single overarching 'package' or way of life (see **Figure 8**).

The consistency in the Recommendations since 2007 increases confidence in the evidence base and in the advice given to policymakers, the scientific community, health professionals and the public.

6.2 Assessing and interpreting evidence: fine-tuning the approach

There has been an increase in the overall amount of evidence since 2007. This has enabled the Panel to fine-tune its approach to assessing and interpreting evidence:

- Growth in the number of cohort studies and the number of cases in existing cohorts, as well as improvement in the quality of these studies, has enabled the Panel to concentrate more on evidence from cohort studies, which are considered the best source of evidence on cancer prevention. This growth has also provided greater confidence in the accumulated evidence.
- Results from pooled analyses of cohort studies have been particularly helpful in adding evidence for subgroup analyses.

- Where possible when reviewing evidence on diet and nutrition, the Panel has increasingly considered the effects of dietary patterns. This is important because people do not eat foods in isolation but in combination, to form an overall diet or eating pattern, which itself is related to other health-linked behaviours such as smoking or physical activity.

  While sophisticated epidemiological or statistical techniques may help to minimise the inevitable effect of confounding, confidence in the nature of the truly causal exposure must always be greater for the aggregated set of dietary factors and other behaviours than for any single food, nutrient or other behavioural marker. Therefore, even where there is no direct evidence on dietary patterns the Panel has aimed to interpret evidence on specific foods in relation to dietary patterns.

- There is more evidence on subtypes of cancer now, such as oesophageal cancer, and therefore more conclusions on the effect of diet, physical activity or body fatness on differential risks of these subtypes. Evidence on subtypes is still emerging. This is important because different exposures might influence the risk of different subtypes in different ways.
- It has been possible to use non-linear analyses more to identify thresholds, or plateaus. For example, there may be a threshold in the level of exposure below which there is no association with the risk of cancer and above which there is. This has proved important, for example, when making Recommendations on the level of consumption of alcoholic drinks.
- Stratified analyses have provided valuable insights, for example, when considering the effect of exposures in relation to smoking status.

6.3 Emerging evidence of note

Emerging evidence that is particularly noteworthy includes:

- Growth in the amount of high-quality data that is available has allowed more sophisticated analyses of how effects on cancer risk change with the level of exposure – for instance on the shape of dose–response associations. For fruit and vegetables, for example, emerging evidence suggests that those people who consume the least, who eat very little or none of these foods, are most at risk of developing certain cancers. It may therefore be more important for these people to increase their consumption levels than for people who already eat more than one or two portions per day.
- The influence of height on cancer risk is becoming more apparent. However, height itself is unlikely to be the actual cause of cancer. It is most likely a marker for developmental factors related to growth and metabolism operating from the earliest stages of life to influence cancer susceptibility. More research is needed to build understanding of precisely how this might happen.
- The importance of the life course in general is emerging more strongly. There is evidence that greater adult height predicts higher risk of several cancers; and for breast cancer specifically, that greater birthweight is associated with higher risk, while greater body fatness in young adulthood predicts lower risk. However, more research is required to help further understand the mechanisms.
- Evidence on cancer survivors is accumulating, though is still at an early stage, and more is needed, particularly from well-conducted trials (some of which are under way).

Figure 8: Our Cancer Prevention Recommendations as an overarching 'package'

While following each individual Recommendation offers cancer protection benefit, most benefit is gained by treating all ten Recommendations as an integrated pattern of behaviours relating to diet, physical activity and other factors that can be considered as a single overarching 'package' or way of life.

Future research directions

7

For further information, see the more detailed **Future research directions** part of the Third Expert Report available online at **wcrf.org/future-research-directions**

As part of the Continuous Update Project (CUP) process, the Panel has discussed the implications of recent findings that emphasise the importance of adopting a more holistic focus, by considering how different patterns of diet and physical activity combine to create a metabolic state that is more, or less, conducive to the development of cancer (rather than focusing on singular effects of specific dietary factors such as individual foods, see **Section 6.1: An important shift in emphasis to a more holistic focus** of this Summary).

These discussions have led the Panel to identify six areas where research is needed:

1. **Biological mechanisms by which diet, nutrition and physical activity affect cancer processes**
2. **The impact of diet, nutrition and physical activity throughout the life course on cancer risk**
3. **Better characterisation of diet, nutrition, body composition and physical activity exposures**
4. **Better characterisation of cancer-related outcomes**
5. **Stronger evidence for the impact of diet, nutrition and physical activity on outcomes in cancer survivors**
6. **Globally representative research on specific exposures and cancer**

These areas are discussed in the following sections and are for consideration by the research community and funding organisations generally. More detailed information on all six areas can be found in the full Future research directions[1] part of the Third Expert Report available online.

7.1 Biological mechanisms by which diet, nutrition and physical activity affect cancer processes

Though not yet completely understood, the last few years have seen a rapid development in the characterisation of the complex and interacting intracellular and intercellular processes that lead to cancer, and the generally consistent structural and behavioural characteristics of cancer cells (hallmarks of cancer – see **Section 1**). However, despite evidence of various types and from several sources implicating nutritional factors as key determinants of cancer patterns in populations, relatively little research has been devoted to methodically exploring the impact of nutrition on these fundamental biological processes.

All biological processes depend on a supply of energy and nutrients that are necessary for normal function, and a nutritional perspective would aim to characterise, in a methodical way, the tolerance of these processes to variations in the supply of energy or nutrients at the cell or tumour level, and the extent to which whole body exposures (diet, activity, body composition) impact on the tumour nutritional microenvironment.

Examining the impact of diet and nutrition in the epithelial tissue niches from which most common tumours arise, and in the emerging tumour microenvironment, offers opportunities to reveal the critical mechanisms by which diet and nutrition can both potentiate and prevent the development of cancer [114–118]. The metabolic and phenotypic plasticity of cells, including myofibroblasts, immune cells and adipocytes, in microenvironmental niches, is integral to the fate of potentially

[1] The more detailed Future research directions part of the Third Expert Report is available online at wcrf.org/future-research-directions

malignant cells [119]. The role of diet and specific nutrients in maintaining and perturbing appropriate metabolism and function in this microenvironmental context is a research priority.

7.2 The impact of diet, nutrition and physical activity throughout the life course on cancer risk

The risk of several adult cancers varies with markers of aspects of growth and development in early life – including birthweight and adult attained height – as well as with body mass index (BMI) during or at the end of childhood growth.

Nutritional factors are key determinants of patterns of growth from conception onwards. Limitation of energy or nutrient supply acts as a potential constraint on growth, and if this occurs during particular periods of growth it can lead to adaptations in the fetus or child that may persist into adulthood, with consequences for the adult phenotype. Such phenotypical alterations include susceptibility to cardiometabolic disease and may also include susceptibility to cancer.

However, the precise mechanisms through which nutritional factors may influence growth and development, and their relation to later cancer risk, remain to be determined.

7.3 Better characterisation of diet, nutrition, body composition and physical activity exposures

In the CUP, the collation and interpretation of the evidence available in the published literature has highlighted inherent limitations of dietary measurements when it comes to precisely and accurately characterising dietary intake, body composition, relevant metabolic processes and other nutritional states, and physical activity.

Incorporating the following markers and measures into study designs could help to establish causal relationships between diet, nutrition, physical activity and disease, and to avoid bias and measurement error:

- better and/or new markers of dietary intake or metabolism and physical activity.
- more objective methods of measuring the effect of exposures, such as the use of Mendelian randomisation.
- better measures of body composition that take into account the importance of not only body fatness but also muscle mass.

7.4 Better characterisation of cancer-related outcomes

The diagnosis, characterisation and treatment of cancer is increasingly complex. Emerging understanding of molecular phenotypes enables definitions of cancers that go beyond simple anatomic classifications. Future study designs must accommodate and standardise the assessment of this phenotypic diversity so that disease endpoints are comparable. In addition, the current literature is not always consistent in the description and definition of cancer outcomes, including the genomic evolution of the tumour over time and with treatment.

Better characterisation of risk according to cancer subtypes, and studies that address the molecular variability of cancer as well as other outcomes, whether cancer-specific (for example, cancer incidence, progression and recurrence) or not (for example, other non-communicable diseases and quality of life), are therefore important.

7.5 Stronger evidence for the impact of diet, nutrition and physical activity on outcomes in cancer survivors

There is emerging but still limited data on the effect of diet, nutrition and physical activity in cancer survivors, regarding outcomes, including prognosis and quality of life during and after treatment. In addition, the review of the evidence for breast cancer survivors has identified various research gaps in terms of the quality of the studies to address each phase of survival and across diverse cancer types and subtypes (see **Section 4.4: Research gaps in cancer survivors** of this Summary).

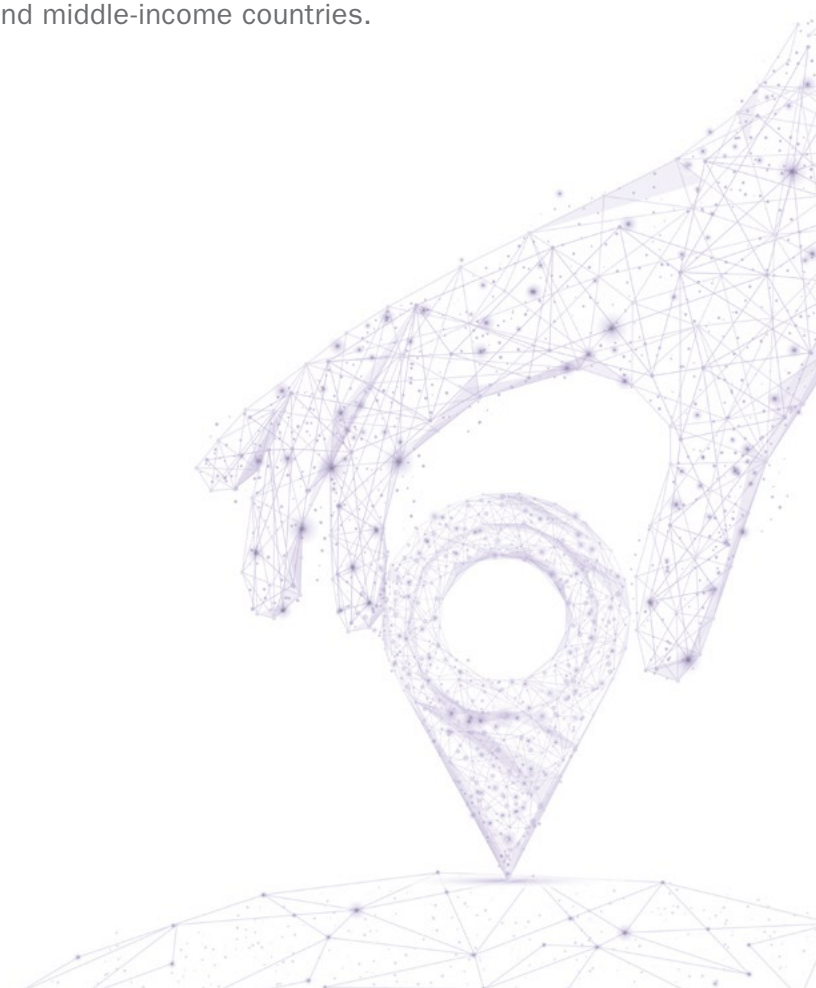
Diet, nutrition and physical activity, and their interplay with genetic, epigenetic and hormonal factors, may play an important role in influencing response to and side effects from treatment, quality of life during and after treatment, and risk of metastasis and recurrence, as well as overall and cancer-specific mortality. More research is critically needed in this area.

7.6 Globally representative research on specific exposures and cancer

The majority of epidemiological studies are conducted in high-income countries such as the UK, the USA and Australia. There is limited or no data from some countries, especially low- and middle-income countries. Most of the evidence has been based on studies conducted in populations of European ancestry and some in Asian populations. However, there is a need for research comparing associations by ethnicity and by genetic ancestry.

Patterns of cancer incidence and prevalence vary considerably according to geographical region. Furthermore, some strong evidence for particular exposures and cancers is relevant only to specific geographic regions, such as the relationship between liver cancer and exposure to aflatoxins in parts of Africa and Asia.

Both observations make the case for future studies to address the lack of data from low- and middle-income countries.



Conclusions

The publication of the Third Expert Report, including this Summary, is an important milestone in the life of the Continuous Update Project (CUP). Like its predecessors, the Third Expert Report provides a comprehensive analysis, using the most meticulous methods, of the current state of the evidence on preventing and surviving cancer through diet, nutrition, maintaining a healthy weight and physical activity, and presents the latest Cancer Prevention Recommendations.

This landmark achievement has been made possible by the significant efforts of large numbers of people from around the world; many others have a role in helping to maximise the impact of those efforts for the ultimate benefit of all (see **Box 10**).

The Cancer Prevention Recommendations provide a tangible way to reduce the incidence of cancer by helping people to maintain a healthy weight and adopt healthy patterns of eating, drinking and physical activity throughout life, and by informing policy action. The Recommendations are for use by individuals, researchers, medical and health professionals, policymakers, civil society organisations and other cancer organisations, as well as the media.

A significant body of evidence suggests that following the Recommendations works in real life. Studies evaluating adherence to the Cancer Prevention Recommendations from the last Expert Report, published in 2007, have shown that the more people adhere to the Recommendations, the greater the reductions in the risk of some specific cancers, of cancer as a whole and of death [1–3]. Moreover, these studies have shown that benefits extend beyond cancer to other non-communicable diseases.

Box 10: The benefits of working in partnership

The landmark publication of the Third Expert Report has been made possible by the collective efforts of many people around the world. Others, not directly involved in the production of this Report but who share the goals of preventing cancer and improving cancer survival, also have a role to play.

Disseminating findings, promoting the Recommendations and guiding future research

WCRF and AICR are committed to disseminating the findings of this Third Expert Report, promoting the Cancer Prevention Recommendations and using the findings to help inform and guide future research.

Support in this effort is encouraged from the wider community of people with an interest in preventing cancer and improving survival, whether they be individuals, researchers, medical and health professionals, policymakers, civil society organisations and other cancer organisations, as well as the media. Together, our voice is louder, our reach is further and the benefits will be greater.

The publication of the Third Expert Report is part of an ongoing process. While the Cancer Prevention Recommendations offer broad health benefits right now, the Report has also revealed important gaps and inadequacies in the evidence that can help the research community and funding organisations by guiding plans for future studies.

It is worth emphasising the importance of considering how different overall patterns of diet and physical activity combine to create a metabolic state that is more, or less, conducive to the development of cancer (rather than focusing on singular effects of specific dietary factors such as individual foods).

The future holds promise of greater understanding of how diet, nutrition and physical activity can influence the risk of cancer and its progression, as well as its role in the care and management of those living with and beyond cancer. The greatest benefit for public health and for cancer survivors will come from collaborative efforts of all stakeholders (see **Box 10**).

This Third Expert Report offers the most robust basis for a future where avoidable cancers are minimised, and where the public and cancer survivors, and those caring for them, know how they can best adapt their ways of living to reduce cancer risk and improve outcome and quality of life after diagnosis.

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Abbreviations

AICR	American Institute for Cancer Research
BMI	Body mass index
CHD	Coronary heart disease
CUP	Continuous Update Project
CVD	Cardiovascular disease
DNA	Deoxyribonucleic acid
HCAs	Heterocyclic amines
IARC	International Agency for Research on Cancer
IGF-I	insulin-like growth factor 1
MAPK	mitogen-activated protein kinase
mTOR	mechanistic/mammalian target of rapamycin
NCDs	Non-communicable diseases
PAHs	Polycyclic aromatic hydrocarbons
RCT	Randomised control trial
RNS	Reactive nitrogen species
ROS	Reactive oxygen species
SLR	Systematic literature review
VEGF	Vascular endothelial growth factor
WCRF	World Cancer Research Fund
WHO	World Health Organization

Glossary

Acetaldehyde

The major metabolic product of ethanol, which is generated by ethanol dehydrogenase and subsequently metabolised to acetate by aldehyde dehydrogenase.

Adenine

A purine derivative and one of the four possible nitrogenous bases in nucleotides and nucleic acids (DNA and RNA). Base pairs with thymine.

Adenocarcinoma

Cancer of glandular epithelial cells.

***Adenomatous polyposis coli (APC)* gene**

A gene that provides instructions for making the APC protein, which plays a critical role in several cellular processes. The protein acts as a tumour suppressor, keeping cells from growing and dividing too fast or in an uncontrolled way.

Adipocytes

Cells of adipose tissue, where fats (triglycerides) are stored.

Adipose tissue

Body fat. Tissue comprising mainly cells containing triglyceride (adipocytes). It acts as an energy reserve, provides insulation and protection, and secretes metabolically active hormones.

Adiposity

The degree of body fatness; can be measured indirectly in a variety of ways including body mass index (see **body mass index**) and percentage body fat.

Aflatoxins

Naturally occurring mycotoxins that are produced by many species of Aspergillus, a fungus, most notably Aspergillus flavus and Aspergillus parasiticus. Aflatoxins are toxic and carcinogenic to animals, including humans.

Alcohol

An organic compound that contains a hydroxyl group bound to a carbon atom. Releases energy when metabolised in the body. Commonly ethanol C_6H_5OH.

Angiogenesis

The process of generating new blood vessels.

Anthropogenic

Originating in human activity, usually related to environmental pollution and pollution.

Anthropometric measures
Measures of body dimensions.

Apoptosis
The death of cells that occurs as a normal and controlled part of the cell cycle.

Bias
In epidemiology, consistent deviation of an observed result from the true value in a particular direction (systematic error) due to factors pertaining to the observer or to the study type or analysis (see **selection bias**).

Bile
A greenish-yellow fluid secreted by the liver and stored in the gallbladder. Bile plays an important role in the intestinal absorption of fats. Bile contains cholesterol, bile salts, and waste products such as bilirubin.

Bioactive constituents
Compounds that have an effect on a living organism, tissue or cell. In nutrition, bioactive compounds are distinguished from nutrients.

Bioactivity
The effect of a given agent on a living organism or on living tissue.

Biological mechanisms
System of causally interacting processes that produce one or more effects.

Body composition
The composition of the body in terms of the relative proportions of water and adipose and lean tissue. Can also be described as the proportions of fat (lipid) and fat-free mass. May also include the content of micronutrients, such as iron, and the distribution of adipose tissue, for example, central/peripheral or visceral/subcutaneous.

Body mass index (BMI)
Body weight expressed in kilograms divided by the square of height expressed in metres (BMI = kg/m^2). Provides an indirect measure of body fatness.

C-reactive protein
A specific protein whose concentration in the blood rises in response to inflammation.

Caffeine
An alkaloid found in coffee, tea, kola nuts, chocolate, and other foods that acts as a stimulant and a diuretic.

Calcium
An essential nutrient for many regulatory processes in all living cells, in addition to playing a structural role in the skeleton. Calcium plays a critical role in the complex hormonal and nutritional

regulatory network related to vitamin D metabolism, which maintains the serum concentration of calcium within a narrow range while optimising calcium absorption to support host function and skeletal health.

Cancer
Any disorder of cell growth that results in the invasion and destruction of surrounding healthy tissue by abnormal cells and which may spread to distant sites. Cancer cells arise from normal cells whose nature is permanently changed.

Carcinogen
Any substance or agent capable of causing cancer.

Carcinogenesis
The process by which a malignant tumour is formed.

Carcinoma
Malignant tumour derived from epithelial cells, usually with the ability to spread into the surrounding tissue (invasion) and produce secondary tumours (metastases).

Carotenoids
A diverse class of compounds providing colour to many plants. Carotenoids are often classified in two groups: as those providing the host with vitamin A, such as beta-carotene, and the non-pro-vitamin A carotenoids, such as lycopene, which provides the familiar red colour of tomatoes.

Case-control study
An epidemiological study in which the participants are chosen on the basis of their disease or condition (cases) or lack of it (controls), to test whether distant or recent history of an exposure such as tobacco smoking, genetic profile, alcohol consumption or dietary intake is associated with the disease.

Cell
Structural and functional unit of most living organisms. Can exist independently or as part of a tissue or organ.

Cell cycle
The highly regulated process by which cells replicate and divide, allowing tissues to grow and remain healthy.

Cell proliferation
An increase in the number of cells as a result of increased cell division.

Checkpoint
Point in the cell cycle of eukaryotic cells at which progress can be halted if the appropriate conditions are not met.

Chronic
Describing a condition or disease that is persistent or long lasting.

Cirrhosis
A condition in which normal liver tissue is replaced by scar tissue (fibrosis), with nodules of liver regenerative tissue.

Colon
Part of the large intestine extending from the caecum to the rectum.

Colonisation sites
The first site in a different organ from which the cancer originates that metastatic tissue colonises.

Colonocyte
An epithelial cell of the colon.

Compliance
The extent to which people such as study participants follow an allocated treatment programme.

Cytokines
Cell-signalling molecules that aid cell-to-cell communication in immune responses and stimulate the movement of cells toward sites of inflammation, infection and trauma.

Deoxyribonucleic acid (DNA)
The double-stranded, helical molecular chain found within the nucleus of each cell, which carries the genetic information.

Diet, nutrition and physical activity
In the CUP, these three exposures are taken to mean the following: **diet**, the food and drink people habitually consume, including dietary patterns and individual constituent nutrients as well as other constituents, which may or may not have physiological bioactivity in humans; **nutrition**, the process by which organisms obtain energy and nutrients (in the form of food and drink) for growth, maintenance and repair, often marked by nutritional biomarkers and body composition (encompassing body fatness); and **physical activity**, any body movement produced by skeletal muscles that requires energy expenditure.

Dietary fibre
Constituents of plant cell walls that are not digested in the small intestine. Several methods of analysis are used, which identify different components. The many constituents that are variously included in the definitions have different chemical and physiological features that are not easily defined under a single term. The different analytical methods do not generally characterise the physiological impact of foods or diets. Non-starch polysaccharides are a consistent feature and are fermented by colonic bacteria to produce energy and short chain fatty acids including butyrate. The term ‘dietary fibre’ is increasingly seen as a concept describing a particular aspect of some dietary patterns.

Dietary supplement
A substance, often in tablet or capsule form, which is consumed in addition to the usual diet. Dietary supplements typically refer to vitamins or minerals, though phytochemicals or other substances may be included.

DNA adduct
A chemical that binds to DNA. This distorts the DNA structure and disrupts its replication, increasing the likelihood of errors in DNA replication, subsequent mutations and possibly cancer.

Dose–response
A term derived from pharmacology that describes the degree to which an association or effect changes as the level of an exposure changes, for instance, intake of a drug or food.

Effect modification
Effect modification (or effect-measure modification) occurs when the effect of an exposure differs according to levels of another variable (the modifier).

Enabling characteristic
Property a cancer cell exhibits which facilitates the attainment and sustainment of the 'hallmarks of cancer'.

Endogenous
Substances or processes that originate from within an organism, tissue or cell.

Energy
Energy, measured as calories or joules, is required for all metabolic processes. Fats, carbohydrates, proteins, and alcohol from foods and drinks release energy when they are metabolised in the body.

Energy balance
The state in which the total energy absorbed from foods and drink equals total energy expended, for example, through basal metabolism and physical activity. Also the degree to which intake exceeds expenditure (positive energy balance) or expenditure exceeds intake (negative energy balance).

Enzyme
Protein that acts as a catalyst in biochemical reactions. Each enzyme is specific to a particular reaction or group of similar reactions. Many require the association of certain non-protein cofactors in order to function.

Epigenetics
Relating to the control of gene expression through mechanisms that do not depend on changes in the nucleotide sequence of DNA, for example, through methylation of DNA or acetylation of histone.

Essential nutrient
A substance that is required for normal metabolism that the body cannot synthesise at all or in sufficient amounts, and thus must be consumed.

Ethanol
An organic compound in which one of the hydrogen atoms of water has been replaced by an alkyl group. See **alcohol**.

Exposure
A factor to which an individual may be exposed to varying degrees, such as intake of a food, level or type of physical activity, or aspect of body composition.

Extracellular matrix
The material that surrounds cells in animal tissues. Contains an aqueous lattice of proteins and other molecules.

Familial
Relating to or occurring in a family or its members.

Fat
Storage lipids of animal tissues, mostly triglyceride esters. See **adipose tissue**.

Folate
A salt of folic acid. Present in leafy green vegetables, peas and beans, and fortified breads and cereals.

Free radicals
An atom or molecule or that has one or more unpaired electrons. A prominent feature of radicals is that they have high chemical reactivity, which explains their normal biological activities and how they inflict damage on cells. There are many types of radicals, but those of most importance in biological systems are derived from oxygen and known collectively as reactive oxygen species.

Functional capacity
The optimal or maximum level at which the body, organ or tissue can function.

Gene
Unit of heredity composed of DNA. Visualised as a discrete particle, occupying specific position (locus) on a chromosome, that determines a particular characteristic.

Gene expression
The manifestation of the effects of a gene by the production of the particular protein, polypeptide or type of RNA whose synthesis it controls. The transcription of individual genes can be ‘switched on’ or ‘switched off’ according to the needs and circumstances of the cell at a particular time.

Genetic code
Means by which genetic information in DNA is translated into the manufacture of specific proteins by the cell. Represented by codons, which take the form of a series of triplets of bases in DNA, from which is transcribed a complementary sequence of codons in messenger RNA. The sequence of these codons determines the sequence of amino acids during protein synthesis.

Genomic instability
Abnormal rate of genetic change in a cell population which becomes evident as proliferation continues.

Genotoxic
Referring to chemical agents that damage the genetic information within a cell, causing mutations, which may lead to cancer.

Glucose
A six-carbon sugar, the main product of photosynthesis, that is a major energy source for metabolic processes. It is broken down by glycolysis during cellular respiration.

Growth factors
Various chemicals, particularly polypeptides, that have a variety of important roles in the stimulation of cell growth and replication. They bind to cell surface receptors.

Guanosine
A nucleoside consisting of one guanine molecule linked to a ribose sugar molecule in DNA.

Hallmarks of cancer
Key phenotypic characteristics in structure and function that represent an essential part of the biology of a cancer cell.

Hepatitis
Inflammation of the liver, which can occur as the result of a viral infection or autoimmune disease, or because the liver is exposed to harmful substances, such as alcohol.

Heterocyclic amines (HCAs) and polycyclic aromatic hydrocarbons (PAHs)
Potentially carcinogenic chemicals formed when muscle meat, including beef, pork, fish or poultry, is cooked using high-temperature methods.

Heterogeneity
A measure of difference between the results of different studies addressing a similar question. In meta-analysis, the degree of heterogeneity may be calculated statistically using the I^2 test.

High-income countries
As defined by the World Bank, countries with an average annual gross national income per capita of US$12,236 or more in 2016. This term is more precise than and used in preference to ‘economically developed countries’.

Homeostasis
Regulation of an organism’s internal environment within a controlled range so that physiological processes can proceed at optimum rates.

Hormone
A substance secreted by specialised cells that affects the structure and/or function of cells or tissues in another part of the body.

Hyperinsulinemia
High blood concentrations of insulin.

Immune response
The production of antibodies or specialised cells, for instance, in response to foreign proteins or other substances.

Immune system
Complex network of cells, tissues, and organs that work together to defend against external agents such as microorganisms.

In vitro
Processes that occur outside the body, in a laboratory apparatus.

In vivo
Describing biological processes as they are observed to occur within living organisms.

Incidence rates
The number of new cases of a condition appearing during a specified period of time expressed relative to the size of the population; for example, 60 new cases of breast cancer per 100,000 women per year.

Inflammation
The immunologic response of tissues to injury or infection. Inflammation is characterised by accumulation of white blood cells that produce several bioactive chemicals (cytokines), causing redness, pain, heat and swelling. Inflammation may be acute (such as in response to infection or injury) or chronic (as part of several conditions, including obesity).

Insulin
A protein hormone secreted by the pancreas that promotes the uptake and utilisation of glucose, particularly in the liver and muscles. Inadequate secretion of, or tissue response to, insulin leads to diabetes mellitus.

Insulin resistance
A pathological condition in which cells fail to respond normally to the hormone insulin.

***KRAS* gene**
Provides instructions for making the K-Ras protein, which is involved in cell signalling pathways, cell growth, cell maturation and cell death. Mutated forms are associated with some cancers.

Lactation
The production and secretion of milk by the mammary glands.

Lipid peroxidation
The oxidative degradation of lipids. It is the process in which free radicals ‘steal’ electrons from the lipids in cell membranes, resulting in cell damage.

Low-income countries
As defined by the World Bank, countries with an average annual gross national income per capita of US$1,005 or less in 2016. This term is more precise than and used in preference to ‘economically developing countries’.

Macrophage
Large phagocytic cell forming part of the body's immune system. It can ingest pathogenic microorganisms or cell debris.

Malignancy
A tumour with the capacity to spread to surrounding tissue or to other sites in the body.

Mendelian randomisation
A method of using natural variation in genes of known function to mimic a potential causal effect of a modifiable exposure on disease. The design helps to avoid problems from reverse causation and confounding.

Metabolism
The sum of chemical reactions that occur within living organisms.

Metabolites
Various compounds that take part in or are formed by chemical, metabolic reactions.

Metastasis/metastatic spread
The spread of malignant cancer cells to distant locations around the body from the original site.

Micronutrient
Vitamins and minerals present in foods and required in the diet for normal body function in small quantities conventionally of less than 1 gram per day.

Mitogen-activated protein kinase (MAPK) pathway
A chain of proteins that transmits chemical signals from outside the cell to the cell's nucleus to activate transcription factors that control gene expression.

Mutation
A permanent change in the nucleotide sequence of the genome (an organism's complete set of DNA).

N-nitroso compound
A substance that may be present in foods treated with sodium nitrate, particularly processed meat and fish. It may also be formed endogenously, for example, from haem and dietary sources of nitrate and nitrite. N-nitroso compounds are known carcinogens.

Neutrophils
A type of white blood cell that fights infection by ingesting microorganisms and releasing enzymes that kill microorganisms.

Non-communicable diseases (NCDs)
Diseases which are not transmissible from person to person. The most common NCDs are cancer, cardiovascular disease, chronic respiratory diseases and diabetes.

Nucleotide
Organic compound consisting of a nitrogen-containing purine or pyrimidine base linked to a sugar (ribose or deoxyribose) and phosphate group.

Nutrient
A substance present in food and required by the body for maintenance of normal structure and function, and for growth and development.

Nutrition
Process by which organisms obtain energy and nutrients (in the form of food and drink) for growth, maintenance and repair.

Obesity
Excess body fat to a degree that increases the risk of various diseases. Conventionally defined as a BMI of 30kg/m^2 or more. Different cut-off points have been proposed for specific populations.

Oestradiol
The principal female sex hormone produced mainly by the ovaries before menopause and by adipose tissue after. It promotes the onset of secondary sexual characteristics and controls the menstrual cycle.

Oestrogen
The female sex hormones, produced mainly by the ovaries during reproductive life and also by adipose tissue.

Oxidative stress
Overproduction of reactive oxygen species that may damage tissues.

p53
A protein central to regulation of cell growth. Mutations of the p53 gene are important causes of cancer.

Pathogenesis
The origin and development of disease. The mechanisms by which causal factors increase the risk of disease.

Phase I metabolising enzyme
Enzymes in the first phase of detoxification (modification) that introduce reactive and polar groups.

Phase II metabolising enzyme
Enzymes in the second phase of detoxification (conjugation) that conjugate active substances from phase one to charged species that are more easily excreted, for example, in bile.

Phenotype
The observable characteristics displayed by an organism; depends on both the genotype (the genetic makeup of a cell) and environmental factors.

Physical activity
Any movement using skeletal muscles that requires more energy than resting.

Phytochemicals
Non-nutritive bioactive plant substances that may have biological activity in humans.

Policy
A course of action taken by a governmental body including, but not restricted to, legislation, regulation, guidelines, decrees, standards, programmes and fiscal measures. Policies have three interconnected and evolving stages: development, implementation and evaluation. Policy development is the process of identifying and establishing a policy to address a particular need or situation. Policy implementation is a series of actions taken to put a policy in place, and policy evaluation is the assessment of how the policy works in practice.

Prevalence
The total number of individuals who have a characteristic, disease or health condition at a specific time, related to the size of the population, for example, expressed as a percentage of the population.

Processed meat
Meats transformed through salting, curing, fermentation, smoking or other processes to enhance flavour or improve preservation.

Proliferation
Increase in the number of cells, for example, in a tissue.

Protein
Polymer of amino acids linked by peptide bonds in a sequence specified by mRNA with a wide variety of specific functions including acting as enzymes, antibodies, storage proteins and carrier proteins.

Randomised controlled trial (RCT)
A study in which a comparison is made between one intervention (often a treatment or prevention strategy) and another (control). Sometimes the control group receives an inactive agent (a placebo). Groups are randomised to one intervention or the other, so that any difference in outcome between the two groups can be ascribed with confidence to the intervention. Sometimes, neither investigators nor subjects know to which intervention they have been randomised; this is called ‘double-blinding’.

Reactive nitrogen species (RNS)
Nitrogen-containing radical species or reactive ions, such as nitric oxide (NO) and peroxynitrite (ONOO-), which are able to damage DNA, such as by inducing DNA strand breaks or base modifications.

Reactive oxygen species (ROS)
Oxygen-containing radical species or reactive ions that can oxidise DNA (remove electrons), for example, hydroxyl radical (OH–), hydrogen peroxide (H_2O_2) or superoxide radical (O^2–).

Resilience
Property of a tissue or of a body to resume its former condition after being stressed or disturbed.

Retinoid
Compounds chemically related to or derived from vitamin A. They may be used for treatment of some cancers.

Selection bias
Bias arising from the procedures used to select study participants and from factors influencing participation.

Statistical power
The power of any test of statistical significance, defined as the probability that it will reject a false null hypothesis.

Stem cell
Cell that is not differentiated but can undergo unlimited division to form other cells, which can either remain stem cells or differentiate to form specialised cells.

Stress
A state of physiological or psychological strain caused by adverse stimuli that tends to disturb the functioning of an organism.

Stromal cells
Connective tissue cells of an organ.

Systematic literature review (SLR)
A means of compiling and assessing published evidence that addresses a scientific question with a predefined protocol and transparent methods.

Systemic
Describing something that occurs throughout the body, not just locally.

Tissue
A collection of one or more types of cells of similar structure organised to carry out particular functions.

Tumorigenesis
The process of tumour development.

Tumour
A mass of neoplastic and other cells.

Visceral obesity
Form of obesity due to excessive deposition of fat in the omentum and around the abdominal viscera, rather than subcutaneously (peripheral obesity). Poses a greater risk of diabetes mellitus, hypertension, metabolic syndrome and cardiovascular disease than peripheral obesity.

Vitamin
One of a number of organic compounds required from food or drinks by living organisms in relatively small amounts to maintain normal structural function.

References

1. Romaguera D, Vergnaud AC, Peeters PH, *et al.* Is concordance with World Cancer Research Fund/American Institute for Cancer Research guidelines for cancer prevention related to subsequent risk of cancer? Results from the EPIC study. *Am J Clin Nutr* 2012; 96(1): 150–163.
2. Kohler LN, Garcia DO, Harris RB, *et al.* Adherence to diet and physical activity cancer prevention guidelines and cancer outcomes: a systematic review. *Cancer Epidemiol Biomarkers Prev* 2016; 25: 1018–28.
3. Vergnaud AC, Romaguera D, Peeters PH, *et al.* Adherence to the World Cancer Research Fund/American Institute for Cancer Research guidelines and risk of death in Europe: results from the European Prospective Investigation into Nutrition and Cancer cohort study. *Am J Clin Nutr* 2013; 97: 1107–20.
4. Ervik M, Lam F, Ferley J, *et al. Cancer Today*. 2016. International Agency for Research on Cancer. Accessed 23/06/2017; available from http://gco.iarc.fr/today
5. Townsend N, Wilson L, Bhatnagar P, *et al.* Cardiovascular disease in Europe: epidemiological update 2016. *Eur Heart J* 2016; 37: 3232–45.
6. Canadian Cancer Statistics Advisory Committee. *Canadian Cancer Statistics*. 2017. Canadian Cancer Society. Accessed 20/09/2017; available from cancer.ca/Canadian-Cancer-Statistics-2017-EN.pdf
7. Torre LA, Siegel RL, Ward EM, *et al.* Global cancer incidence and mortality rates and trends – an update. *Cancer Epidemiol Biomarkers Prev* 2016; 25: 16–27.
8. Allemani C, Weir HK, Carreira H, *et al.* Global surveillance of cancer survival 1995–2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). *Lancet* 2015; 385: 977–1010.
9. Jemal A Vineis P, Bray F, *et al. The Cancer Atlas, Second Edition*. 2014. American Cancer Society. Accessed 23/06/2017; available from http://canceratlas.cancer.org/the-burden/cancer-survivorship/
10. Bloom DE, Cafiero ET, Jan-Llopis E, *et al. The Global Economic Burden of Noncommunicable Diseases: A Report by the World Economic Forum and the Harvard School of Public Health*. 2011.
11. Kankeu HT, Saksena P, Xu K, *et al.* The financial burden from non-communicable diseases in low- and middle-income countries: a literature review. *Health Res Policy Syst* 2013; 11: 31.
12. World Health Organization (WHO). *Cancer Prevention*. Accessed 15/06/2017; available from http://www.who.int/cancer/prevention/en/
13. Hanahan D and Weinberg RA. Hallmarks of cancer: the next generation. *Cell* 2011; 144: 646–74.
14. National Cancer Institute. *Causes and Prevention: The Genetics of Cancer*. 2017. Accessed 05/03/2018; available from https://www.cancer.gov/about-cancer/causes-prevention/genetics
15. International Agency for Research on Cancer (IARC). *List of Classifications by Cancer Sites with Sufficient or Limited Evidence in Humans: Volumes 1–120*. Accessed 20/11/2017; available from http://monographs.iarc.fr/ENG/Classification/Table4.pdf
16. Sheweita SA and Tilmisany AK. Cancer and phase II drug-metabolizing enzymes. *Curr Drug Metab* 2003; 4: 45–58.
17. Jackson SP and Bartek J. The DNA-damage response in human biology and disease. *Nature* 2009; 461: 1071–8.
18. Norbury CJ and Zhivotovsky B. DNA damage-induced apoptosis. *Oncogene* 2004; 23: 2797.
19. Wiseman H and Halliwell B. Damage to DNA by reactive oxygen and nitrogen species: role in inflammatory disease and progression to cancer. *Biochem J* 1996; 313 (Pt 1): 17–29.
20. Aguilera A and Gomez-Gonzalez B. Genome instability: a mechanistic view of its causes and consequences. *Nat Rev Genet* 2008; 9: 204–17.
21. Negrini S, Gorgoulis VG and Halazonetis TD. Genomic instability – an evolving hallmark of cancer. *Nat Rev Mol Cell Biol* 2010; 11: 220–8.
22. Albano E. Alcohol, oxidative stress and free radical damage. *Proc Nutr Soc* 2006; 65: 278–90.
23. NCD Risk Factor Collaboration. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet* 2017; 390: 2627–42.
24. Quail DF, Olson OC, Bhardwaj P, *et al.* Obesity alters the lung myeloid cell landscape to enhance breast cancer metastasis through IL5 and GM-CSF. *Nat Cell Biol* 2017; 19: 974–87.109

25. O'Flanagan CH, Rossi EL, McDonell SB, *et al.* Metabolic reprogramming underlies metastatic potential in an obesity-responsive murine model of metastatic triple negative breast cancer. *NPJ Breast Cancer* 2017; 3: 26.

26. Hoffmeister M, Blaker H, Kloor M, *et al.* Body mass index and microsatellite instability in colorectal cancer: a population-based study. *Cancer Epidemiol Biomarkers Prev* 2013; 22: 2303–11.

27. Amankwah EK, Friedenreich CM, Magliocco AM, *et al.* Anthropometric measures and the risk of endometrial cancer, overall and by tumor microsatellite status and histological subtype. *Am J Epidemiol* 2013; 177: 1378–87.

28. Donohoe CL, Lysaght J, O'Sullivan J, *et al.* Emerging concepts linking obesity with the hallmarks of cancer. *Trends Endocrinol Metab* 2017; 28: 46–62.

29. Chan DS, Bandera EV, Greenwood DC, *et al.* Circulating c-reactive protein and breast cancer risk: systematic literature review and meta-analysis of prospective cohort studies. *Cancer Epidemiol Biomarkers Prev* 2015; 24: 1439–49.

30. Heikkila K, Ebrahim S and Lawlor DA. A systematic review of the association between circulating concentrations of C reactive protein and cancer. *J Epidemiol Community Health* 2007; 61: 824–33.

31. Lippmann D, Lehmann C, Florian S, *et al.* Glucosinolates from pak choi and broccoli induce enzymes and inhibit inflammation and colon cancer differently. *Food Funct* 2014; 5: 1073–81.

32. Gilsing AM, Franssen F, de Kok TM, *et al.* Dietary heme iron and the risk of colorectal cancer with specific mutations in KRAS and APC. *Carcinogenesis* 2013; 34: 2757–66.

33. Seitz HK and Stickel F. Molecular mechanisms of alcohol-mediated carcinogenesis. *Nat Rev Cancer* 2007; 7: 599–612.

34. Boffetta P and Hashibe M. Alcohol and cancer. *Lancet Oncol* 2006; 7: 149–56.

35. Hankinson SE, Willett WC, Manson JE, *et al.* Alcohol, height, and adiposity in relation to estrogen and prolactin levels in postmenopausal women. *J Natl Cancer Inst* 1995; 87: 1297–302.

36. Key TJ, Appleby PN, Reeves GK, *et al.* Circulating sex hormones and breast cancer risk factors in postmenopausal women: reanalysis of 13 studies. *Br J Cancer* 2011; 105: 709–22.

37. Gunter MJ, Hoover DR, Yu H, *et al.* Insulin, insulin-like growth factor-I and risk of breast cancer in postmenopausal women. *J Natl Cancer Inst* 2009; 101: 48–60.

38. McTiernan A. Mechanisms linking physical activity with cancer. *Nat Rev Cancer* 2008; 8: 205–11.

39. Choudhury F, Bernstein L, Hodis HN, *et al.* Physical activity and sex hormone levels in estradiol- and placebotreated postmenopausal women. *Menopause* 2011; 18: 1079–86.

40. Oh H, Arem H, Matthews CE, *et al.* Sitting, physical activity, and serum oestrogen metabolism in postmenopausal women: the Women's Health Initiative Observational Study. *Br J Cancer* 2017; 117: 1070–8.

41. Friedenreich CM, Neilson HK and Lynch BM. State of the epidemiological evidence on physical activity and cancer prevention. *Eur J Cancer* 2010; 46: 2593–604.

42. Bray I, Gunnell D, Holly JM, *et al.* Associations of childhood and adulthood height and the components of height with insulin-like growth factor levels in adulthood: a 65-year follow-up of the Boyd Orr cohort. *J Clin Endocrinol Metab* 2006; 91: 1382–9.

43. Gunnell D, Okasha M, Smith GD, *et al.* Height, leg length, and cancer risk: a systematic review. *Epidemiol Rev* 2001; 23: 313–42.

44. Albanes D, Jones DY, Schatzkin A, *et al.* Adult stature and risk of cancer. *Cancer Research* 1988; 48: 1658–62.

45. Hill AB. The environment and disease: association or causation? *Proc R Soc Med* 1965; 58: 295–300.

46. World Health Organization (WHO). *Global Database on Body Mass Index: BMI classification*. 2017. Accessed 28/09/2017; available from http://apps.who.int/bmi/index.jsp?introPage=intro_3.html

47. World Health Organization (WHO). *Child Growth Standards*. 2017. Accessed 2017 20/11/2017; available from http://www.who.int/childgrowth/standards/chts_bfa_girls_z/en/

48. World Health Organization (WHO). *Waist Circumference and Waist-Hip Ratio: Report of a WHO Expert Consultation*. 2008.

49. Lauby-Secretan B, Scoccianti C, Loomis D, *et al.* Body fatness and cancer – viewpoint of the IARC Working Group. *N Engl J Med* 2016; 375: 794–8.

50. Singh GM, Danaei G, Farzadfar F, *et al.* The age-specific quantitative effects of metabolic risk factors on cardiovascular diseases and diabetes: a pooled analysis. *PLoS One* 2013; 8: e65174.

51. Wormser D, Kaptoge S, Di Angelantonio E, *et al.* Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. *Lancet* 2011; 377: 1085–95.

52. Jiang L, Rong J, Wang Y, *et al.* The relationship between body mass index and hip osteoarthritis: a systematic review and meta-analysis. *Joint Bone Spine* 2011; 78: 150–5.

53. Jiang L, Tian W, Wang Y, *et al.* Body mass index and susceptibility to knee osteoarthritis: a systematic review and meta-analysis. *Joint Bone Spine* 2012; 79: 291–7.

54. Vernon G, Baranova A and Younossi ZM. Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. *Aliment Pharmacol Ther* 2011; 34: 274–85.

55. World Health Organization (WHO). *Factsheet: Physical Activity and Adults*. 2017. Accessed 28/09/2017; available from http://www.who.int/dietphysicalactivity/factsheet_adults/en/

56. Saris WH, Blair SN, van Baak MA, *et al.* How much physical activity is enough to prevent unhealthy weight gain? Outcome of the IASO 1st Stock Conference and consensus statement. *Obes Rev* 2003; 4: 101–14.

57. World Health Organization (WHO). *Global Recommendations on Physical Activity for Health: 5–17 years old*. 2010.

58. Sadeghirad B, Duhaney T, Motaghipisheh S, *et al.* Influence of unhealthy food and beverage marketing on children's dietary intake and preference: a systematic review and meta-analysis of randomized trials. *Obes Rev* 2016; 17: 945–59.

59. Boyland EJ, Nolan S, Kelly B, *et al.* Advertising as a cue to consume: a systematic review and meta-analysis of the effects of acute exposure to unhealthy food and nonalcoholic beverage advertising on intake in children and adults. *Am J Clin Nutr* 2016; 103: 519–33.

60. Salmon J, Campbell KJ and Crawford DA. Television viewing habits associated with obesity risk factors: a survey of Melbourne schoolchildren. *Med J Aust* 2006; 184: 64–7.

61. Coon KA and Tucker KL. Television and children's consumption patterns. A review of the literature. *Minerva Pediatr* 2002; 54: 423–36.

62. Pearson N and Biddle SJ. Sedentary behavior and dietary intake in children, adolescents, and adults: a systematic review. *Am J Prev Med* 2011; 41: 178–88.

63. Marsh S, Ni Mhurchu C and Maddison R. The non-advertising effects of screen-based sedentary activities on acute eating behaviours in children, adolescents, and young adults: a systematic review. *Appetite* 2013; 71: 259–73.

64. Lee IM, Shiroma EJ, Lobelo F, *et al.* Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet* 2012; 380: 219–29.

65. Kohl HW, 3rd, Craig CL, Lambert EV, *et al.* The pandemic of physical inactivity: global action for public health. *Lancet* 2012; 380: 294–305.

66. Arem H, Moore SC, Patel A, *et al.* Leisure time physical activity and mortality: a detailed pooled analysis of the dose-response relationship. *JAMA Intern Med* 2015; 175: 959–67.

67. Piepoli MF, Hoes AW, Agewall S, *et al.* 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J* 2016; 37: 2315–81.

68. Masala G, Bendinelli B, Occhini D, *et al.* Physical activity and blood pressure in 10,000 Mediterranean adults: The EPIC-Florence cohort. *Nutr Metab Cardiovasc Dis* 2017; 27: 670–8.

69. Wendel-Vos GC, Schuit AJ, Feskens EJ, *et al.* Physical activity and stroke. A meta-analysis of observational data. *Int J Epidemiol* 2004; 33: 787–98.

70. Ford ES, Kohl HW, 3rd, Mokdad AH, *et al.* Sedentary behavior, physical activity, and the metabolic syndrome among U.S. adults. *Obes Res* 2005; 13: 608–14.

71. Rebar AL, Stanton R, Geard D, *et al.* A meta-meta-analysis of the effect of physical activity on depression and anxiety in non-clinical adult populations. *Health Psychol Rev* 2015; 9: 366–78.

72. Cosman F, de Beur SJ, LeBoff MS, *et al.* Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int* 2014; 25: 2359–81.

73. Boeing H, Bechthold A, Bub A, *et al.* Critical review: vegetables and fruit in the prevention of chronic diseases. *Eur J Nutr* 2012; 51: 637–63.

74. Li M, Fan Y, Zhang X, *et al.* Fruit and vegetable intake and risk of type 2 diabetes mellitus: meta-analysis of prospective cohort studies. *BMJ Open* 2014; 4: e005497.

75. Miller V, Mente A, Dehghan M, *et al.* Fruit, vegetable, and legume intake, and cardiovascular disease and deaths in 18 countries (PURE): a prospective cohort study. *Lancet* 2017; 390: 2037–49.

76. Popkin BM, Adair LS and Ng SW. Now and then: the global nutrition transition: the pandemic of obesity in developing countries. *Nutr Rev* 2012; 70: 3–21.

77. U.S. Department of Health and Human Services and U.S. Department of Agriculture. *2015–2020 Dietary Guidelines for Americans. 8th Edition*. December 2015.

78. Davey GK, Spencer EA, Appleby PN, *et al.* EPIC-Oxford: lifestyle characteristics and nutrient intakes in a cohort of 33 883 meat-eaters and 31 546 non meat-eaters in the UK. *Public Health Nutr* 2003; 6: 259–69.

79. Pan A, Sun Q, Bernstein AM, *et al.* Red meat consumption and mortality: results from 2 prospective cohort studies. *Arch Intern Med* 2012; 172: 555–63.

80. Yang C, Pan L, Sun C, *et al.* Red meat consumption and the risk of stroke: a dose-response meta-analysis of prospective cohort studies. *J Stroke Cerebrovasc Dis* 2016; 25: 1177–86.

81. Pan A, Sun Q, Bernstein AM, *et al.* Red meat consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. *Am J Clin Nutr* 2011; 94: 1088–96.

82. Scientific Advisory Committee on Nutrition. Iron and Health. 2010. Public Health England. Accessed 30/01/2017; available from https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/339309/SACN_Iron_and_Health_Report.pdf

83. European Food Safety Authority Panel on Dietetic Products Nutrition and Allergies. Scientific opinion on the safety of caffeine. *EFSA Journal* 2015. European Food Safety Authority (EFSA). Accessed 30/01/2017; available from http://www.efsa.europa.eu/sites/default/files/consultation/150115.pdf

84. Popkin BM and Hawkes C. Sweetening of the global diet, particularly beverages: patterns, trends, and policy responses. *Lancet Diabetes Endocrinol* 2016; 4: 174–86.

85. Malik VS. Sugar sweetened beverages and cardiometabolic health. *Curr Opin Cardiol* 2017; 32: 572–9.

86. Scientific Advisory Committee on Nutrition. *Carbohydrates and Health*. 2015. Public Health England. Accessed 30/01/2017; available from https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/445503/SACN_Carbohydrates_and_Health.pdf

87. Department of Health. UK Chief Medical Officers' Low Risk Drinking Guidelines. 2016. Accessed 30/01/2017; available from https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/545937/UK_CMOs__report.pdf

88. Parry CD, Patra J and Rehm J. Alcohol consumption and non-communicable diseases: epidemiology and policy implications. *Addiction* 2011; 106: 1718–24.

89. Adolescent Division of the Ministry of Health and Family Welfare (MoHFW). National Iron-plus Initiative Guidelines for Control of Iron Deficiency Anemia. 2013. Government of India. Accessed 30/01/2017; available from https://www.nhm.gov.in/images/pdf/programmes/child-health/guidelines/Control-of-Iron-Deficiency-Anaemia.pdf

90. Development Initiatives. *Global Nutrition Report 2017: Nourishing the SDGs*. 2017. Accessed 29/09/2017; available from https://www.globalnutritionreport.org/files/2017/11/Report_2017.pdf

91. World Health Organization (WHO). Global Health Observatory Data Repository: Infant Nutrition – Data by World Bank income group. 2017. Accessed 28/09/2017; available from http://apps.who.int/gho/data/view.maineuro.1720?lang=en

92. World Health Organization (WHO). Global Health Observatory Data Repository: Infant Nutrition – Data by Country 2017. Accessed 28/09/2017; available from http://apps.who.int/gho/data/node.main.52?lang=en

93. World Health Organization (WHO). Infant and Young Child Feeding: Model Chapter for Textbooks for Medical Students and Allied Health Professionals. Session 2 – The physiological basis of breastfeeding. 2009. Accessed 30/09/2017; available from https://www.ncbi.nlm.nih.gov/books/NBK148970/

94. World Health Organization/UNICEF. Guideline: Updates on HIV and infant feeding: the duration of breastfeeding, and support from health services to improve feeding practices among mothers living with HIV. 2016.

95. World Health Organization (WHO). *Global Nutrition Targets 2025:* Policy brief series. 2014. Accessed 13/06/2017; available from http://www.who.int/nutrition/global-target-2025/en/

96. Stuebe A. The risks of not breastfeeding for mothers and infants. *Rev Obstet Gynecol* 2009; 2: 222–31.

97. Victora CG, Bahl R, Barros AJD, *et al.* Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *Lancet* 2016; 387: 475–90.

98. International Agency for Research on Cancer (IARC). IARC *Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 100, Part C: Arsenic, metals, fibres and dusts*. 2012.

99. FAO/World Health Organization. *Summary of Evaluations Performed by the Joint FAO/WHO Expert Committee on Food Additives*. 2006.

100. World Health Organization (WHO). *WHO Framework on Convention on Tobacco Control*. 2005. Accessed 10/08/2017; available from http://apps.who.int/iris/bitstream/10665/42811/1/9241591013.pdf?ua=1

101. World Cancer Research Fund International/American Institute for Cancer Research. *Continuous Update Project: Diet, Nutrition, Physical Activity and the Prevention of Cancer. Summary of Strong Evidence*. 2017. Available from wcrf.org/cupmatrix

102. Roberto CA, Swinburn B, Hawkes C, *et al.* Patchy progress on obesity prevention: emerging examples, entrenched barriers, and new thinking. *Lancet* 2015; 385: 2400–9.

103. World Cancer Research Fund/American Institute for Cancer Research. *Policy and Action for Cancer Prevention. Food, Nutrition and Physical Activity: a Global Perspective*. 2009.

104. World Health Organization (WHO). *Global Action Plan for the Prevention and Control of Noncommunicable Diseases* 2013–2020. Accessed 23/06/2017; available from http://apps.who.int/iris/bitstream/10665/94384/1/9789241506236_eng.pdf?ua=1

105. World Health Organization (WHO). *Seventieth World Health Assembly, Provisional agenda item 15.1, Preparation for the third high-level meeting of the General Assembly on the prevention and control of non-communicable diseases, to be held in 2018, Annex 1, Draft updated Appendix 3 to the Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013–2020*. Accessed 10/08/2017; available from http://who.int/ncds/management/WHO_Appendix_BestBuys.pdf?ua=1

106. World Health Organization (WHO). *Noncommunicable Disease Progress Monitor 2015*. Accessed 04/07/2017; available from http://apps.who.int/iris/bitstream/10665/184688/1/9789241509459_eng.pdf?ua=1

107. United Nations. *Transforming Our World: The 2030 Agenda for Sustainable Development*. 2015. Accessed 23/06/2017; available from https://sustainabledevelopment.un.org/content/documents/21252030%20Agenda%20for%20Sustainable%20Development%20web.pdf

108. United Nations. World population projected to reach 9.8 billion in 2050, and 11.2 billion in 2100. 2017. United Nations Department of Economic and Social Affairs. Accessed 20/11/2017; available from https://www.un.org/development/desa/en/news/population/world-population-prospects-2017.html

109. Xia T, Zhang Y, Crabb S, *et al.* Cobenefits of replacing car trips with alternative transportation: a review of evidence and methodological issues. *J Environ Public Health* 2013; 2013: 14.

110. Hawkes C, Jewell J and Allen K. A food policy package for healthy diets and the prevention of obesity and diet related non-communicable diseases: the NOURISHING framework. *Obes Rev* 2013; 14 Suppl 2: 159–68.

111. World Cancer Research Fund International. *NOURISHING: Methods for Compiling and Updating the Database*. 2017. Accessed 14/06/2017; available from http://www.wcrf.org/int/policy/nourishing-framework/methodology

112. World Cancer Research Fund/American Institute for Cancer Research. *Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective*. Washington DC: AICR. 1997.

113. World Cancer Research Fund/American Institute for Cancer Research. *Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective*. Washington DC: AICR. 2007. Available from wcrf.org/about-the-report

114. Kwon OJ and Xin L. Prostate epithelial stem and progenitor cells. *Am J Clin Exp Urol* 2014; 2: 209–18.

115. Ingthorsson S, Briem E, Bergthorsson JT, *et al.* Epithelial plasticity during human breast morphogenesis and cancer progression. *J Mammary Gland Biol Neoplasia* 2016; 21: 139–48.

116. Donne ML, Lechner AJ and Rock JR. Evidence for lung epithelial stem cell niches. *BMC Dev Biol* 2015; 15: 32.

117. Roberts KJ, Kershner AM and Beachy PA. The stromal niche for epithelial stem cells: a template for regeneration and a brake on malignancy. *Cancer Cell* 2017; 32: 404–10.

118. Koelwyn GJ, Quail DF, Zhang X, *et al.* Exercise-dependent regulation of the tumour microenvironment. *Nat Rev Cancer* 2017; 17: 620–32.

119. DeGregori J. Connecting cancer to its causes requires incorporation of effects on tissue microenvironments. *Cancer Res* 2017; 77: 6065–8.

Our Cancer Prevention Recommendations

Be a healthy weight
Keep your weight within the healthy range and avoid weight gain in adult life

Be physically active
Be physically active as part of everyday life – walk more and sit less

Eat a diet rich in wholegrains, vegetables, fruit and beans
Make wholegrains, vegetables, fruit, and pulses (legumes) such as beans and lentils a major part of your usual daily diet

Limit consumption of 'fast foods' and other processed foods high in fat, starches or sugars
Limiting these foods helps control calorie intake and maintain a healthy weight

Limit consumption of red and processed meat
Eat no more than moderate amounts of red meat, such as beef, pork and lamb. Eat little, if any, processed meat

Limit consumption of sugar sweetened drinks
Drink mostly water and unsweetened drinks

Limit alcohol consumption
For cancer prevention, it's best not to drink alcohol

Do not use supplements for cancer prevention
Aim to meet nutritional needs through diet alone

For mothers: breastfeed your baby, if you can
Breastfeeding is good for both mother and baby

After a cancer diagnosis: follow our Recommendations, if you can
Check with your health professional what is right for you

Not smoking and avoiding other exposure to tobacco and excess sun are also important in reducing cancer risk.

Following these Recommendations is likely to reduce intakes of salt, saturated and trans fats, which together will help prevent other non-communicable diseases.

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