World Cancer Research Fund International

CUP GLOBAL
Cancer Update Programme

Unifying research on nutrition, physical activity and cancer

Diet, nutrition, physical activity and body weight for people living with and beyond colorectal cancer

The latest evidence, our guidance for patients, carers and health professionals, and recommendations for future research

American Institute for Cancer Research

World Cancer Research Fund

Wereld Kanker Onderzoek Fonds

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Introduction

This report:

- **Outlines the prevalence of colorectal cancer and the growing population of people surviving colorectal cancer**
- **Describes how we are developing guidance and recommendations in the Global Cancer Update Programme, including how we have incorporated input from health professionals and patients**
- **Reports the current evidence relating to the impact of diet, nutrition, physical activity and body weight on outcomes after a colorectal cancer diagnosis**
- **Reports the Global Cancer Update Programme expert panel judgements on the evidence in those living with and beyond colorectal cancer**
- **Discusses research gaps and recommendations for future research**
- **Presents guidance and makes recommendations for those living with and beyond colorectal cancer**

A separate review on the impact of diet, nutrition, physical activity and body weight and health-related quality of life and fatigue after a diagnosis of colorectal cancer was also conducted and will be reported separately.

This report focuses on those living with and beyond colorectal cancer, World Cancer Research Fund International has produced an accompanying report with guidance and recommendations for those living with and beyond breast cancer.

World Cancer Research Fund network

OUR VISION

Our vision is a world where no one develops a preventable cancer, and people living with and beyond cancer are enabled to live longer, healthier lives.

OUR MISSION

We champion the latest and most authoritative scientific research from around the world on cancer prevention and survival through diet, weight and physical activity, so that we can help people make informed lifestyle choices to reduce their cancer risk.

OUR NETWORK

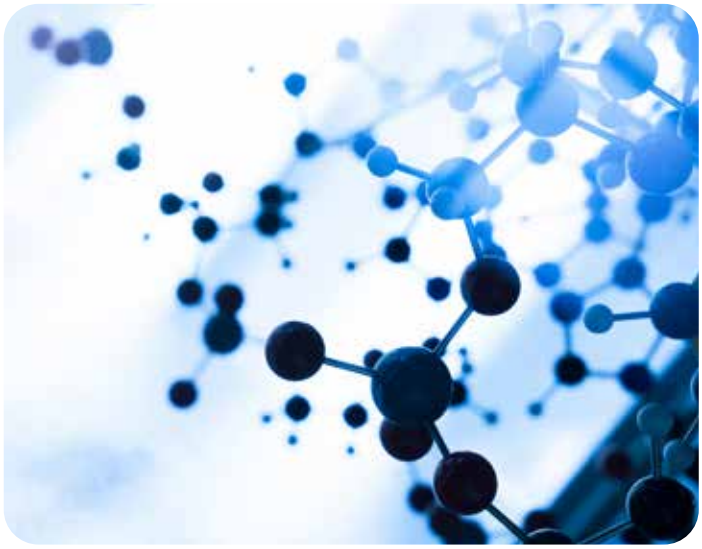
As an international network of charities, we've been funding life-saving research into cancer prevention and survival, influencing global healthcare policy, and educating the public since 1982. WCRF Network comprises: American Institute for Cancer Research (AICR) in the US, Wereld Kanker Onderzoek Fonds (WKOF) in the Netherlands, World Cancer Research Fund (WCRF) in the UK and a presence in Asia with a science ambassador based in Hong Kong. Together, we help people worldwide live longer, healthier lives, free from the devastating effects of cancer.

Global Cancer Update Programme

The Global Cancer Update Programme (CUP Global) analyses global research on how diet, nutrition, physical activity and body weight affect cancer risk and survival. It is produced by World Cancer Research Fund International (WCRF International) in partnership with American Institute for Cancer Research (AICR), World Cancer Research Fund in the UK (WCRF) and Wereld Kanker Onderzoek Fonds (WKOF) in the Netherlands.

This report is from WCRF International's CUP Global - the world's largest source of scientific research on cancer prevention and survivorship focused upon analysing the evidence related to diet, nutrition, physical activity and body weight. The research in this report builds on the 2018 report *Survivors of breast and other cancers* which was published as part of the Third Expert Report produced by WCRF/ AICR titled *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective* [1].

Many world-renowned experts contribute to CUP Global. An expert panel evaluates the strength of the evidence from systematic reviews, develops guidance and recommendations, makes recommendations for future research and provides input on the direction of the work. Topic-specific expertise for key areas of work is provided via expert committees; of particular relevance to the current report is the cancer survivors expert committee. Additional expertise is provided via formal observers to the panel, representing key organisations in the field (World Health Organization, International Agency for Research on Cancer, National Cancer Institute and Union for International Cancer Control). See page 33 for a full list of contributors to the work in this report.



Key aims of CUP Global

The transition period in 2020/21 enabled WCRF International to develop 7 key aims for the new programme of research under the new name of the Global Cancer Update Programme (CUP Global):

Development of population or disease-specific guidance and recommendations – for specific stages of life (eg children, young adults, older adults), specific populations (eg childhood and adult cancer survivors) and specific cancer subtypes (eg ER, PR positive and triple-negative breast cancer, Lynch syndrome, cancers with a genetic component vs sporadic).

Clarification of existing knowledge to develop greater understanding of cancer prevention and survivorship – eg the role and impact of specific dietary patterns, the biological mechanisms that cause or prevent cancer.

Efficient and targeted approaches and keeping the evidence current – eg through the application of automated approaches and analytical tools, and the use of a dedicated scanning exercise and data prioritisation (including rapid reviews) to target or trigger an evidence update.

Collaborations and input from experts and external stakeholders – utilising experts from across the world, as well as continuing to work in collaboration with the research team at Imperial College London.

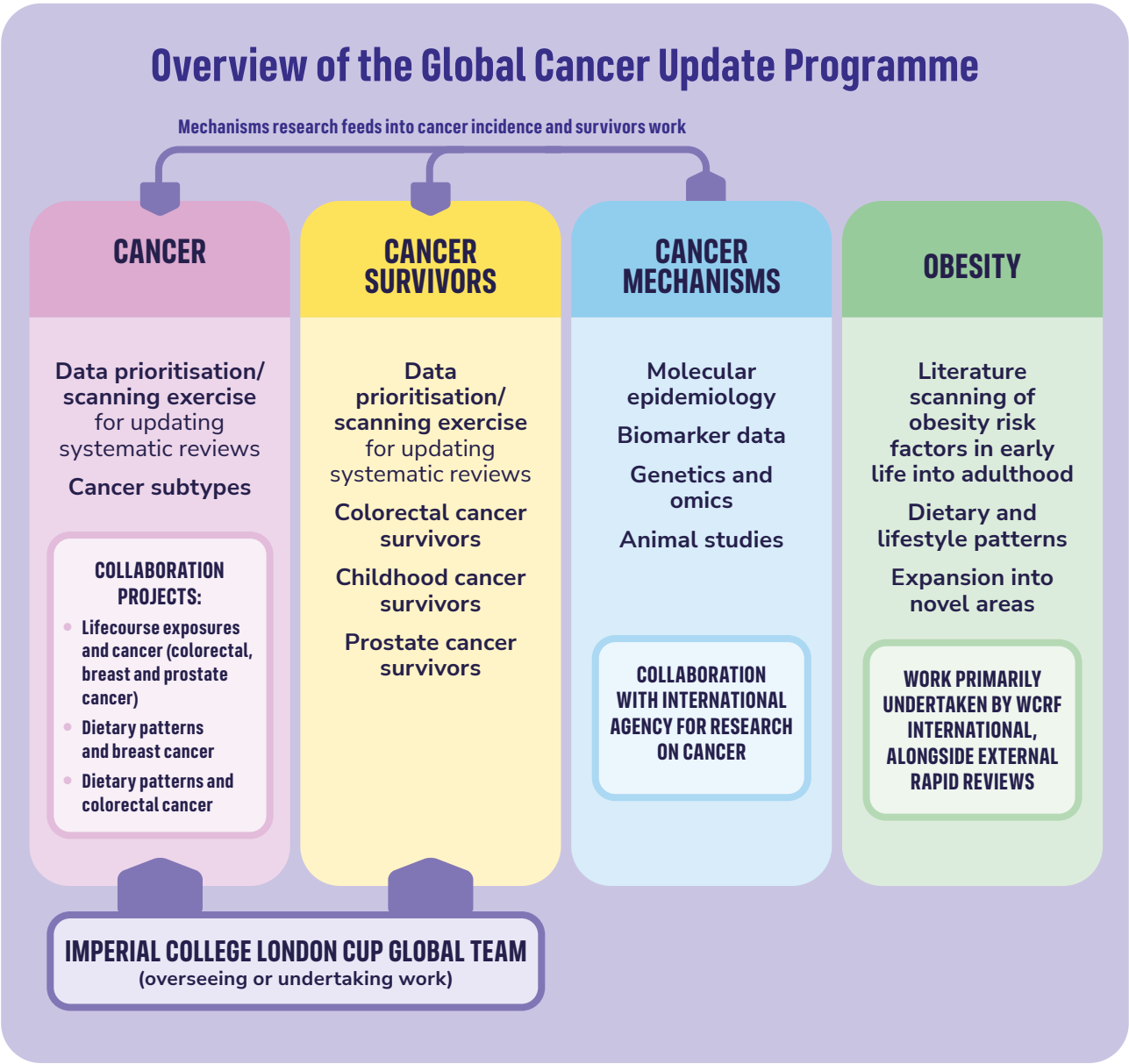
Varied and targeted outputs – to enable greater reach and scope within the scientific community (through academic papers), as well as targeted communications for other audiences (including dissemination events).

Globally representative research – most epidemiological studies are conducted in high-income countries, such as those in Europe, the US and Australia, with limited or no data from other countries, especially low- and middle-income countries. Cancer incidence and prevalence vary considerably according to geographical region, making the case for future CUP Global studies to address the limited data from low- and middle-income countries.

Strong public involvement – we recognise the importance of user involvement at all stages of the work, from identifying research priorities, promoting involvement in funded research and selecting successful research funding applications, to making recommendations and disseminating findings.

Areas of research focus in CUP Global

The current work is organised into 4 areas: cancer incidence, cancer survivors, cancer mechanisms and obesity. The mechanisms work supports the cancer incidence and survivors work through developing a clearer understanding of the biological processes that underpin associations between diet, nutrition, physical activity, body weight and cancer. This current report is part of the cancer survivors work area, with the systematic reviews conducted by the CUP Global team at Imperial College London.



Executive summary

Background

Colorectal cancer is the third most commonly diagnosed cancer globally, accounting for 1 in 10 (9.6%) new cancer cases worldwide in 2022. At the same time, progress in early detection and treatment has significantly increased the number of years lived after a diagnosis. Survival rates differ between countries, but worldwide there are an estimated 5 million people living with and beyond colorectal cancer. There is increasing demand for reliable, evidence-based guidance on diet and physical activity from health professionals and people living with and beyond cancer.

This report is from World Cancer Research Fund International's Global Cancer Update Programme (CUP Global) - the world's largest source of scientific research on cancer prevention and survivorship through diet, nutrition, physical activity and body weight. The research in this report builds on the 2018 report *Survivors of breast and other cancers* which was published as part of the Third Expert Report produced by WCRF/AICR on *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective*. At that time, research on cancer survival was limited, but there was enough evidence to conclude that people living with and beyond cancer should follow our Cancer Prevention Recommendations. These outline an integrated pattern of behaviours that the evidence consistently shows is linked to reduced cancer risk.

The increasing recognition of the importance of diet, nutrition, physical activity and body weight in cancer survival provides the rationale for the current work.

Aims of this report

This report summarises the latest research on diet, nutrition, physical activity and body weight for people living with and beyond colorectal cancer. It also presents guidance for patients and recommendations for future research. This information can be used to develop materials for those responsible for the care of patients and patients themselves. We intend for this work to supplement our existing Cancer Prevention Recommendations. Whilst we recommend that people living with and beyond cancer follow these as much as they can, they were not specifically developed for this group. Our new guidance adds to these recommendations by highlighting specific behaviours which evidence suggests may be beneficial for people living with and beyond colorectal cancer.

The evidence underpinning this report

The CUP Global research team at Imperial College London carried out a comprehensive analysis investigating the extent to which certain modifiable risk factors impact mortality (cancer-specific and all-cause) and risk of cancer recurrence in people after a colorectal cancer diagnosis. Three systematic reviews were carried out covering different exposures (diet, physical activity and sedentary behaviour, body weight). One review analysed data from 69 publications on diet and colorectal cancer outcomes, the review on physical activity and sedentary behaviour included 20 publications and the review on body weight included 85 publications.

An independent panel of experts graded the strength of the evidence from each review using WCRF International's pre-determined criteria to give a final evidence judgement for each exposure.

The panel judged the strength of much of the evidence as 'limited' which hampered the expert panel's ability to develop recommendations. Despite this, we consider it important that people living with and beyond cancer can access reliable information based on the latest evidence that has been judged by our expert panel. The guidance described here has been developed using a robust and transparent process, incorporating input from expert clinicians and scientists, along with user input from health professionals and patients.

As an evidence-based organisation, we have used the best available evidence to develop this process and produce practical guidance on diet, physical activity and body weight for people living with and beyond colorectal cancer.

Recommendations for future research

WCRF International, our panel of experts and the cancer survivors expert committee are continually discussing how the evidence base within survivorship research can be strengthened. We have agreed upon several key areas:

- Well-designed clinical trials and prospective cohorts are needed. These studies should account for differences in cancer sub-types, treatment types and other patient characteristics.

- Studies should aim to use the most accurate methods possible for assessing diet, nutrition, physical activity and body weight within populations living with and beyond cancer. They should include more accurate reporting of the timing of exposures.

- Novel methods for understanding the biological processes and mechanisms that underpin the associations we find in our cancer survivorship research are much needed.

- Research should aim to study more diverse populations.

By highlighting gaps in the evidence base, current research enables us to look to the future with insights on where further (high quality) research is needed. Observational studies can also help to identify promising exposures for testing in randomised-controlled trials. This allows us to develop new areas of investigation, with the aim of future new findings being used to develop specific recommendations for this group and to further confirm the benefits of following our recommendations and guidance.

Guidance for people living with and beyond colorectal cancer

The below guidance has been developed using the best available evidence and consultation with experts in the field and individuals living with and beyond colorectal cancer.

Evidence comes from the 3 systematic reviews described in the full report, along with previous evidence reviewed for the Third Expert Report which led to the development of WCRF/AICR's Cancer Prevention Recommendations.

Summary of our guidance for those living with and beyond colorectal cancer

EVIDENCE	GUIDANCE
General guidance **WCRF/AICR's recommendations for cancer prevention** Nutritional factors and physical activity appear to predict outcomes in people living with and beyond cancer, but there is insufficient evidence that changing these improves outcomes.	**We suggest that people consider following as many of WCRF/AICR's cancer prevention recommendations as they are able to.**
New specific guidance on physical activity **Physical activity** People who are more physically active have better health outcomes after a diagnosis of colorectal cancer, but it is uncertain whether increasing physical activity will improve these outcomes.	**We suggest that people consider increasing their physical activity. However, physical activity should be increased under the supervision of health care professionals.** Note: It may be particularly important for any increases in physical activity to be gradual, particularly for patients suffering from side-effects of their treatment surgery, or medication that may restrict their ability to be physically active, such as neuropathy or musculoskeletal issues.
New specific guidance on diet **Diet** ***Wholegrains*** People who eat more wholegrains have better health outcomes after a diagnosis of colorectal cancer. But it is uncertain that increasing wholegrains improves these outcomes.	**We suggest that people consider increasing their wholegrain intake.** Note: Some patients may report difficulty consuming or digesting wholegrain foods following their treatment. This may be a particular issue following colon or rectal surgery. It is advisable that patients who increase (or reintroduce) wholegrain foods into their diet do so gradually and as and when they can; this should be done under the supervision of a health professional, particularly after surgical intervention.
Coffee People who consume more coffee (both caffeinated and decaffeinated) have better health outcomes after a diagnosis of colorectal cancer. But it is uncertain that increasing coffee improves these outcomes.	**We suggest that people consider increasing their coffee intake.** Note: Caffeinated coffee can have a laxative effect or cause palpitations, so it is advisable for patients to consider this when consuming coffee, or other caffeine-containing beverages (eg black or green tea) and foods (eg dark chocolate).
Sugary drinks People who consume less sugary drinks have better health outcomes after a diagnosis of colorectal cancer. But it is uncertain that decreasing sugary drinks improves these outcomes.	**We suggest that people consider decreasing their sugary drink intake.**

Recommendations are based on strong evidence.

Guidance is based on evidence graded as 'limited suggestive'. Limitations in the evidence meant that the panel could not be confident that associations were causal, so we cannot be sure that changing the exposures would change the outcomes. Despite the limitations in the evidence, this represents the best advice based on the current evidence and expert opinion.

Health outcomes include all-cause mortality and cancer outcomes.

Background

Incidence and survival from colorectal cancer

The global burden of cancer is increasing due to a growing and aging population alongside increases in risk factors, most notably obesity; other contributing risk factors include smoking, physical inactivity and unhealthy dietary patterns [2]. In recent decades, progress in the early detection and treatment of cancer has led to a dramatic increase in the number of people living with and beyond cancer (LWBC). In addition, therapeutic control of tumour growth and progression in patients with recurrent disease has led to a diagnosis becoming a prolonged chronic condition with a long lifespan and acceptable quality of life. Within this report, we define this group as all people who have been diagnosed with cancer, including before, during and after treatment [3].

Colorectal cancer is the third most common cancer, with nearly 2 million new cases worldwide and accounting for 9.6% of new cases in 2022 [4]. Survival rates differ between countries, but it is estimated that there are more than 5 million people living with and beyond colorectal cancer globally [5]

It is essential that the long-term health needs of people LWBC, beyond those directly related to their cancer, be considered. Cancer prevention is a crucial component of the World Health Organization's (WHO) global target of a 25% reduction in deaths from cancer and other non-communicable diseases (NCDs) in people aged 30 to 69 by 2025 [6]. However, achieving this target (referred to as 25 x 25) requires the deployment of more effective health systems to improve survival, alongside more effective prevention [7].

Research has historically focused on understanding exposures influencing cancer development. Despite growing numbers of people LWBC, until recently there has been relatively little available research focused on diet, nutrition, physical activity and body weight as levers for improving post-diagnostic survival and quality of life. Although there has been a substantial growth in research, the increase in people LWBC has resulted in greater demand for reliable, evidence-based guidance for health professionals and people LWBC concerning diet, physical activity and body weight. Our work with researchers, health professionals and patients has also highlighted the need for more tailored advice for people LWBC. Numerous studies have explored the views of people LWBC about their needs, preferences and experiences of accessing dietary information (including weight-related information). Studies commonly show a preference for receiving information directly from health-professionals, however, people also report that information can be too generic and sometimes conflicting [8].

Our current report aims to help fill this gap by providing information based on the latest available research.

Our previous work and recommendations

WCRF/AICR previously produced a set of Cancer Prevention Recommendations (see **Appendix 1**), based on evidence judgements made by a panel of independent experts and published in 2018 as part of The Third Expert Report *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective* [9]. The panel concluded that following these recommendations would *'convincingly or probably'* contribute to reducing cancer risk. These recommendations were based on evidence for reducing the risk of developing cancer and did not specifically focus on studies including patients following a cancer diagnosis.

The first report on cancer survivors was published in 2014; this examined literature linking diet, nutrition, physical activity and body weight to survival and occurrence of new primary cancers in people living with and beyond breast cancer [10]. At the time, the panel was unable to draw firm conclusions on the effect of diet, nutrition, physical activity or body weight upon outcomes in this group. However, the panel agreed that the conclusions underpinning the Cancer Prevention Recommendations were also likely to be relevant for people LWBC (generally, not just after a diagnosis of breast cancer) and recommended that, as far as possible, they should aim to follow these recommendations once acute treatment had finished. In addition, the panel judged that following these recommendations was unlikely to be harmful to people LWBC who have completed treatment. However, the evidence was inadequate to make specific recommendations for this group with confidence. The current work builds upon this and signals an increasing focus for the WCRF Network in the cancer survivorship area.

About this report

Purpose of the report

This report brings together the findings from a series of new systematic reviews on the links between diet, nutrition, physical activity and body weight and health outcomes in people after a diagnosis of colorectal cancer and the interpretation of this evidence by our panel of experts. This has been used to develop guidance. The systematic reviews, carried out by the CUP Global team at Imperial College London, examine how diet, nutrition, physical activity and body weight affect survival and recurrence after a colorectal cancer diagnosis [11-14].

As the evidence base for people LWBC continues to develop, we hope to expand our guidance to include information for different cancer types. Further to this, as the evidence base improves in quality, we hope to develop cancer survival recommendations to accompany those we have for cancer prevention.

Who the report is for

The information included in this report is aimed at those with an interest in improving the survival and quality of life of people living with and beyond colorectal cancer. This group includes:

- Healthcare professionals involved in the clinical and supportive care of people living with and beyond colorectal cancer at various stages of their cancer journey. This could be: oncologists; surgeons; cancer nurse specialists; nurse practitioners; dietitians; physiotherapists; other medical professionals; pharmacists; nutritionists and nutritional therapists; and any other relevant healthcare professionals.
- Civil society, patient and charitable organisations (eg cancer charities).
- Researchers working in the areas of diet, nutrition, physical activity, body weight and cancer.
- Policymakers in public health settings.
- People living with and beyond cancer. We will be developing resources specifically for patients and their families, but these reports can be accessed by anyone wanting to read more about the science underpinning the guidance.

This report aims to inform:

- The development of appropriate public-facing outputs and resources for people living with and beyond colorectal cancer including patients who have completed the acute phase of their cancer treatment.
- The development of resources for healthcare professionals working with patients living with and beyond colorectal cancer.
- How the quality and interpretation of future research can be improved to make it more relevant to the specific considerations of people LWBC.
- Policymakers about the strength and limitations of current evidence on diet, nutrition, physical activity and body weight and key outcomes within this group.

Approach

WCRF International's Global Cancer Update Programme (CUP Global) has a robust process for reviewing and interpreting evidence to ensure that our recommendations and guidance are supported by the best available research. Recommendations for the public are generally developed from evidence judged as 'strong' by the independent expert panel. The literature on how diet, nutrition, physical activity and body weight influence long-term health for people LWBC is, despite growth in recent years, in its infancy compared with that for cancer incidence. Researching the modifiable behaviours that might influence health-related outcomes among those LWBC is also highly complex.

The term 'cancer survivor' (or 'living with and beyond cancer' (LWBC)) covers a wide variety of circumstances beginning at diagnosis through cancer treatment to the end of life. In this report, the term 'living with and beyond cancer' (LWBC) will be used. The definition LWBC here does not include people living with a diagnosis of benign tumour or conditions defined as premalignant. Using a single term to cover people LWBC to encompass all of these stages cannot do justice to the heterogenous, complex and emotional reality of living with cancer. Each stage of survivorship has its own particular characteristics, and the impact of interventions or exposures, including those related to diet, nutrition, physical activity and body weight, can vary considerably. The experience of LWBC also varies depending upon the site-specific cancer diagnosed. That is why, when it comes to survival-related information, we are producing guidance for individual cancers rather than cancer overall.

Despite the challenges, it is important that people LWBC can access sound information. Therefore, along with recommendations for how future research can address these challenges, it is important to maximise how the currently available evidence is used. The processes developed in CUP Global, and described in this report, utilise the evidence as it currently stands through a robust transparent process, incorporating input from expert clinicians and scientists, along with user input from health professionals and patients. This enables us to provide people LWBC with information based on the best available evidence while taking into account its limitations.

Using evidence to develop guidance and recommendations

Summary of steps taken

RECOMMENDATIONS- typically developed using strong evidence
GUIDANCE- developed using less strong evidence with input from expert clinicians, scientists and patients and their healthcare providers

Factors considered

- Is there potential patient benefit? (on cancer or other outcomes)
- Is there evidence of harm in this population?
- Are there specific population groups (eg age, sex, race and ethnicity, other socio-demographic characteristics) or clinical populations (eg cancer subtype, treatment) which need to be considered?
- Taking into account the broader context, is there possible harm/ benefit for other health outcomes or any environmental considerations?
- Does the current research allow for a degree of confidence?
- What is the likely impact of a recommendation/ guidance?

What we mean by 'guidance'

Guidance in this report refers to statements developed with input from experts (scientists, health professionals and patients). This differs from clinical guidelines and our recommendations - which we developed based around a strong evidence base. The current guidance is a way of providing information for healthcare professionals and patients in areas where the evidence is less strong based on the judgement criteria. However, it is noteworthy that a substantial body of evidence was reviewed by the panel to be able to develop this guidance.

STEP 1

Gathering evidence through systematic reviews carried out by CUP Global team at Imperial College London

Three systematic reviews were carried out by the CUP Global team at Imperial College London: these examined the relationship between post-diagnosis diet, physical activity and sedentary behaviour and body weight and all-cause mortality, colorectal cancer mortality, colorectal cancer recurrence, second primary cancers or cardiovascular disease mortality (hereafter referred to as 'health outcomes').

Published papers available here:
https://onlinelibrary.wiley.com/toc/10970215/2024/155/3

The protocol was developed by the research team at Imperial College London with input from the Protocol Expertise Group. The peer reviewed protocol is available online [15].

PubMed and Embase databases were searched from inception to 28th February 2022. Relevant exposures were measured post-diagnosis and included any type of physical activity (and sedentary behaviour), diet (food, food components, nutrients, dietary patterns, supplements) and adiposity[1] (body mass index (BMI); waist circumference; waist-to-hip ratio; changes in weight or BMI).

Randomised controlled trials (RCTs) and observational longitudinal studies (or pooled analyses of individual data of these studies) were included if they reported outcome data on all-cause mortality, colorectal cancer mortality, colorectal cancer recurrence, second primary cancers or cardiovascular disease mortality. Most studies reported all-cause mortality, colorectal cancer mortality and/ or colorectal cancer recurrence, with more limited data available for other outcomes.

The results from each review are summarised below; these are supported by a selection of forest plots to illustrate the results, see **Appendix 2**, please refer to the papers to access all of the results and forest plots.

[1]The term 'body weight' is used in this report hereafter as a simpler term for adiposity; it includes body mass index, waist circumference, waist-to-hip ratio

Physical activity findings

A total of 20 publications (16 studies) were included in the review, reporting findings from 13 cohort studies and 3 observational follow-up analyses from randomised controlled trials (RCTs). There were no primary RCTs. There were more than 82,000 patients, of whom approximately 7,800 died of any cause, 1,700 died of colorectal cancer and 2,100 had another colorectal cancer diagnosis.

Most studies looked at the effect of recreational physical activity, such as leisure activity and walking, with limited data on other types of activity and sedentary behaviour. Higher levels of recreational physical activity were associated with a lower risk of all-cause mortality, colorectal cancer mortality and cancer recurrence. Few studies examined change in physical activity (pre-to-post diagnosis or post-diagnosis) and results on this were inconsistent.

Diet findings

A total of 69 publications were included – 63 publications reporting the findings from 35 observational studies and 6 publications reporting the findings from 5 RCTs. Overall, there were more than 30,000 patients of whom more than 8,700 died of any cause, 2,100 died of colorectal cancer and 3,700 had another colorectal cancer diagnosis. The RCTs covered a range of interventions - one nutritional behavioural intervention and 4 interventions of different nutritional supplements. The observational studies looked at a wide range of dietary exposures.

Higher intakes of wholegrains and coffee (both caffeinated and decaffeinated coffee) were associated with a lower risk of all-cause mortality. Conversely, a higher intake of sugary drinks was associated with higher risk of all-cause mortality (in these studies, sugary drinks refer to drinks sweetened with sugar, for example, sugar-sweetened carbonated and non-carbonated soft drinks). Following certain healthier 'dietary and lifestyle patterns' and 'dietary patterns' was associated with lower all-cause mortality and unhealthy dietary patterns was associated with higher all-cause mortality. Other dietary factors were not associated with mortality or recurrence.

Body weight findings

A total of 85 publications (reporting the findings from 124 studies) were included. All of the studies were observational, with no relevant RCTs found. Overall, there were more than 294,000 patients of whom approximately 44,000 died of any causes, 16,000 died of colorectal cancer and 24,600 had another colorectal cancer event. Most evidence was related to body mass index (BMI), with non-linear relationships seen for all-cause mortality, colorectal cancer mortality and recurrence.

STEP 2

Evidence judged by the CUP Global panel

An independent panel of experts, convened by WCRF international, graded the strength of the evidence described above using pre-defined grading criteria (shown in **Appendix 3** and 10]). WCRF International's grading criteria are designed to judge, for observational studies, whether an association is causally linked to a particular health outcome, or, for RCTs, whether a specific intervention affects the risk of developing specific health outcomes.

The panel considered several factors when judging the evidence, including: the amount of evidence; the consistency, magnitude and precision of the summary estimates; whether there was a dose-response relationship; study design and risk of bias; generalisability; the presence of biological plausibility and mechanisms. The evidence levels used within the grading criteria were 'strong' (either 'convincing' or 'probable') or 'limited' (either 'suggestive' or 'no conclusion'), with an additional 'strong' grading of 'substantial effect on risk unlikely' where there is strong evidence that the exposure or intervention does not affect the risk of an outcome.

Summary of panel judgements of evidence

The panel made the following judgements based on the evidence from the systematic reviews. (see **Appendix 4** for a summary of the evidence judgements).

Physical activity

- Higher levels of recreational physical activity after diagnosis were associated with a lower risk of death overall and of cancer recurrence. The evidence was judged as limited (suggestive) because the panel could not be sure of the direction of these associations. Other evidence was judged as limited (no conclusion).

Diet

The following associations were judged by the panel as limited (suggestive):

- 'Healthy' dietary or dietary and lifestyle patterns were associated with lower risk of all-cause mortality, and 'unhealthy' dietary patterns with higher risk.
- Higher intakes of wholegrains were associated with lower risk of all-cause mortality.
- Higher intakes of coffee (overall, caffeinated, decaffeinated) were associated with lower risk of all-cause mortality.
- Higher intakes of sugary drinks were associated with higher risk of all-cause mortality.

This evidence was judged as limited (suggestive) due to limitations in methodological quality. Other evidence was judged as limited (no conclusion) due to limitations in the quantity and quality of both the observational and RCT evidence.

Body weight

The panel judged all the evidence on body weight as limited (no conclusion). Despite there being a substantial quantity of evidence for some exposures and outcomes, limitations in study quality precluded stronger conclusions being made.

STEP 3

Recommendations for future research

The work of the CUP Global panel in judging the evidence from these reviews highlighted a number of limitations that should be addressed in future research. In particular, it was agreed that there is a need not just for more research but also improved methodologies, so that future research can address these limitations. In other words, more of the same types of data or studies are unlikely to strengthen our understanding of the influence of modifiable behaviours related to diet, nutrition, physical activity and body weight on outcomes for people LWBC. Improved research would allow for stronger evidence conclusions, which could then be turned into information for the public. This work will help the WCRF Network to support those LWBC to live healthier and longer lives.

In addition, research that can more clearly define the potential health and economic benefits from intervening to improve diet, nutrition, physical activity and body weight in those LWBC may help to achieve greater buy-in from key decision makers.

It is also important that health professionals, researchers, policy makers and other relevant stakeholders are aware of the limitations of current research when offering advice or making decisions that may impact the long-term health of those LWBC.

The key issues that future research should aim to address include:

- Conducting well-designed clinical trials and prospective cohorts that account for differences in cancer sub-types, timing and types of treatment (eg surgery, medication), and other patient characteristics (eg co-morbidities, age, race, ethnicity). These factors should be accurately reported.
- Using more accurate methods to assess 'usual' pre-diagnosis dietary intake, physical activity and body weight, with more accurate reporting of the timing of exposures, and accurate measurement of potential confounding factors.
- Providing further information on the biological pathways that may explain the relationships between diet, nutrition, physical activity, body weight and cancer/non-cancer outcomes.
- Increasing diversity and inclusivity of study populations and accurate characterisation of samples.

The above key issues are outlined in more detail in the table below, along with potential solutions. While many of these issues are generally applicable to research on diet, nutrition, physical activity and body weight involving those LWBC, where there are specific considerations for colorectal cancer these are noted.

It is also important to note that despite limitations, observational studies can help to identify promising exposures for testing in more robust study designs (eg appropriately conducted RCTs).

Research recommendations

RESEARCH CONSIDERATION Reverse causation

ISSUES AND POTENTIAL SOLUTIONS

The observational design of many studies on diet, physical activity and body weight makes it difficult to exclude the possibility of reverse causation. The disease and treatments received may affect a patient's dietary choices and ability to do physical activity, while their dietary and physical activity choices may also affect disease outcomes. Reverse causality is also a particular issue when interpreting associations between body weight and survival outcomes, and it is challenging to disentangle intentional and unintentional weight loss. This is an inherent problem for observational studies in cancer survivorship populations.

Future research could attempt to address this through:

- *Well-conducted intervention studies where the impact of specific diet, physical activity and/or weight management interventions on survival or other outcomes is the primary research question. However, such studies can be costly and challenging to conduct.*
- *More accurate reporting of the timing of exposures in studies (eg before, during and/or after treatment) and/or analyses of existing studies that account for treatment timing.*
- *Measuring body weight both pre- and post-diagnosis will enable better exploration of these associations. Collecting and reporting pre-diagnosis body weight data is challenging but is possible in cohort studies. However, depending on the type of cancer and treatment pathway, this may introduce bias.*
- *Methods for better understanding the impact of treatment on modifiable risk factors as well as outcomes should be considered. This includes how treatment might result in changes in diet, physical activity levels and body weight, as well as quality of life, morbidity and mortality.*
- *Stage of disease at diagnosis has a clear impact on outcomes, for example, whether the cancer is metastatic or has already impacted health (eg cachexia), by impacting behaviour and affecting treatment options and effectiveness. Future studies need to develop better ways of collecting stage data and including it within analysis.*

Colorectal cancer specific considerations:

The disease and treatments received will likely affect a patient's dietary choices and ability to do physical activity, so reverse causality should be considered.

Better reporting of the timing of exposures may be especially important for dietary studies in populations living with and beyond colorectal cancer. The disease presentation (eg from screening, compared to symptomatic or emergency [bowel obstruction]) can vary, as can the impact of bowel surgery (eg the need for subsequent low fibre diet in some cases).

RESEARCH CONSIDERATION Residual confounding

ISSUES AND POTENTIAL SOLUTIONS

It is rarely possible to control for all factors that may affect the outcome of interest in cohort studies. Treatment-related factors may interact with behaviours (eg by changing the way that a person eats or the energy they have for recreational exercise) and make interpretation complicated. In addition, the presence of other co-morbidities among people with cancer, such as cardiovascular disease or type 2 diabetes, may also impact exposures and outcomes of interest.

Future research should consider how to better account for confounding factors. Suggestions for how future research could attempt to address this include:

- *Accurate reporting of disease state, presentation of disease, disease stage, treatment factors (treatment mode, completion, dose) and any co-morbidities.*
- *Accurate reporting and appropriate adjustment for confounders, including information on timing of confounders in relation to exposure and outcome of interest.*
- *Studies often use recalled data – this can introduce bias – novel ways of more accurately recording such data could be considered.*
- *The use of longitudinal data has the potential to overcome some of the limitations of current studies.*
- *Consideration of the impact of other factors on outcomes, including patient genetic cancer risk, as well as broader social determinants of health (eg socio-economic status, race and ethnicity).*
- *Consideration of whether some confounders also act as effect modifiers.*
- *Appropriate sample sizes to offer sufficient study power to account for confounders.*

Colorectal cancer specific considerations:

Better reporting on the presentation of the disease (eg presentation via polyp vs emergency bowel obstruction) and the type of surgery, which will impact post-operative diet and nutritional considerations both in the immediate and longer-term, is important. This information may help with classifying participants and improve study interpretation.

RESEARCH CONSIDERATION Time-varying impacts

ISSUES AND POTENTIAL SOLUTIONS

There is a growing body of evidence demonstrating that the impact of a risk factor upon a health outcome changes over time and across the lifecourse. Considering this in future studies will allow for better understanding of potentially dynamic associations.

Repeated dietary, nutritional, physical activity or body weight assessments can account for changes in the exposure over time or changes in behaviour after diagnosis (eg cutting out unhealthy foods). This is important because a single measure post-diagnosis is unlikely to accurately capture 'usual' behaviour pre-diagnosis.

RESEARCH CONSIDERATION Indirect effects

ISSUES AND POTENTIAL SOLUTIONS

Some risk factors, such as body weight, may adversely affect outcomes by limiting the treatment options available to a patient. They may also alter the efficacy of treatment. For instance, obesity may impact the risk of complications, pain management and surgical options.

One solution to overcome this may be to conduct trials in patients where more in-depth and repeated information on these factors is available. For example, there is potential to look at computed tomography (CT) derived body composition measurements in studies of metastatic cancer where patients have regular CTs.

RESEARCH CONSIDERATION More accurate data on diet, nutrition, physical activity and body weight

ISSUES AND POTENTIAL SOLUTIONS

Despite there now being large amounts of data collected related to cancer survival, the quality of published research in this area does not allow for strong conclusions to be drawn. Future studies should consider improving the quality and accuracy of the patient data they collect. Best practice and quality assurance within the research field could be considered. For example:

- *Ensuring that validated questionnaires (eg food frequency questionnaires) are used to collect dietary components. Dietary components also need to be appropriately defined to avoid misclassification. The development of online data collection software enables data to be collected more easily in large samples and should be considered.*
- *Objective measures of physical activity (eg accelerometery) should be considered to better capture the amount, intensity and type of activity, and any changes in patterns of activity over time.*
- *Most studies use BMI as a measure of adiposity, but this does not distinguish between lean body mass and fat mass and does not provide information about fat distribution. Future studies should consider collecting more detailed information on this in addition to BMI.*

RESEARCH CONSIDERATION Study cohorts specific to cancer survivorship

ISSUES AND POTENTIAL SOLUTIONS

Existing data are largely from cohorts not specifically designed to look at cancer survivorship but rather incidence. The level of information about exposures and other details of participants may therefore be insufficient to fully assess the impact of modifiable risk factors upon survivor-specific outcomes.

There are also different patterns of cancer recurrence based on the type of cancer (the 'natural history' of the disease) that can affect study outcomes. This should be considered in the study design.

Initiatives for establishing cancer survivor cohorts, to increase size and study power, have been discussed and some are currently underway. Given the increasing size of survivor populations – the inclusion of people LWBC in studies should be seen as a priority.

RESEARCH CONSIDERATION Increased diversity and inclusivity within research

ISSUES AND POTENTIAL SOLUTIONS

Research should aim to study more diverse populations as published research currently tends to focus on populations from countries in Europe, North America and China.

More inclusive and representative study populations are needed, including greater diversity in terms of geography, race and ethnicity, socio-economic status and other factors known to impact long-term health and life expectancy.

There is also a growing body of evidence that diverse research teams are better able to understand and overcome challenges within their work. Research organisations should consider the diversity of their research teams – and seek out diverse ways of thinking about research focused upon cancer survivorship.

RESEARCH CONSIDERATION More accurate characterisations of study populations

ISSUES AND POTENTIAL SOLUTIONS

Cancer patients represent a diverse group of individuals. Study populations should be well-characterised. This will help to improve the quality of the available data and the accuracy of study outcomes. Studies should better define and report on their study populations, including:

- Cancer sub-types
- Potential influence of disease-specific factors, such as treatment type, stage (eg metastatic vs early-stage), time since diagnosis
- Socio-demographic determinants (eg age, sex, race and ethnicity, socio-economic factors, menopausal status).

RESEARCH CONSIDERATION Improved understanding of underlying mechanisms

ISSUES AND POTENTIAL SOLUTIONS

Increased knowledge of the potential biological pathways underpinning the associations between exposures and outcomes seen in epidemiological studies would improve our understanding of causality. This is an active area of work within CUP Global.

For example, there are multiple mechanisms that underpin the associations between physical activity and cancer progression. These include the role of sex hormones, metabolic dysregulation, inflammation, immune function, oxidative stress and genetic mutations. It remains unclear if physical activity influences these pathways independently or if it exerts its action via reductions in adipose tissue.

RESEARCH CONSIDERATION More multi-disciplinary research collaborations

ISSUES AND POTENTIAL SOLUTIONS

There is a clear need for more collaboration between specialists so that expertise on cancer, diet, nutrition, physical activity and body weight can be brought together more effectively. As our understanding of biological mechanisms increases and becomes more complex – research teams will likely benefit from the inclusions of experts in this field.

Multidisciplinary teams and projects would help to address some of the key issues with the current research discussed here.

STEP 4

Development of guidance and recommendations with input from the panel, cancer survivors expert committee and users

WCRF International worked with the CUP Global panel and cancer survivors expert committee in 2023 to develop a process for producing guidance. The guidance presented in this document is based on evidence judged by the panel to be at least 'limited suggestive'. Oncology experts from the panel and expert committee provided direction on which evidence gradings were suitable for developing into guidance.

User input

Input from individuals living with and beyond colorectal cancer

When developing this report, we recognised the importance of getting input from those who would be directly using the public facing information produced from it. This included those living with and beyond colorectal cancer and the health professionals who will be communicating and relaying the guidance to them. Involving direct users in the development of guidance is important to enhance patient care as it allows them to identify patient focused issues and ensures it most closely matches their lived experience.

We held interviews with 3 people living with and beyond colorectal cancer to contribute to the report. Interviewees were identified using People in Research (NIHR), 2 of the interviewees had previous experience in reviewing patient materials through their work with other organisations. Before the interviews, each participant was sent a draft example of a patient-facing material intended to communicate our guidance. During the interview, 2 sets of questions were asked: one set on their experiences of accessing advice on health information (specifically around diet and physical activity) and the other set more specifically relating to our guidance.

Their feedback was used to develop, revise or refine the guidance statements and supporting information within this report and will be used further by the WCRF network when developing patient facing outputs based on this report. The interviews also suggested the use of real-world examples of how to incorporate the guidance into their lives, with inclusive examples for those who have barriers to, for example, exercises since their cancer diagnosis. They demonstrated to us the conflicting information regarding diet and physical activity during their diagnosis, stressing that this guidance was welcomed. They also emphasised the need for accessible language that was both direct and yet empowering and non-judgmental.

Input from health professionals:

In our ongoing conversations with healthcare professionals, it is clear that there is an unmet need for cancer-specific information about what those LWBC can do to improve their health and potentially outcomes. With this in mind, we sought input from healthcare professionals – firstly, about the need for our new guidance and, secondly, how they might use it.

We received feedback from clinical cancer nurse specialists and cancer dieticians, both in the UK and US, on a draft example of the information that we could provide them to support their conversations with patients LWBC. As a result of their feedback, the document was restructured for clarity.

Within our conversations with individuals LWBC and healthcare professionals it was noted that it would be useful to link to information that was already available. Therefore, references to other organisations, where possible, were included – for example, WHO recommendations on the amount of physical activity required to confer a health benefit.

The reviewers, especially those not based in the UK, provided feedback on the need for language to be inclusive and have a consideration of global audiences. We will carefully consider this when we are developing public-facing outputs based on the current guidance.

Our guidance for those living with and beyond colorectal cancer

Current evidence and guidance statements are provided below for those living with and beyond colorectal cancer. These reflect the strength of the scientific evidence and expert opinion. Additional information on specific considerations for interpreting the guidance statements is also provided. It is important that changes to diet, nutrition, physical activity and body weight are discussed with a healthcare professional, as appropriate.

Much of the evidence on which the guidance in this report is based comes from observational studies rather than intervention studies. This means that any associations found cannot confidently be assumed to be causal, for instance because of confounding or reverse causation. So, even if people who are found to experience a particular diet, physical activity or body weight exposure have better outcomes, if the exposure is not causal, then changing it cannot be assumed to change the outcome. This problem is a main reason why the evidence is regarded as weak and this guidance is less secure than our firm recommendations. Nevertheless it represents the best advice, based on current evidence and expert opinion.

In developing the guidance, we include a description of the association between the exposure (eg diet) and health outcomes, followed by a brief outline of our guidance. For each guidance statement, we have provided a supporting summary statement of the evidence grading.

This guidance is based on the evidence described in this report, with outcomes collectively referred to as 'health outcomes'. See steps 1 and 2 for information about the specific health outcomes.

Our existing WCRF/AICR recommendations for cancer prevention

WCRF/AICR have previously developed a set of 10 cancer prevention recommendations, these include following a healthy diet, being physically active and maintaining a healthy body weight. These are based on decades of research and many studies have now shown that following them reduces the risk of developing cancer, as well as reducing the risk of other chronic diseases [9].

One of these recommendations is that people LWBC follow the cancer prevention recommendations as much as possible (see **Appendix 1**). This recommendation was made by the expert panel, as part of the Third Expert Report, based on the best available evidence at the time. The panel made this recommendation with caution because, although nutritional factors and physical activity appear to predict outcomes in people LWBC, there was insufficient evidence that changing these improves outcomes for this group.

Guidance statement:

People who follow WCRF/AICR's Cancer Prevention Recommendations are predicted to have better outcomes after a colorectal cancer diagnosis.

We suggest that people consider following as many of these recommendations as they are able to.

The finding from the reviews described in this report (that healthy dietary and lifestyle patterns and healthy dietary patterns are associated with a lower risk of all-cause mortality, and unhealthy dietary patterns with a higher risk) are consistent with this guidance.

In addition to this general guidance, we have used the more recent evidence from the current reviews to develop guidance specifically for people living with and beyond colorectal cancer. These are outlined below.

Physical activity

There is limited evidence suggesting that higher levels of recreational physical activity might improve health outcomes.

Guidance statement:

People who are more physically active have better health outcomes after a diagnosis of colorectal cancer. While it is uncertain that increasing physical activity will improve these outcomes, we suggest that people consider increasing their physical activity (with appropriate support from their healthcare team).

Physical activity should be introduced gradually and the type and intensity of activity should be appropriate to an individual's fitness level and physical capabilities.

Whilst this guidance is primarily focused on the period after treatment completion, we recognise that people may be using it at any time in their cancer journey. It may be particularly important for any increases in physical activity to be gradual, particularly for patients suffering from side-effects of their treatment, surgery or medication that may restrict their ability to be physically active, such as neuropathy or musculoskeletal issues. In this instance, individuals may wish to seek advice from their healthcare professional. A referral to a physiotherapist or exercise specialist who can provide individualised advice may be appropriate.

There are numerous wider benefits of regular physical activity [16], including:

- Reducing the risk of developing other conditions, such as cardiovascular disease and type 2 diabetes
- Helping maintain a healthy body weight
- Reducing the risk of depression and anxiety
- Reducing the risk of falls, as well as hip and vertebral fractures, in older adults
- Helping improve sleep and cognitive health
- Helping keep joints and muscles healthy

Additional information:

International guidelines on physical activity from the World Health Organization (WHO) [16] recommend that adults (aged 19 to 64 years):

- Should do at least **150–300 minutes of moderate-intensity** aerobic physical activity, or at least **75–150 minutes of vigorous-intensity** aerobic physical activity (or an equivalent combination of these) throughout the week.
- Should also do **muscle-strengthening activities** (at moderate or greater intensity) that involve all major muscle groups on two or more days a week, as these provide additional health benefits.
- **May do more than 300 minutes** of moderate-intensity aerobic physical activity or more than 150 minutes of vigorous-intensity aerobic physical activity (or an equivalent combination of these) throughout the week **for additional health benefits**.
- **Should limit the amount of time spent being sedentary**. Replacing sedentary time with physical activity of any intensity (including light intensity) provides health benefits.

For adults aged 65 years and above, WHO additionally recommends:

- Doing varied multicomponent physical activity that emphasises functional balance and strength training at moderate or greater intensity, on 3 or more days a week, to enhance functional capacity and to prevent falls.

Please note that these general physical activity guidelines may not be applicable to all people.

Wholegrains

There is limited evidence suggesting that higher consumption of wholegrains after a diagnosis might improve health outcomes.

Guidance statement:

People who eat more wholegrains after a diagnosis of colorectal cancer might have better health outcomes. While it is uncertain that increasing wholegrains is beneficial, we suggest that people consider increasing their wholegrain intake.

Wholegrain foods include:

- Oats, barley, rye
- Bulgur wheat
- Quinoa
- Brown and wild rice
- Wholewheat pasta
- Wholegrain breakfast cereals
- Wholemeal bread, wraps, chapatis, pittas

Additional information:

Some patients may report difficulty consuming or digesting wholegrain foods following their treatment. This may be a particular issue following colon or rectal surgery. It is advisable that patients who increase (or reintroduce) wholegrain foods into their diet do so gradually and as and when they can; this should be done under the supervision of a health professional, particularly after surgical and/or radiotherapy intervention. If a patient experiences any ongoing issues with consuming wholegrain (or other) foods following treatment, they should seek the advice of a medical professional or dietitian who can provide advice suited to individual patient needs.

Coffee

There is limited evidence suggesting that higher consumption of caffeinated and decaffeinated coffee after a diagnosis might improve health outcomes.

Guidance statement:

People who consume more coffee (both caffeinated and decaffeinated) have better health outcomes. Whilst it is uncertain that increasing coffee is beneficial, we suggest that people consider increasing their coffee intake.

Additional information:

Caffeinated coffee can have a laxative effect or cause palpitations, so it is advisable for patients to consider this when consuming coffee, or other caffeine-containing beverages (eg black or green tea) and foods (eg dark chocolate). It is also advisable for patients to consider how caffeine fits with any overall health concerns, such as sleep.

Sugary drinks

There is limited evidence suggesting that lower consumption of sugary drinks after a diagnosis might improve health outcomes.

Guidance statement:

People who consume less sugary drinks have better health outcomes. Whilst it is uncertain that reducing sugary drinks is beneficial, we suggest that people consider reducing their consumption of sugary drinks.

Sugary drinks include:

- Sugar-sweetened caffeinated and non-caffeinated colas
- Other sugar-sweetened carbonated soft drinks
- Non-carbonated drinks sweetened with sugar (for example, juice drinks with added sugar)

Please note: We recommend that individuals living with and beyond a cancer diagnosis speak to their healthcare team before making any changes related to diet, nutrition, physical activity or body weight. Any healthcare professionals using this guidance should consider where a patient is in their cancer journey and interpret the guidance appropriately to suit each person's individual needs.

Acknowledgments

Global Cancer Update Programme panel (carried out judgement of colorectal cancer evidence, developed guidance for people living with and beyond colorectal cancer)

Professor Lord John Krebs, University of Oxford, UK (Panel Chair); Professor Matty Weijenberg, Maastricht University, NL (Panel Deputy Chair); Professor Monica Baskin, University of Pittsburgh, US (Chair of Expert Committee on Cancer Incidence); Professor Sarah Lewis, University of Bristol, UK (Chair of Expert Committee on Cancer Mechanisms); Professor Ellen Copson, University of Southampton, UK (Chair of Expert Committee on Cancer Survivors); Professor Jaap Seidell, VU University, NL (Chair of the Expert Committee on Obesity); Professor Rajiv Chowdhury, Florida International University, US (Global Representative); Lynette Hill, UK (Public Representative)

Formal observers to the Global Cancer Update Programme panel

Dr Carolina Espina, International Agency for Research on Cancer, FR; Dr Jason Montez, World Health Organization, CH; Professor Mathilde Touvier, French National Institute of Health and Medical Research, FR; Shalini Jayasekar Zürn, Union for International Cancer Control, CH; Dr Emily Tonorezos, National Cancer Institute, US

Global Cancer Update Programme cancer survivors expert committee (contributed to judgement of colorectal cancer evidence and the development of guidance for people living with and beyond colorectal cancer)

Professor Ellen Copson, University of Southampton, UK (Chair); Professor Andrew Renehan, University of Manchester, UK (Deputy Chair); Professor Anne May, University Medical Centre Utrecht, NL; Professor Anne Tjonneland, Danish Cancer Society Research Centre, DK; Professor Galina Velikova, University of Leeds, UK; Professor Karen Steindorf, DKFZ and NCT, DE; Dr Martijn Bours, Maastricht University, NL; Dr Melissa Hudson, St. Jude Children's Research Hospital, US; Professor Rod Skinner, Newcastle University, UK; Professor Wendy Demark-Wahnefried, University of Alabama, US; Professor Folakemi Odedina, Mayo Clinic, US

Imperial College London research team (carried out the systematic literature reviews)

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Previously in Imperial College London research team:
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User involvement

Patients and health professionals providing feedback on the guidance and recommendation, including patient representatives via People in Research (NIHR)

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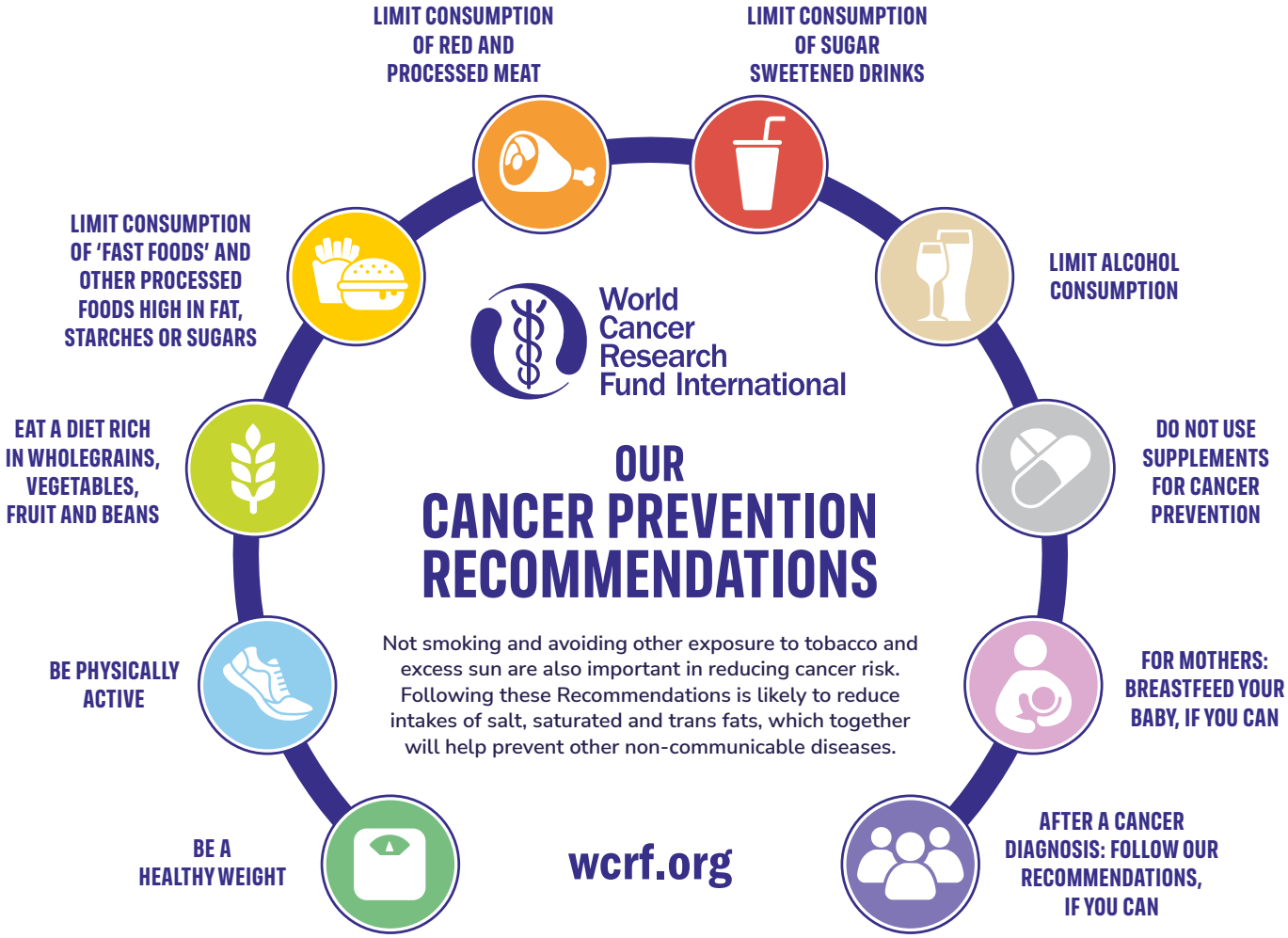
Appendix 1: WCRF/ AICR Cancer Prevention Recommendations

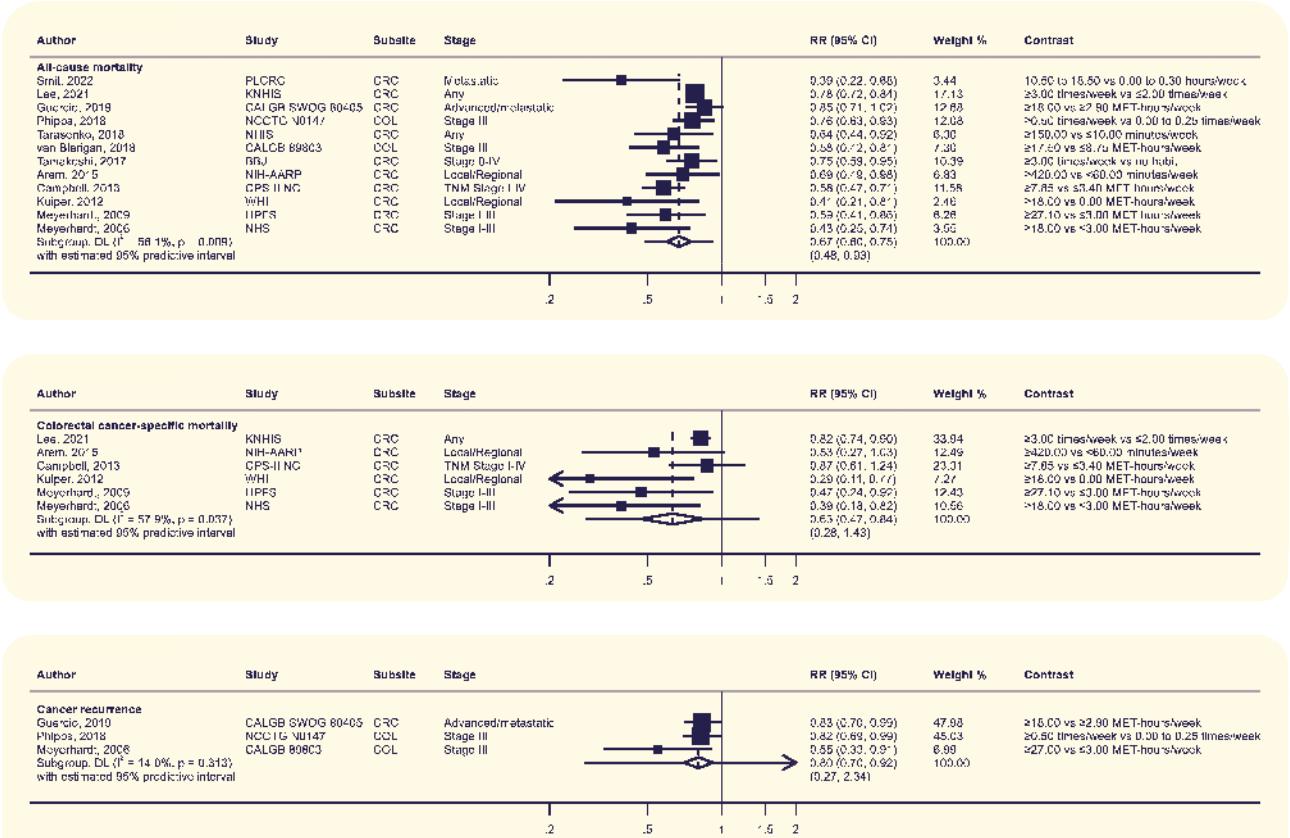


Appendix 2: Selection of forest plots illustrating findings from systematic reviews

The below forest plots are a selection shown to illustrate the results from the reviews, please refer to the papers to access all of the results and forest plots.

Recreational physical activity after diagnosis and health outcomes

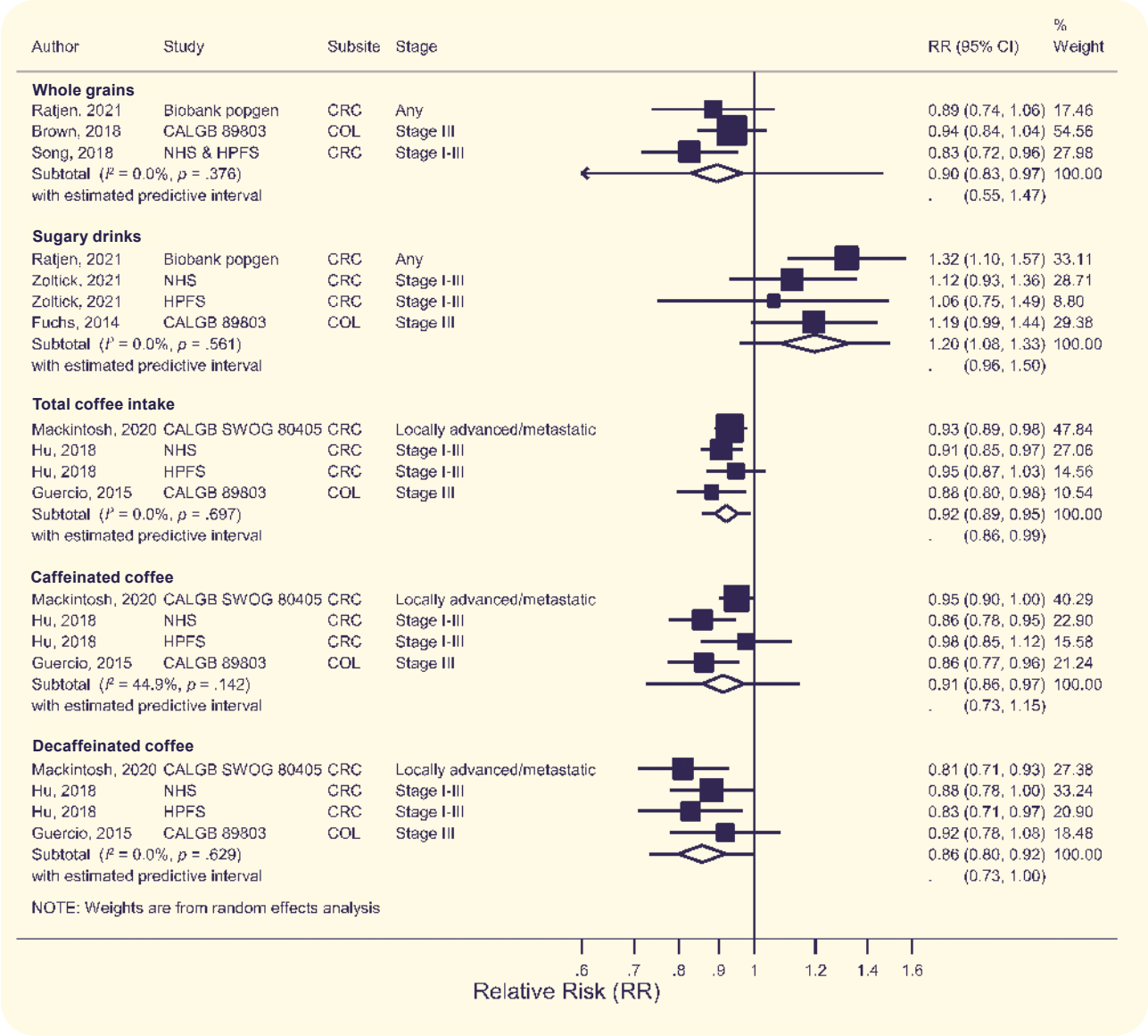
Relative risk (95% CI) of outcomes after colorectal cancer diagnosis for the highest compared with the lowest level of recreational physical activity.



Citation: Markozannes G, Becerra-Tomás N, Cariolou M, Balducci K, Vieira R, Kiss S, et al. Post-diagnosis physical activity and sedentary behaviour and colorectal cancer prognosis: A Global Cancer Update Programme (CUP Global) systematic literature review and meta-analysis. Int J Cancer. 2024;155(3):426-44. (Plots taken from Supplementary Figure S4)

Dietary intake after diagnosis and health outcomes

Linear dose-response meta-analysis of post-diagnosis dietary intake in relation to all-cause mortality.



Linear dose–response meta-analyses of post-diagnosis intake of whole grains, sugary drinks, and total, caffeinated, and decaffeinated coffee in relation to all-cause mortality (associations presented are those graded as 'limited—suggestive'). Forest plot shows the linear dose–response results (per 1 serving/day intake of whole grains and sugary drinks; and per 1 cup/day intake of coffee) from the inverse variance DerSimonian–Laird random-effects model. Each diamond represents the summary relative risk (RR) estimate, the diamond's width is the 95% confidence interval (CI), and the diamond's horizontal line is the 95% prediction interval (PI). Each square and the horizontal line across the square represents the RR estimate of the individual study and its 95% CI. CI, confidence interval; COL, colon cancer; CRC, colorectal cancer; RR, relative risk. Study abbreviations: CALGB 89803, Cancer And Leukemia Group B 89803; CALGB SWOG 80405, Cancer And Leukemia Group B (Alliance) Southwest Oncology Group 80405; HPFS, Health Professionals Follow-Up Study; NHS, Nurses' Health Study.

Citation: Chan DSM, Cariolou M, Markozannes G, Balducci K, Vieira R, Kiss S, et al. Post-diagnosis dietary factors, supplement use and colorectal cancer prognosis: A Global Cancer Update Programme (CUP Global) systematic literature review and meta-analysis. Int J Cancer. 2024;155(3):445-70. (Figure 4)

Appendix 3: Summary of grading criteria

EVIDENCE GRADES	GRADING CRITERIA FOR EVIDENCE ON DIET, NUTRITION, PHYSICAL ACTIVITY AND SURVIVAL FOLLOWING CANCER		Het	PB	Mec
STRONG EVIDENCE	CONVINCING	Evidence of an effect from at least 2 well-designed independent RCTs	NO	NO	NOT REQUIRED
	PROBABLE	Evidence from at least 2 well-designed independent RCTs	SOME	NO	NOT REQUIRED
		OR Evidence from 1 well-designed RCT plus evidence from well-designed cohort studies	NO	NO	REQUIRED
		OR Evidence from at least 1 well-designed pooling study (of cohort studies)	NO	NO	REQUIRED
		OR Evidence from at least 3 independent well-designed cohort studies	NO	NO	REQUIRED
LIMITED SUGGESTIVE	LIMITED SUGGESTIVE	Evidence from at least 2 well-designed RCTs but the confidence interval may include the null	SOME	NO	NOT REQUIRED
		OR Evidence from 1 well-designed RCT but the confidence interval may include the null	NO	-	REQUIRED
		OR Evidence from a well-designed pooling study (of cohort studies)	SOME	NO	NOT REQUIRED
		OR Evidence from a well-designed pooling study (of cohort studies) but the confidence interval may include the null	SOME	NO	REQUIRED
		OR Evidence of an effect from at least 2 cohort studies	NO	NO	NOT REQUIRED
	LIMITED - NO CONCLUSION	Any of the following reasons: - Too few studies available - Inconsistency of direction of effect - Poor quality of studies	–	–	–
STRONG EVIDENCE	SUBSTANTIAL EFFECT ON RISK UNLIKELY	Evidence of the absence of an effect (a summary estimate close to 1.0) from any of the following: a. A meta-analysis of RCTs b. At least two well-designed independent RCTs c. A well-designed pooling study (of cohort studies) d. At least 2 well-designed cohort studies - Absence of a dose-response relationship (in cohort studies)	NO	–	ABSENCE

Note: Special upgrading factors: (a) Presence of a plausible biological gradient ('dose response') in the association. Such a gradient need not be linear or even in the same direction across the different levels of exposure, so long as this can be explained plausibly. (b) A particularly large summary effect size (a relative risk of 2.0 or more, or 0.5 or less, depending on the unit of exposure), after appropriate control for confounders. (c) Evidence from appropriately controlled experiments demonstrating one or more plausible and specific mechanisms. (d) All plausible known residual confounders or biases including reverse causation would reduce a demonstrated effect, or suggest a spurious effect when results show no effect. Special considerations important for evidence for colorectal cancer survivors including the following potential confounding variables—the type of tumour, type of treatment, amount of treatment received and the dissemination of the disease.

Abbreviations: Het, substantial unexplained heterogeneity or some unexplained heterogeneity; PB, publication bias; Mec, strong and plausible mechanistic evidence is required, not required (but desirable), or absent.

Appendix 4: Summary of panel conclusions

The below table summarises the evidence judgements made by the expert panel as part of our ongoing work to examine how diet, weight and physical activity exposures affect outcomes following a colorectal cancer diagnosis.

LIVING WITH AND BEYOND COLORECTAL CANCER (HEALTH OUTCOMES)					
2024	Diet, nutrition and physical activity for colorectal cancer survivors				
		DECREASES RISK		INCREASES RISK	
		EXPOSURE	OUTCOME	EXPOSURE	OUTCOME
STRONG EVIDENCE	CONVINCING				
	PROBABLE				
LIMITED EVIDENCE	LIMITED–SUGGESTIVE	Healthy dietary patterns[1] Wholegrains Coffee[2] Recreational physical activity	All mortality All mortality All mortality All mortality Recurrence	Unhealthy dietary patterns[3] Sugary drinks	All mortality All mortality
	LIMITED–NO CONCLUSION	Nuts and peanuts, red and processed meat, dairy products, artificially sweetened beverages, alcohol, dietary glycaemic index, dietary glycaemic load, dietary insulin load, dietary insulin index, marine omega-3 polyunsaturated fatty acids, circulating 25-hydroxyvitamin D, supplemental calcium, circulating folate and folic acid concentrations, dietary calcium Recreational physical activity (for colorectal cancer mortality), total physical activity, level of recreational physical activity (by frequency, duration, intensity, volume), pre-to-post diagnosis and post-diagnosis physical activity change, sedentary behaviour[4] Post diagnosis body fatness[5], weight change and BMI change (pre-to-post diagnosis or post-diagnosis (any period) or during / after cancer treatment)			
STRONG EVIDENCE	SUBSTANTIAL EFFECT ON RISK UNLIKELY				

Abbreviations:

All mortality, all-cause mortality

Footnotes:

[1] Refers to predefined healthy dietary patterns and healthy dietary and lifestyle patterns

[2] Total coffee, caffeinated coffee and decaffeinated coffee

[3] Refers to predefined unhealthy dietary patterns

[4] Measured by time sitting whilst watching TV

[5] BMI, waist circumference

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American Institute for Cancer Research

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