World Cancer Research Fund

American Institute for Cancer Research

CUP Continuous Update Project

Analysing research on cancer prevention and survival

# Diet, nutrition and physical activity: Energy balance and body fatness

2018

## The determinants of weight gain, overweight and obesity

World Cancer Research Fund International

World Cancer Research Fund UK

Wereld Kanker Onderzoek Fonds

World Cancer Research Fund 世界癌症研究基金會

# Contents

# WORLD CANCER RESEARCH FUND NETWORK

## Our Vision

We want to live in a world where no one develops a preventable cancer.

## 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 choices to reduce their cancer risk.

As a network, we influence policy at the highest level and are trusted advisors to governments and to other official bodies from around the world.

## Our Network

World Cancer Research Fund International is a not-for-profit organisation that leads and unifies a network of cancer charities with a global reach, dedicated to the prevention of cancer through diet, weight and physical activity.

The World Cancer Research Fund network of charities is based in Europe, the Americas and Asia, giving us a global voice to inform people about cancer prevention.

CUP Continuous Update Project

Analysing research on cancer prevention and survival

THIRD EXPERT REPORT

## Our Continuous Update Project (CUP)

The Continuous Update Project (CUP) is World Cancer Research Fund (WCRF) Network's ongoing programme to analyse cancer prevention and survival research related to diet, nutrition and physical activity from all over the world. Among experts worldwide it is a trusted, authoritative scientific resource which informs current guidelines and 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 at Imperial College London. An independent panel of experts carries out ongoing evaluations of this evidence, and their findings form the basis of the WCRF Network's Cancer Prevention Recommendations (see inside back cover).

Through this process, the CUP ensures that everyone, including 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 launch of World Cancer Research Fund Network's Third Expert Report, *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective*, in 2018 brings together the very latest research from the CUP's review of the accumulated evidence on cancer prevention and survival related to diet, nutrition and physical activity. Diet, nutrition and physical activity: Energy balance and body fatness is one of many parts that make up the CUP Third Expert Report. For a full list of contents, see dietandcancerreport.org

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.

## How to cite the Third Expert Report

**This part:** World Cancer Research Fund/American Institute for Cancer Research. Continuous Update Project Expert Report 2018. Diet, nutrition and physical activity: Energy balance and body fatness. Available at dietandcancerreport.org

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## Key

See online **glossary** (wcrf.org/dietandcancer/glossary) for definitions of terms highlighted in *italics*.

References to other parts of the Third Expert Report are highlighted in purple.

# Executive summary

## Background and context

Overweight and obesity, characterised by excess body fat, are widely considered to be one of the most pressing public health concerns of the 21st century. Over the last five decades, the global *prevalence* of people living with overweight and obesity has increased dramatically. Current estimates show that 1.97 billion adults are living with overweight or obesity [1], with numbers projected to rise if trends remain unchanged. Although the rate of increase has begun to slow in some *high income countries* (albeit at a high prevalence), the rate of increase of obesity has tended to accelerate in *low and middle income countries*. These accelerations have occurred in tandem with considerable changes in food systems and dietary patterns, commonly termed the '*nutrition transition*' [2, 3]. Overweight and obesity are occurring at an ever earlier age, increasing lifetime exposure to the associated risks.

Our Continuous Update Project (CUP) has identified 12 cancers causally linked to greater body fatness including cancers of the mouth, pharynx and larynx, oesophagus (*adenocarcinoma*), stomach (cardia), pancreas, gallbladder, liver, colorectum, breast (postmenopause), ovary, endometrium, prostate (advanced), and kidney (see Exposures: Body fatness and weight gain). Three additional cancer sites were reviewed by the World Health Organization's International Agency for Research on Cancer which concluded that greater body fatness is a cause of thyroid cancer, multiple myeloma and meningioma [4]. In addition, having overweight or obesity is associated with other comorbidities, including higher risks of type 2 diabetes, high blood pressure, heart disease and stroke.

The increasing prevalence of overweight and obesity has global and national economic implications. These can be direct, through costs to social and healthcare systems, or indirect, through increased absences from work or people living with obesity being unable to work. The costs of obesity are well characterised in high-income countries; however, they have been difficult to assess globally due to a lack of data from lower-income countries.

Maintenance of stable body weight in adulthood depends on the close matching of energy intake (through food and drink) and energy expenditure (through the body's basic functions and *physical activity*) over the long term, called *energy balance*. Under normal circumstances energy balance is achieved through interaction between the body's regulatory systems, including appetite, with important roles for learning, memory and physical activity. These interactions can be influenced by a variety of factors, both internal (for example, genetic variation) and external (for example, changes in the composition of food and drink and the social circumstances in which they are consumed).

In addition to the findings in this report related to diet, nutrition and physical activity, other established influences on energy balance and body weight include:

### Genetics

- Identical twin studies have identified many genetic variants that contribute to weight gain, principally by influencing appetite. However, *mutations* and chromosomal rearrangements known to cause obesity, such as congenital *leptin* deficiency, Prader-Willi Syndrome and Bardet-Biedl syndrome, are rare.

### Epigenetics and maternal programming

- The womb environment is an important determinant of fetal phenotype and

disease risk in later life. Factors such as nutrition or infection influence the pattern of fetal gene expression and risk of excess weight gain, overweight and obesity.

- Infants of mothers who have obesity tend to have greater fetal size and increased fat mass – both risk factors for obesity.

**Gut microbiota**

- There is early but growing evidence that the bacteria residing in the colon – the *microbiome* – may be involved with the development of overweight and obesity, although the mechanisms are not fully established.

**Psychosocial factors**

- Psychosocial factors which can influence body weight, including risk of overweight or obesity, include stress, discrimination, depressive mood and emotional eating disorders.

**Environmental and policy factors**

- Overweight and obesity are complex issues, influenced by many factors outside of people's direct personal control. Broadly, these are economic, social and environmental factors that operate at global, national and local levels. At a personal level these are experienced as the availability, affordability, awareness and acceptability of healthy diets and physical activity, relative to unhealthy diets and physical inactivity. For a full overview of the role of *policy* in public health, see Recommendations and public health and policy implications.

## How the research was conducted

Because of the large number of studies covering a wide range of *exposures*, and because published reviews address relevant research questions, a pragmatic approach was taken based primarily on a '*review of published reviews*'. This review collated and analysed the global scientific research on diet, nutrition and physical activity and risk of weight gain, overweight and obesity. The results were independently assessed by a panel of leading international scientists in order to draw conclusions about which of these factors increase or decrease the risk of weight gain, overweight and obesity.

Where available, quantification of exposures in relation to outcomes has been reported as in the published reviews. However, because of the methods used (a 'review of published reviews'), reliable summary estimates of quantified thresholds were not able to be calculated for this report.

Throughout the CUP, a standardised process has been used, assessing the likelihood of observed relationships being causal. To achieve this, standardised criteria for grading the evidence and standardised terminology for describing the strength of the evidence have been used. A description of the definitions of, and criteria for, the terminology of 'convincing' and 'probable' (referring to the likelihood of causality), and 'limited – suggestive', 'limited – no conclusion' and 'substantial effect on risk unlikely', appears in **Appendix 1**. For more information on the process, see Judging the evidence.

## Findings

### Integration of the evidence

Each 'singular' exposure has been judged to show a relationship with weight maintenance or weight gain, on the basis of either strong or limited evidence. However, the CUP Panel has greater confidence that any effects on energy balance can be ascribed to clusters of the individual exposures (including both strong and limited evidence). In part this is because such singular exposures often cluster together with other exposures that may have a similar effect, for example, people who are physically active tend to have healthier lifestyles

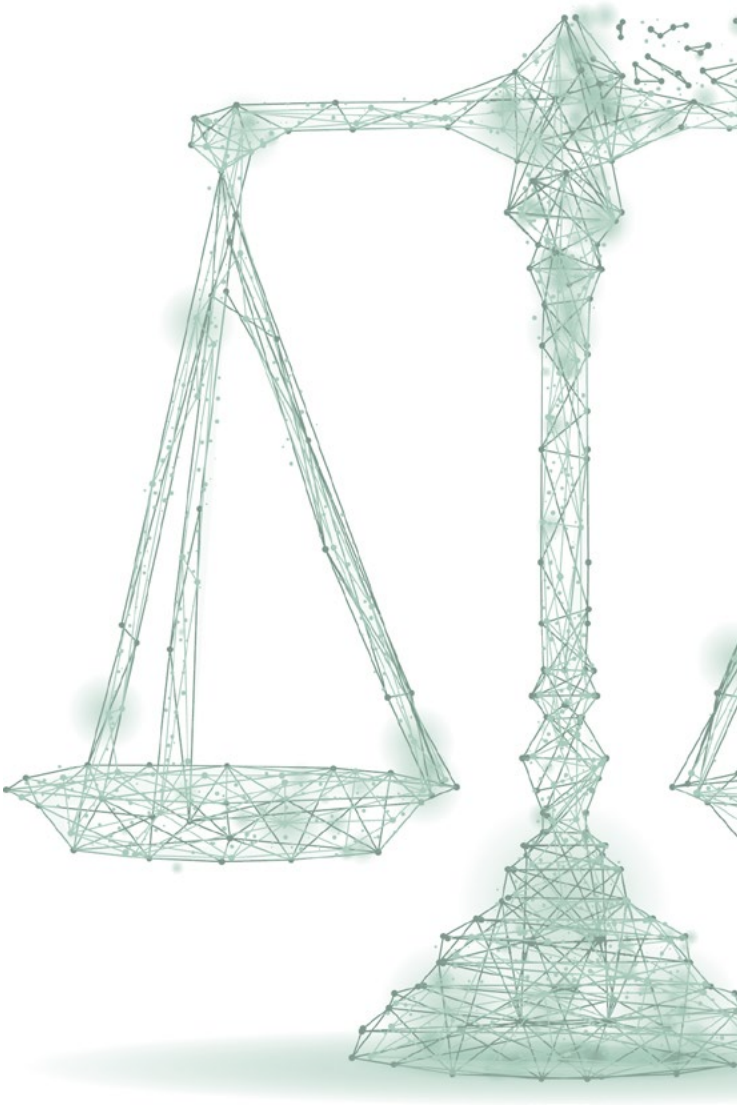
in other respects [5]. Increased aerobic *physical activity*, including walking, alongside consumption of foods containing *dietary fibre*, particularly wholegrains, fruit and vegetables, and higher adherence to a *'Mediterranean type' dietary pattern* is more likely to decrease the risk of weight gain, overweight and obesity than modifying any given single exposure. Conversely, increased sedentary time, including screen time, in combination with a 'Western type' diet, and consumption of sugar sweetened drinks, 'fast foods', and refined grains is more likely to increase the risk of weight gain, overweight and obesity than any exposure in isolation. Conclusions drawn for each individual exposure, based on the strength of the evidence, are listed below.

**There is strong evidence that:**

- **walking decreases** the risk of weight gain, overweight and obesity
- **aerobic physical activity decreases** the risk of weight gain, overweight and obesity
- **consuming foods containing dietary fibre decreases** the risk of weight gain, overweight and obesity
- **consuming a 'Mediterranean type' dietary pattern decreases** the risk of weight gain, overweight and obesity
- **having been breastfed decreases** the risk of excess weight gain, overweight and obesity in children
- **greater screen time increases** the risk of weight gain, overweight and obesity
- **consuming sugar sweetened drinks increases** the risk of weight gain, overweight and obesity
- **consuming 'fast foods' increases** the risk of weight gain, overweight and obesity
- **consuming a 'Western type' diet increases** the risk of weight gain, overweight and obesity

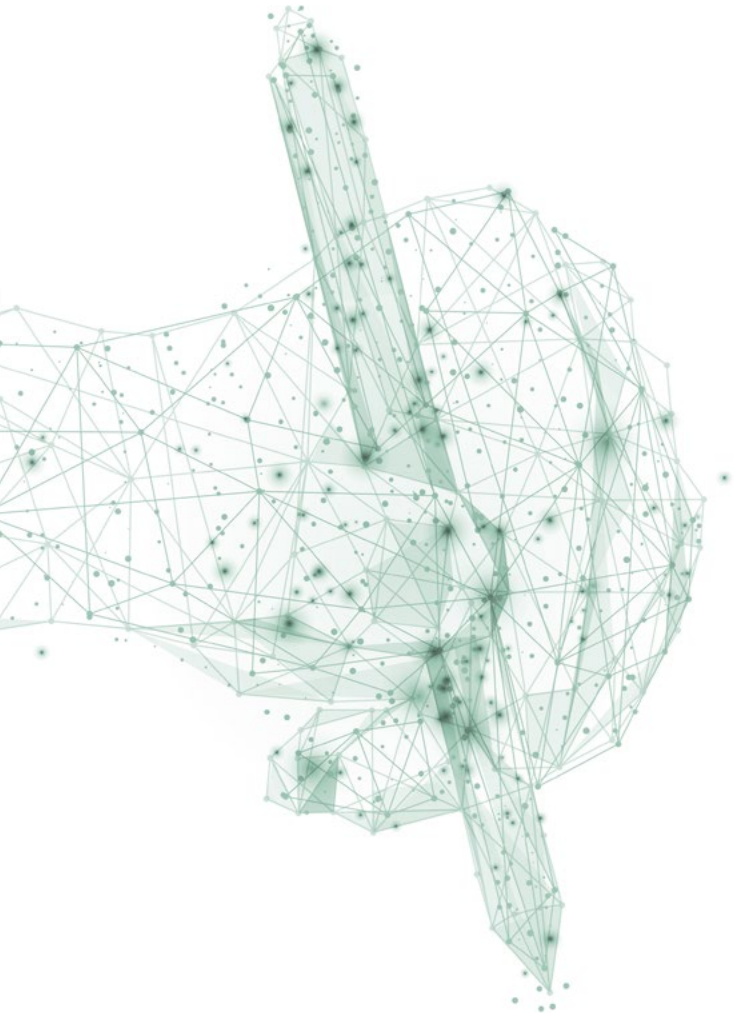
**There is limited evidence that:**

- **consuming wholegrains might decrease** the risk of weight gain, overweight and obesity
- **consuming fruit and vegetables might decrease** the risk of weight gain, overweight and obesity
- **breastfeeding (lactation) might decrease** the risk of weight gain, overweight and obesity for the mother
- **sedentary behaviours might increase** the risk of weight gain, overweight and obesity
- **consuming refined grains might increase** the risk of weight gain, overweight and obesity



## Recommendations

Our Cancer Prevention Recommendations – for preventing cancer in general – include maintaining a healthy weight, being physically active, eating a healthy diet and limiting alcohol consumption (if consumed at all). The Cancer Prevention Recommendations are listed on the inside back cover of this report, with full details available at dietandcancerreport.org.



## References


[1] NCD Risk Factor Collaboration (NCD-RisC). 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.

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[4] 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.

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## DIET AND PHYSICAL ACTIVITY AND WEIGHT GAIN, OVERWEIGHT AND OBESITY IN ADULTS AND CHILDREN[1]: A SUMMARY MATRIX

| WCRF/AICR GRADING | | DECREASES RISK OF WEIGHT GAIN, OVERWEIGHT AND OBESITY | INCREASES RISK OF WEIGHT GAIN, OVERWEIGHT AND OBESITY |
|---|---|---|---|
| STRONG EVIDENCE | Convincing | **Walking** | **Screen time (children)[2]**<br>**Sugar sweetened drinks[3]** |
| | Probable | **Aerobic physical activity**<br>**Foods containing dietary fibre**<br>**'Mediterranean type' dietary pattern[4]**<br>**Having been breastfed[5]** | **Screen time (adults)[2]**<br>**'Fast foods'[6]**<br>**'Western type' diet[7]** |
| LIMITED EVIDENCE | Limited – suggestive | Wholegrains[8]<br>Fruit and vegetables<br>Lactation (mother) | Sedentary behaviours[9]<br>Refined grains[8] |
| | Limited – no conclusion | Vegetarian or vegan diets, adherence to dietary guidelines, dietary variety, eating breakfast, family meals, eating in the evening, eating frequency, snacking, pulses (legumes), nuts, fish, dairy, confectionery, water, artificially sweetened drinks, fruit juice, coffee and tea, alcoholic drinks, total carbohydrate, glycaemic load, total protein, caffeine, catechins, strength training, energy density, sleep | |
| STRONG EVIDENCE | Substantial effect on risk unlikely | None identified | |

The factors identified in the matrix as increasing or decreasing risk of weight gain, overweight or obesity do so by promoting excess energy intake (positive energy balance, increased risk) relative to the level of energy expenditure (in particular physical activity), or appropriate energy balance (decreased risk), through a complex interplay of physiological, psychological and social influences.[10]

1 The evidence for these conclusions comes mostly from studies of adults, except where specified. However, the CUP Panel judged that the conclusions for adults, unless there is evidence to the contrary, also apply to children aged 5 years and over.

2 With the available evidence, the Panel could make separate conclusions for children and adults in relation to screen time. Screen time is a marker of sedentary behaviour and may also be associated with low levels of physical activity, consumption of energy-dense snacks and drinks, and exposure to marketing of such foods and drinks.

3 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.

4 There are recognised scores for quantifying adherence to a 'Mediterranean type' dietary pattern but it is unclear exactly what such a diet comprises. It generally describes a diet rich in fruits and vegetables, with modest amounts of meat and dairy, some fish and wine, and rich in unrefined olive oil. Traditionally it is also associated with high levels of physical activity. Currently most countries around the Mediterranean do not consume such a diet.

5 The evidence relates principally to excess weight gain, overweight and obesity in childhood, but overweight and obesity in childhood tends to track into adult life.

6 'Fast foods' are readily available convenience foods that tend to be energy dense and are often consumed frequently and in large portions. Most of the evidence is from studies of foods such as burgers, fried chicken pieces, chips (French fries) and high-calorie drinks (containing sugars, such as cola, or fat, such as shakes), as typically served in international franchise outlets. Many other foods can also be prepared quickly, but the speed of preparation is not the important factor, even though it is characteristic of this group of foods.

7 Such diets are characterised by high intakes of free sugars, meat and dietary fat, which are probably the factors responsible for the effects on weight. The overall conclusion includes all these factors.

8 Refined grains refers to the grains themselves, or products of such grains, that have been mechanically processed to remove one or more of the bran, germ or endosperm. This is in contrast to wholegrains (or their products), which contain all three constituents.

9 Sedentary behaviours comprise both high levels of physical inactivity and low levels of physical activity.

10 For discussion of the integration of the exposures into clusters, please see **Section 8**.

# 1. Summary of Panel judgements

The Continuous Update Project (CUP) Panel has drawn conclusions about individual *exposures* and whether they decrease or increase the risk of weight gain, overweight and obesity, as outlined below and in **Section 7**.

Several singular exposures (increased *aerobic physical activity*, consumption of wholegrains, foods containing *dietary fibre*, fruit and vegetables) have been judged to show specific associations with decreased risk of weight gain, overweight and obesity, as has a predefined *'Mediterranean type' dietary pattern* (which itself includes these singular exposures). However, the CUP Panel has greater confidence that the overall clustering of the exposures, including higher adherence to a 'Mediterranean type' dietary pattern, is more likely to decrease the risk of weight gain, overweight and obesity than any given single exposure.

Furthermore, several singular exposures have been individually associated with increased risk of weight gain, overweight and obesity: increased sedentary time, including screen time, and consumption of sugar sweetened drinks, 'fast foods' and refined grains. The CUP Panel also judged a 'Western type' diet (characterised by high intakes of free sugars, meat and dietary fat) to be associated with increased risk of weight gain, overweight and obesity; such a diet itself often includes these singular exposures. And similarly, the CUP Panel has greater confidence that the overall clustering of these exposures is more likely to increase the risk of weight gain, overweight and obesity than any exposure in isolation. These groupings include conclusions for both strong and limited evidence.

In addition, the Panel notes the strength of the evidence for having been breastfed and reduced risk of excess weight gain, overweight and obesity in children, and the limited nature of the evidence for lactation and decreased risk in mothers. For a full discussion of the integration of the evidence, please see **Section 8**.

The exposures identified as increasing or decreasing risk of weight gain, overweight or obesity do so by promoting excess energy intake (positive *energy balance*, increased risk) relative to the level of energy expenditure (in particular physical activity), or appropriate energy balance (decreased risk), through a complex interplay of physiological, psychological and social influences. For an explanation of the contextual framework and energy balance, see **Section 3**.

The CUP Panel's judgements for each singular exposure are as follows:

### The CUP Panel concluded:

### Convincing

**Decreased risk**

- **Walking:** Walking protects convincingly against weight gain, overweight and obesity.

**Increased risk**

- **Screen time (children):** Greater screen time is a convincing cause of excess weight gain, overweight and obesity in children. Screen time is a marker of sedentary behaviour and may also be associated with low levels of physical activity, consumption of energy-dense snacks and drinks, and exposure to marketing of such foods and drinks.
- **Sugar sweetened drinks:** Consumption of sugar sweetened drinks is a convincing cause of weight gain, overweight and obesity.

## Probable

### Decreased risk

- **Aerobic physical activity:** Aerobic physical activity probably protects against weight gain, overweight and obesity.
- **Foods containing dietary fibre:** Consumption of foods containing dietary fibre probably protects against weight gain, overweight and obesity.
- **'Mediterranean type' dietary pattern:** Consumption of a 'Mediterranean type' dietary pattern probably protects against weight gain, overweight and obesity.
- **Having been breastfed:** Having been breastfed probably protects against excess weight gain, overweight and obesity in children.

### Increased risk

- **Screen time (adults):** Greater screen time is probably a cause of weight gain, overweight and obesity in adults. Screen time is a marker of sedentary behaviour and may also be associated with low levels of physical activity, consumption of energy-dense snacks and drinks, and exposure to marketing of such foods and drinks.
- **'Fast foods':** Consumption of 'fast foods' is probably a cause of weight gain, overweight and obesity.
- **'Western type' diet:** Consumption of a 'Western type' diet is probably a cause of weight gain, overweight and obesity.

## Limited – suggestive

### Decreased risk

- **Wholegrains:** The evidence suggesting that consumption of wholegrains decreases the risk of weight gain, overweight and obesity is limited.
- **Fruit and vegetables:** The evidence suggesting that consumption of fruits and vegetables decreases the risk of weight gain, overweight and obesity is limited.
- **Lactation:** The evidence that lactation decreases the risk of weight gain, overweight and obesity in the mother is limited.

### Increased risk

- **Sedentary behaviours:** The evidence suggesting that sedentary behaviours increase the risk of weight gain, overweight and obesity is limited.
- **Refined grains:** The evidence suggesting that consumption of refined grains increases the risk of weight gain, overweight and obesity is limited.

Where available, quantification of exposures in relation to outcomes has been reported as in the published reviews (see **Section 7**). However, owing to the methods used (a '*review of published reviews*'), reliable summary estimates of quantified thresholds were not able to be calculated in this report.

For a description of the definitions of, and criteria for, the terminology of 'convincing' and 'probable' (referring to the likelihood of causality), and 'limited – suggestive', 'limited – no conclusion' and 'substantial effect on risk unlikely', see **Appendix 1**.

The Panel judgements for the determinants of weight gain, overweight and obesity are shown in the **Matrix**.

# 2. Measures, trends and implications

## 2.1. Defining weight gain, overweight and obesity

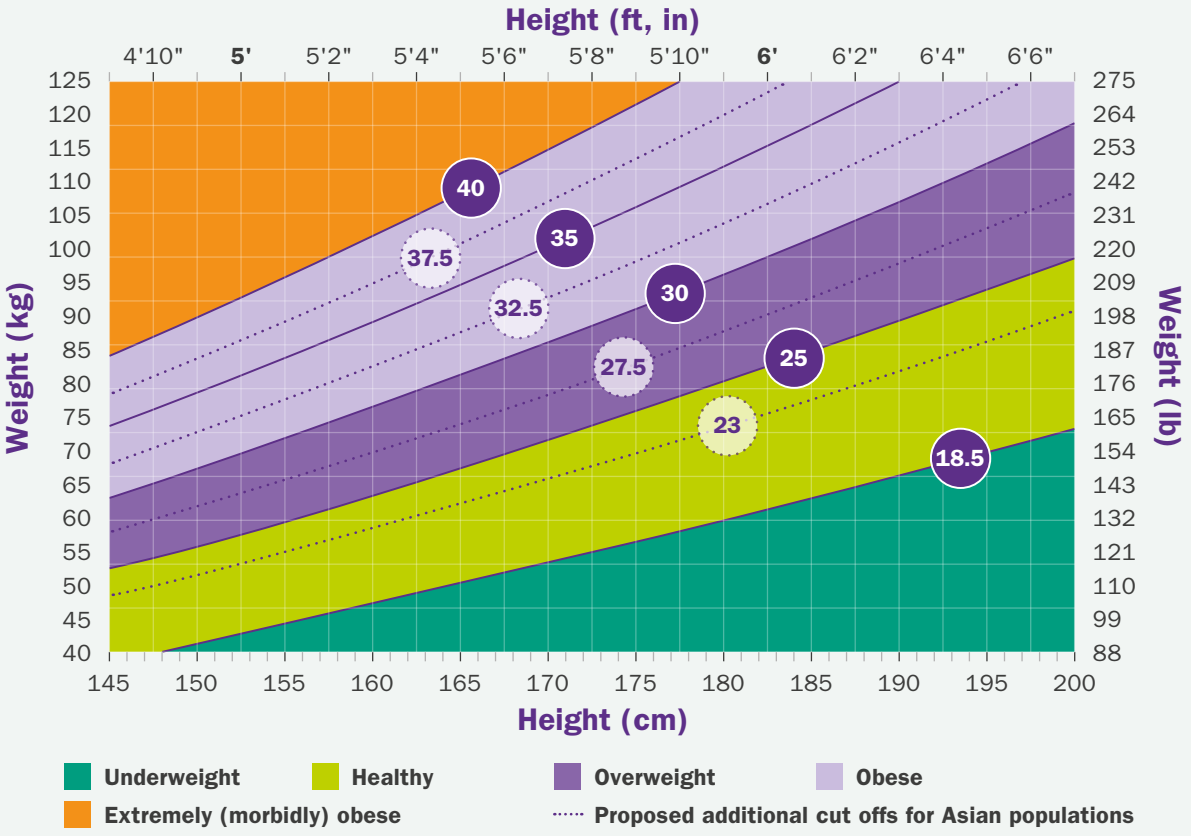
Overweight and obesity are characterised by excess body fat. *Adipose tissue* can accumulate at various sites around the body, including subcutaneously (beneath the skin), around skeletal muscles, or viscerally (around internal organs). Fat may also be deposited ectopically, that is in tissues other than adipose tissue, such as in muscles or the liver. The pattern of fat storage is largely determined by genetic factors, with a typically different pattern in men and women, which also varies with age and between ethnic groups [6, 7].

Numerous *anthropometric measures* can be used to estimate the level of *adiposity*. The most common is the *body mass index* (BMI), a measure of weight adjusted for height, calculated as weight in kilograms divided by height in metres squared ($kg/m^2$). The category thresholds for BMI as proposed by the World Health Organization (WHO) are shown in **Figure 1**. BMI is a population-level measure and does not always provide an accurate approximation of body fatness at an individual level [8]. Category thresholds also vary between ethnic groups. Alternative markers of body fatness include waist circumference, *waist-hip ratio* and other body composition measures such as percentage body fat. There are also measures specifically designed for use during childhood and adolescence. See **Box 1**.

Weight gain is a normal feature for certain stages of life such as during childhood, pregnancy and recovery from illness. However, excessive weight gain, characterised by the accumulation of fat mass to a greater extent than lean mass, can be used as an indicator of overweight and obesity and may better reflect adiposity than total weight.

## Figure 1: Adult height, weight and ranges of body mass index (BMI)

Body mass index (BMI) is a simple index of weight-for-height used to classify underweight, healthy weight and overweight in adults. BMI is defined as weight in kilograms divided by the square of height in metres (kg/m$^2$). The category thresholds for BMI as proposed by the World Health Organization (WHO) are shown.




## Box 1: Anthropometric measures in adults, adolescents and children

***Body mass index (BMI).*** Overweight is defined as a BMI greater than or equal to 25 kg/m². Obesity is defined as a BMI greater than or equal to 30 kg/m². At a population level, BMI is the most commonly used marker of body fatness in epidemiological studies because of its low cost and simplicity to assess, while maintaining high accuracy and precision at the population level [8]. However, it is an imperfect measure at an individual level owing to its failure to differentiate between lean and adipose tissue or account for differences in age or ethnicity [6, 7, 9].

***Waist circumference and waist-hip ratio.*** The WHO reference values for waist circumferences of 94 centimetres (37 inches) in men and 80 centimetres (31.5 inches) in women, and the waist-hip ratio reference values more than 0.90 for men and more than 0.85 for women, are roughly equivalent to a BMI of 25 kg/m² [10]. These are useful measures to identify abdominal adiposity but, as with BMI, are population-level measures and often imperfect at an individual level as they do not distinguish between visceral and subcutaneous fat tissue. Threshold values are lower for people of South Asian origin; further research is required to establish these values for other ethnic groups [9].

***Body fat percentage.*** Other measures of body composition aim to assess 'whole-body' adiposity – most commonly fat mass as a proportion of weight or body fat percentage [11]. Examples of tools used include skinfold thickness and bioelectrical impedance analysis as well as more sophisticated techniques, which directly calculate body fat percentage, such as magnetic resonance imaging, computer tomography and dual-energy X-ray absorptiometry. While these more sophisticated measures are the most accurate, they are not superior to BMI for predicting disease risk in a general population [12]. In addition, their high cost often makes them impractical for use in large scale studies.

***Measures in children and adolescents.*** In children and adolescents, the most commonly used measures of growth and body composition in a clinical setting are weight-for-age, height-for-age and BMI. Reference values for all three measures are age and sex specific, to account for the differences throughout this period of growth and development [13–15]. BMI z-score, also known as BMI standard deviation score, is a measure of how far any individual in a group deviates from the average of that group or from a reference standard. Calculated z-scores correspond to equivalent growth chart percentiles; for example, a BMI z-score of zero lies on the 50$^{th}$ percentile.

The WHO defines weight categories during childhood and adolescence using gender-specific BMI-for-age percentile curves, devised from international reference groups. The WHO thresholds for overweight and obesity are one standard deviation above the mean and two standard deviations above the mean, respectively [15]. Discrepancies in weight category classification can arise when transitioning from adolescence to adulthood, as the conversion from percentile or BMI z-score to the standard adult BMI does not directly align [16]. World Obesity Policy and Prevention (formerly International Obesity Task Force, IOTF) has proposed alternative cut-off points for childhood overweight and obesity, derived from international data. These are based on centiles in children and adolescents that project directly to adult BMI thresholds at 18 years [17, 18].

## 2.2 Trends

Since the mid 1970s, the worldwide *prevalence* of overweight and obesity has increased [1]. There has been a dramatic shift from the proportion of underweight adults being double that of those who had obesity, to obesity equalling or overtaking underweight. This shift has been seen within almost every region of the world. However, since 2000, the rate of increase in BMI among *higher-income countries* has begun to slow. In contrast, rates have continued to increase in countries characterised by low and middle indices of income and/or development resulting in total global prevalence of overweight and obesity continuing to rise, as illustrated in **Figure 2**.

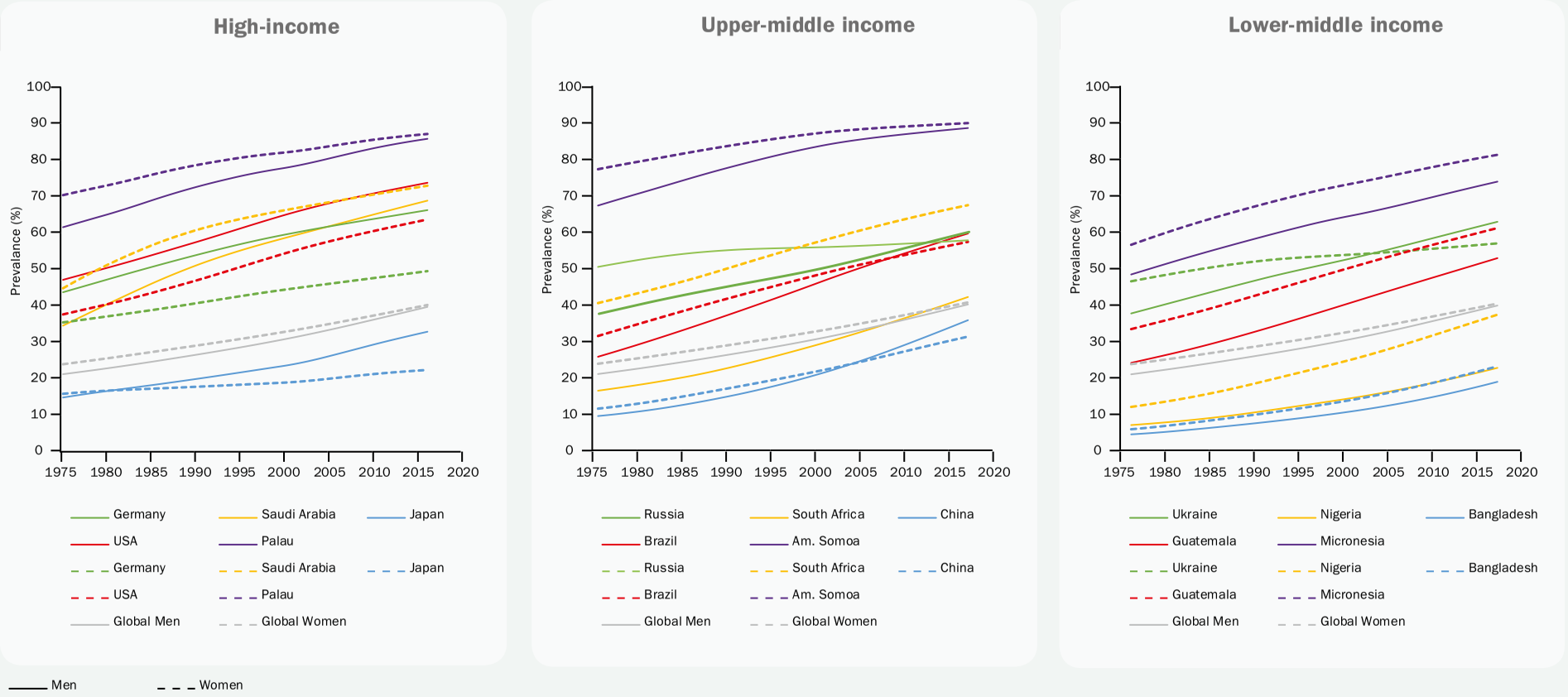
Childhood and adolescent overweight and obesity is following very similar global trends to that seen in adults. Although current figures show there are still more 5 to 19 year olds underweight than with obesity, if trends continue as predicted, child and adolescent obesity will surpass underweight by 2022 [1]. This highlights the importance of monitoring childhood overweight and obesity as it tracks into adulthood.

The last four decades have also seen considerable changes in global nutrition, termed the '*nutrition transition*' [2]. Rapid economic development, globalisation, mass media and new technologies have had a dramatic impact on food systems and dietary patterns. Although this has had some beneficial outcomes such as reducing undernutrition, food insecurity, dietary deficiencies and infectious disease, it has also been accompanied by adverse effects, including increasing rates of overweight and, in particular, a dramatic increase in obesity and diet-related *non-communicable diseases* (NCDs).

Common themes and dietary patterns have appeared across cultural and ethnic groups during this transition. Most notably, there has been a global shift from traditional and relatively unprocessed plant-based diets to those with more processed foods and drinks, which are high in fats and sugars, and more foods from animal sources. This shift has been fuelled by changes in agriculture and industry, resulting in cheaper production of highly processed foods, making them increasingly affordable, particularly for countries characterised by low indices of income and/or development [3]. These changes to dietary patterns have been accompanied by falling levels of *physical activity* and increasingly sedentary lifestyles. This is exacerbated by the decline in manual jobs, changes to transport habits and increases in screen-based technologies that dominate both work and leisure time [19].

This nutrition transition, coupled with falling levels of energy expenditure, has had profound effects on the prevalence of overweight and obesity. Since 1975, the global population has almost doubled [20]. In contrast, the number of adults with overweight and obesity has more than quadrupled, from 463 million in 1975 to 1.97 billion in 2016. Childhood and adolescent overweight and obesity has increased six-fold, from 59 million to 338 million, over the same time period, with numbers projected to rise if trends remain unchanged [1].

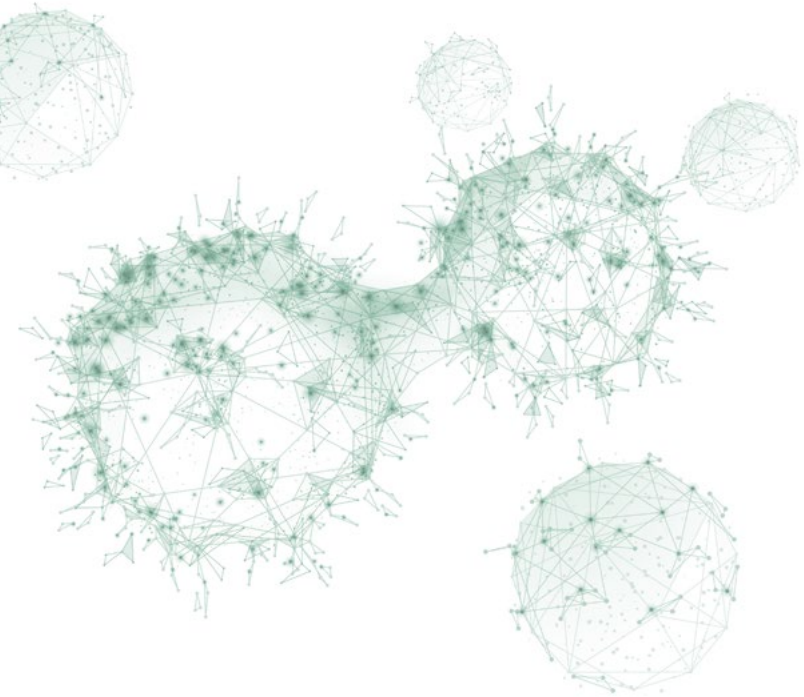
## Figure 2: Estimated age-standardised prevalence of overweight and obesity in adults (aged 20+) across representative countries of low, middle and high-income between 1975 and 2016




Overweight and obesity is categorised as a BMI equal to or greater than 25 kg/m². Countries are categorised as low and low-middle, upper-middle and high income by the World Bank. Income is measured using gross national income per capita. The countries have been chosen on the basis of largest population size for each index of income for four global regions: Europe and Central Asia (green), Africa and the Middle East (yellow), East and South Asia and the Pacific (blue) and the Americas (red); for reference, the country with the highest prevalence of obesity for each income category has been included (purple). Global prevalence is also plotted (light grey). Data obtained with permission from NCD Risk Factor Collaboration (NCD-RisC), see www.ncdrisc.org [1].

## 2.3 Individual Implications

The CUP has identified 12 cancers causally linked to overweight and obesity; see Exposures: Body fatness and weight gain. There is convincing evidence that greater body fatness is a cause of cancers of the oesophagus (*adenocarcinoma*), pancreas, liver, colorectum, breast (postmenopausal) and kidney. Greater body fatness, encompassing weight gain in adult life, is a convincing cause of endometrial cancer. Greater body fatness is also probably a cause of cancers of the mouth, pharynx and larynx, stomach (cardia), gallbladder, ovary and prostate (advanced). Weight gain in adult life is a convincing cause of postmenopausal breast cancer. The CUP analysis also found evidence that greater body fatness throughout life probably protects against premenopausal breast cancer and greater body fatness in young adulthood probably protects against postmenopausal breast cancer. The biological mechanisms linking greater body fatness and cancer are outlined in **Box 2**; for full details see The cancer process.



### Box 2: The obesity-cancer link

**Analyses in the WCRF/AICR Third Expert Report show that greater body fatness is causally linked to 12 cancers; oesophagus (adenocarcinoma), pancreas, liver, colorectum, breast (postmenopausal), kidney, endometrial, stomach (cardia), gallbladder, ovary, prostate (advanced) and cancers of the mouth, pharynx and larynx (see Exposures: Body fatness and weight gain). Research is continuing to uncover the biological mechanisms underlying this relationship, and several cellular and molecular pathways have been implicated. Increasing adiposity leads to systemic changes in metabolic and endocrine pathways that can affect intracellular processes relevant to several hallmarks of cancer (the set of phenotypic characteristics – as opposed to the genetic factors that cause them – acquired by normal cells during the transition to cancer cells [21]). The hallmarks of cancer exacerbated by greater body fatness include sustained proliferative signalling, angiogenesis, immune regulation, invasion and metastasis, genomic instability and altered cellular energetics.**

- **For a full summary of how foods, food constituents, nutrition (including body composition) and physical activity can influence the biological processes that underpin the development and progression of cancer, please see The cancer process.**
- **For a summary of the site-specific mechanisms linking greater body fatness to cancer development and progression, please see Appendix 2 in Exposures: Body fatness and weight gain.**

In addition to increasing the risk of the cancers assessed by the CUP, three additional cancer sites were reviewed by WHO's International Agency for Research on Cancer, which concluded that greater body fatness also increases the risk of thyroid cancer, multiple myeloma and meningioma [4].

As well as cancer, overweight and obesity are associated with numerous other comorbidities [22]. These include metabolic [23], cardiovascular [24], musculoskeletal [25, 26], digestive [27, 28] and mental health disorders [29].

For several comorbidities [30], including some cancers, the increased risk of disease is seen at the top end of the healthy BMI and waist circumference ranges, not just above the conventional WHO thresholds; see Exposures: Body fatness and weight gain.

Although overweight and obesity are risk factors for a number of diseases and disorders, less is understood about how weight loss may affect future risk of developing these comorbidities. It is a complex picture, especially for cancer; see **Box 3**.

### Box 3: Impact of intentional weight loss on risk of disease

**Intentional weight loss has been associated with reducing risk of type 2 diabetes and cardiovascular diseases. Lifestyle interventions, such as calorie-controlled diets and physical activity interventions, can lead to modest weight loss. Losing even small amounts of weight can yield an improvement in key disease markers, such as reducing blood concentrations of triglyceride, low-density lipoprotein (LDL) and glucose [31, 32]. This can reduce risk of future disease development, as well as alleviating symptoms in patients already living with comorbidities [33]. Weight loss through dietary means is also associated with a reduction in premature all-cause mortality in people with obesity [34]. More substantial weight loss, achieved through highly intensive weight management interventions, can result in even better outcomes, including complete remission of disease [35].**

**Prospective observational studies have suggested that intentional weight loss may also be favourable in reducing risk of cancer [36]. However, in the absence of trials and because cancer itself can cause unintentional weight loss, it is difficult to identify cause and effect.**

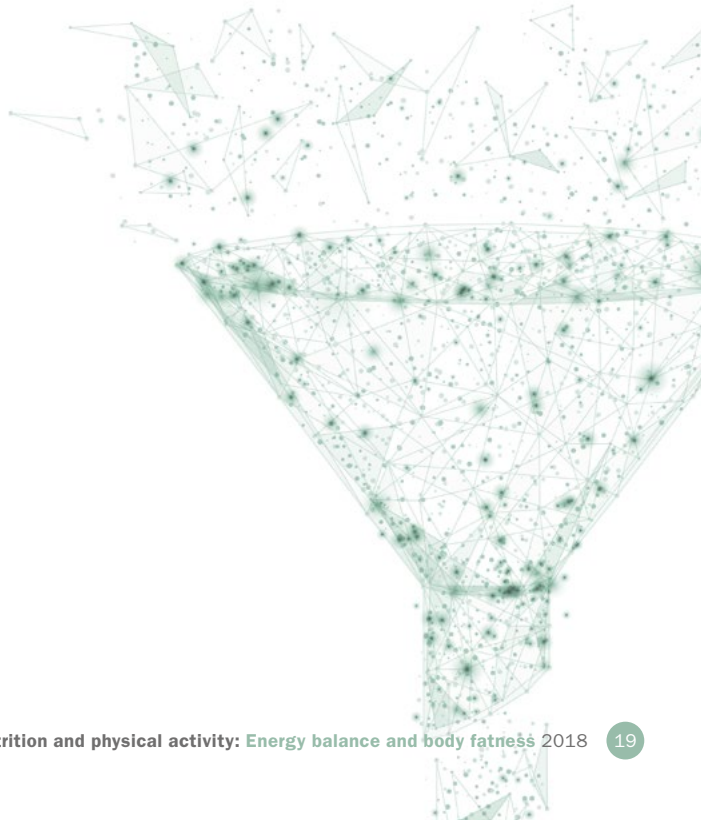
**Bariatric surgery can be a more successful, long-term solution for some patients with obesity-related comorbidities, after nonsurgical measures have been explored. Sustained improvement in key disease markers over several years post-surgery contributes to decreased incidence of disease and overall mortality when compared with those who have not undergone surgery [37]. However, the reduced risk of some diseases is not directly correlated with the degree of weight loss. Bariatric surgery can dramatically improve glycaemic control in patients with type 2 diabetes within days post-surgery, suggesting factors other than weight loss are also involved in the improvement of disease risk following surgery [38].**

In addition to increased risk of numerous comorbidities, overall mortality is higher in people living with overweight or obesity compared with those within the healthy BMI range [39]. Although there is some evidence of benefit from having a higher BMI, between 25 and 35 kg/m$^2$, for specific diseases or periods during the life course, this is unlikely to be attributable to greater body fat. In older people, more than 65 years of age, the association between higher BMI and reduced mortality [40] is considered a marker of maintained lean mass. Greater lean mass is associated with increased resilience, mobility and grip strength as well as longer life expectancy and better overall survival. Survival rates after cardiac events and stroke are better in patients who have higher BMI compared with those who have a healthy BMI [41]. However, BMI is a poor predictor of adiposity at an individual level and may be subject to *biases*, particularly in older populations and patient groups where it is most likely to pose a problem of interpretation [42, 43].

Alongside these implications, both adults and children who have overweight or obesity report experiencing *weight bias* and *obesity stigma* [44, 45]. This may be in relation to work, healthcare, education, social interactions including friends and family, or the media. Obesity stigma is associated with significant physiological and psychological consequences [46] and can affect the quality of care received from clinicians. In some situations, it can ultimately lead to reluctance to seek medical advice, poor health outcomes and greater risk of mortality [47].

## 2.4 Wider implications

Overweight and obesity, and their comorbidities, have huge economic impacts [48, 49], not only in terms of direct costs to social and healthcare systems, but through other indirect costs. There are more absences from work reported for people living with obesity than for the general population, which increases financial costs for businesses. Furthermore, a growing number of people are unable to work at all as a direct result of obesity, its related health issues, discrimination in the recruitment processes, or lack of support and appropriate adjustments in the workplace. At a national level this can lead to reduced productivity of the workforce and increased national or government expenditure to support those not currently employed or unable to work, such as through unemployment benefits. In the UK it is estimated that overweight and obesity cost the National Health Service £5.1 billion between 2006 and 2007 [50]. It is difficult to establish the true cost of overweight and obesity globally owing to a lack of sufficient data in countries characterised by lower indices of income and/or development.



# 3. Fundamental concepts

## 3.1 Energy balance

Humans need energy to maintain the body's basic functions (*basal metabolic rate* or BMR), to digest and assimilate food (diet induced thermogenesis), and for *physical activity*. BMR is largely determined by lean body mass [51, 52]; this varies with body size, sex, age and ethnicity, and also health and nutrition status [53–55]. The major energy cost beyond BMR comes from physical activity. There are also additional energy costs for non-exercise activity thermogenesis and tissue deposition during growth in childhood, puberty, and pregnancy and lactation. Total energy requirements vary considerably between people.

*Energy balance* is achieved when intake of energy, through foods and drinks, matches energy requirements. Positive energy balance means consuming more energy than is expended. A person in positive energy balance will gain weight over time — mainly as fat, but also as lean tissue [56, 57]. Negative energy balance means consuming less energy than is expended, and over time this results in weight loss — again mainly fat, but also lean tissue; the proportions depend on the degree of energy deficiency, starting body composition and type of activity [56–58].

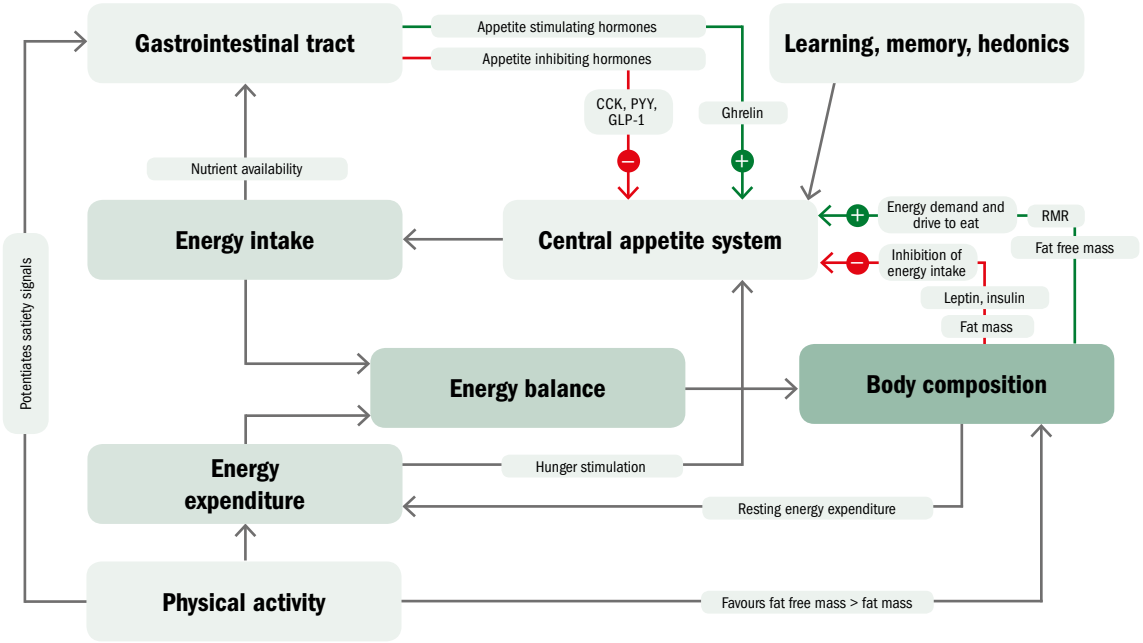
Normally, body weight and energy stores are balanced over several days to weeks. Short-term changes in weight are mostly caused by fluctuations in the body's store of water, not in fat [59]. Thus, between meals and overnight, the short-term stores of carbohydrate (glycogen in liver and muscles) are mobilised and oxidised, with associated loss of water. Longer-term changes in weight over months to years, by contrast, are generally due mainly to alterations in the amount of the body's fat tissue [60, 61]. Therefore, substantial daily fluctuations in weight do not reflect changes in energy stores, whereas consistent weight gain or loss over a longer period of time generally does.

Furthermore, ageing results in a decline in resting energy expenditure, which is mediated by changes to fat free mass and organ metabolic rates [62, 63]. In order to maintain energy balance, food intake needs to decrease, or physical activity needs to increase (particularly resistance training, which favours development and preservation of lean mass). However, both of these options are difficult to achieve because of the stability of food and activity habits acquired over a lifetime, and therefore it is usual to observe weight gain in adult life [64].

## 3.2 Influences on energy balance

Maintenance of stable body weight in adulthood depends on closely matching energy intake from food and drink with the energy expended in basal metabolism and physical activity. Under normal circumstances this is achieved through a complex interplay between regulatory systems involving the gut, the hypothalamus and *hormonal* messengers, together with an important role for *hedonic signals*, and energy expenditure, principally through physical activity (see **Figure 3**).

## Figure 3*: Appetite signals, energy balance and body composition




**Abbreviations used:** CCK = cholecystokinin; PYY = peptide tyrosine tyrosine; GLP-1 = glucagon-like peptide 1; RMR = resting metabolic rate.

The maintenance of energy balance (when energy intake equals energy expenditure) is the result of a complex interplay between neurophysiological and gastrointestinal systems influencing the regulation of food intake. Appetite responds to a variety of factors, including the level of physical activity (the major modifiable determinant of energy expenditure), which promotes increased food intake, and endogenous signals that respond to the amount and characteristics of food and drink consumed. The gastrointestinal tract responds to the composition of the food and drink by secreting hormones that stimulate or inhibit the central appetite system in the brain. Hormone secretion by the gastrointestinal tract is also influenced by physical activity, which leads to an increase in appetite in proportion to the increased energy expenditure. Signals that promote hunger (in the face of reduced intake or increased expenditure) are more powerful than those that suppress intake (in the face of reduced energy expenditure or excess energy intake). Consequently, at low levels of energy expenditure, effective appetite regulation is compromised, and the likelihood of excess energy intake (positive energy balance) is increased when exposed to factors that tend to promote overconsumption, such as higher energy density food and drink. Learning, memory and food hedonics, strongly modulated by the external environment and early experiences, directly influence the central appetite system and can stimulate or inhibit the desire to eat. Body composition, the proportion of fat to fat free mass, influences total energy expenditure (by modifying resting energy expenditure) and energy intake (by modifying the demand for energy and the drive to eat).

*Schematic diagram has been adapted from Figure 2 in Blundell *et al.* (2012) [65] and Figure 1 in MacLean *et al.* (2017) [66], with permission.

When energy intake fails to meet energy expenditure, powerful signals promote hunger and food consumption (where available) and reduce physical activity. When energy intake exceeds expenditure, feelings of *satiation* (the desire to stop eating) and *satiety* (the lack of desire to start eating) are promoted. However, these signals may be overridden by factors relating to the food and drink consumed, or individual susceptibility to overconsumption. For instance, foods that have higher energy density and larger offered portion sizes both increase overall energy intake, at least in the short term [67–70]. Energy taken in liquid form appears to be less effective in inducing satiation or satiety [71], and so may promote overconsumption.

The level of physical activity appears to interact with these processes, so that at low levels of energy expenditure (such as are typical of populations *in high-income countries*, and increasingly in *low- and middle-income countries*) and when food and drink are readily available, adequate suppression of appetite to maintain energy balance is compromised [72], and the resulting positive energy balance leads to gradual but persistent weight gain over time, most of which is *adipose tissue*.

# 4. Other influences on energy balance and body weight

*Energy balance* and body weight are influenced by numerous, interdependent factors. Genetics and *epigenetics*, the gut *microbiome*, and psychosocial and environmental and *policy* factors all contribute to determining body weight, by influencing and interacting with diet, nutrition and *physical activity* patterns. The precise nature of the interactions between these factors remains to be fully established.

## Genetics

Overweight and obesity tend to run in families, consistent with a role for genetics in predisposing an individual to greater body fatness [73]. Having one or two parents who have obesity, in particular the mother, increases the risk of greater body fatness for children [74]. This link may be partially explained by role modelling and learned behaviours from parent to child or the intrauterine environment and early nutrition (see next sub-section). A large number of complex gene-gene and gene-environment interactions are involved. Identical (monozygote) twin studies have identified many genetic variants that contribute to weight gain, principally by influencing appetite. However, *mutations* and chromosomal rearrangements known to cause obesity, such as congenital *leptin* deficiency, Prader-Willi syndrome and Bardet-Biedl syndrome, are rare [75].

## Epigenetics and maternal programming

Nutritional *exposures* during critical windows of fetal development are an important determinant of phenotype, which may influence risk of disease later in life. Maternal nutritional status determines capacity to deliver appropriate nutrients to the fetus. Being underweight or overweight during the periods of gestation and lactation, as well as eating diets lacking in key *micronutrients*, can result in detrimental changes to the

metabolic profile of the developing fetus or infant which can predispose him or her to obesity and metabolic dysfunction [4, 76, 77]. These effects are attributed to epigenetic changes (such as DNA methylation, histone modifications and chromatin remodelling) that silence or upregulate key genes or groups of genes; see also The cancer process. In addition to nutritional factors, the altered hormonal status of mothers who have overweight or obesity results in adverse metabolic and epigenetic changes which predispose to increased risk of obesity for the infant [73]. Transgenerational heritability of these epigenetic modifications is possible if they occur in the epigenome of *germ cells* during fetal development [78]. Children of mothers who have obesity, including those who gain excessive gestational weight, also have greater fetal size (fetal macrosomia) and greater percentage fat mass at birth [79].

### Gut microbiota

There is growing evidence that the bacteria that normally reside in the colon – the microbiome – may be involved with the development of overweight and obesity. The composition of the gut microbiome in people with higher BMIs is different from that of those within the healthy *BMI* range, although the direction of the relationship is not fully established [80]. This altered composition might contribute to increased *adiposity* by several mechanisms, including enhancing *energy harvest* capacity from the diet [81, 82]. Recent studies have suggested that modulation of the gastrointestinal microbiota might help regulate body weight [83, 84].

### Psychosocial factors

Many elements of the social environment can influence the determinants of overweight and obesity. Psychosocial factors that can influence weight gain and increase risk of overweight or obesity include stress, discrimination, depressive mood, personality traits and emotional eating disorders. A stable social environment, such as one with a strong support network, and a cohesive and supportive local community can reduce the risk of weight gain [85].

### Environmental and policy factors

Overweight and obesity are complex and influenced by many factors beyond people's direct personal control. Broadly these economic, social and environmental factors operate at global, national and local levels, which at a personal level are experienced as the availability, affordability, awareness and acceptability of healthy diets and physical activity, relative to unhealthy diets and physical inactivity. Income, social status, education, health and food literacy, healthy child development, and social and physical environments all influence weight gain. These factors influence the health outcomes of individuals, communities and populations and can create health inequalities, with lower *socioeconomic* groups more likely to be impacted by these upstream determinants. Changing the upstream structural factors through public health policy, in the form of laws, regulations or guidelines, is critical in reducing inequalities. A package of policies is needed to address the multiple drivers of weight gain. For a full overview of the role of policy in public health, see Recommendations and public health and policy implications.

# 5. Interpretation of the evidence

## 5.1 General

For general considerations that may affect interpretation of the evidence, see Judging the evidence.

### Availability of intervention data

- In general there is a relative lack of intervention studies, leaving *cohort studies* – which may be subject to *confounding* and *bias* – as the main type of evidence. However, *randomised controlled trials* also have limitations, in particular in investigating the effects of long-term dietary change (see Judging the evidence, Section 2).

## 5.2 Specific

Considerations specific to interpreting and judging the evidence for the determinants of weight gain, overweight and obesity include the following:

### Varied designs, reporting methods and outcomes

- Designs and reporting methods vary between studies, making it difficult to combine data. For most of the *exposures* several measures were used. The non-uniformity of the data means they need to be interpreted carefully, on a study by study basis.

### Self-reported data

- Self-reported anthropometric data often correlate well with measured data, although under-reporting of body weight and over-reporting of height are common [86, 87].
- Self-reported information on food consumption is prone to bias:
  - Consumption of foods or drinks regarded by participants as 'unhealthy', for instance those containing high levels of fat and sugars, tend to be under-reported more than others.
  - Under-reporting of energy intake has been shown to be associated with factors such as age, weight status, perceived body size and other personal characteristics [88–95].
  - Self-reporting bias has also been observed in children [96].
- Self-reported data on *physical activity* is also influenced by biases which can lead to both under- and over-reporting [97].

### Precision of measurement

- Measuring energy intake and expenditure in humans is complex. Current techniques are not sufficiently precise to reliably detect the small imbalances that lead to weight change, against a background of much higher levels of total energy intake and expenditure [98, 99].
- Many studies measure exposures that can be captured easily. However, these exposures may be markers of more important risk factors; for example, total physical activity may be the operative factor in the true relationship, but leisure time physical activity, although not easy to measure, may be easier to capture through questionnaires or surveys.

### Reverse causality

- Although all studies included are prospective, some studies do not allow *reverse causality* to be excluded. For example, a high *BMI* at the start of the study may be associated with low physical activity and may also be independently associated with an increased risk of weight gain. Although many studies *adjust* for potential confounders, this complexity makes residual confounding difficult to exclude, in particular in relation to smoking.

### The role of study funding

- Sources of funding may create conflicts of interest and may bias the results of studies or reviews. For example, studies funded by soft drink companies are more likely to present a conclusion of no significant association between intake of sugar sweetened drinks and *adiposity* than are non-industry-funded studies [100].

### Country level income

- Most epidemiological studies investigating weight gain, overweight and obesity are carried out in *high-income countries*, which may limit the wider application of their findings. This is pertinent given the growing burden of overweight and obesity in many *low- and middle-income countries* [1].

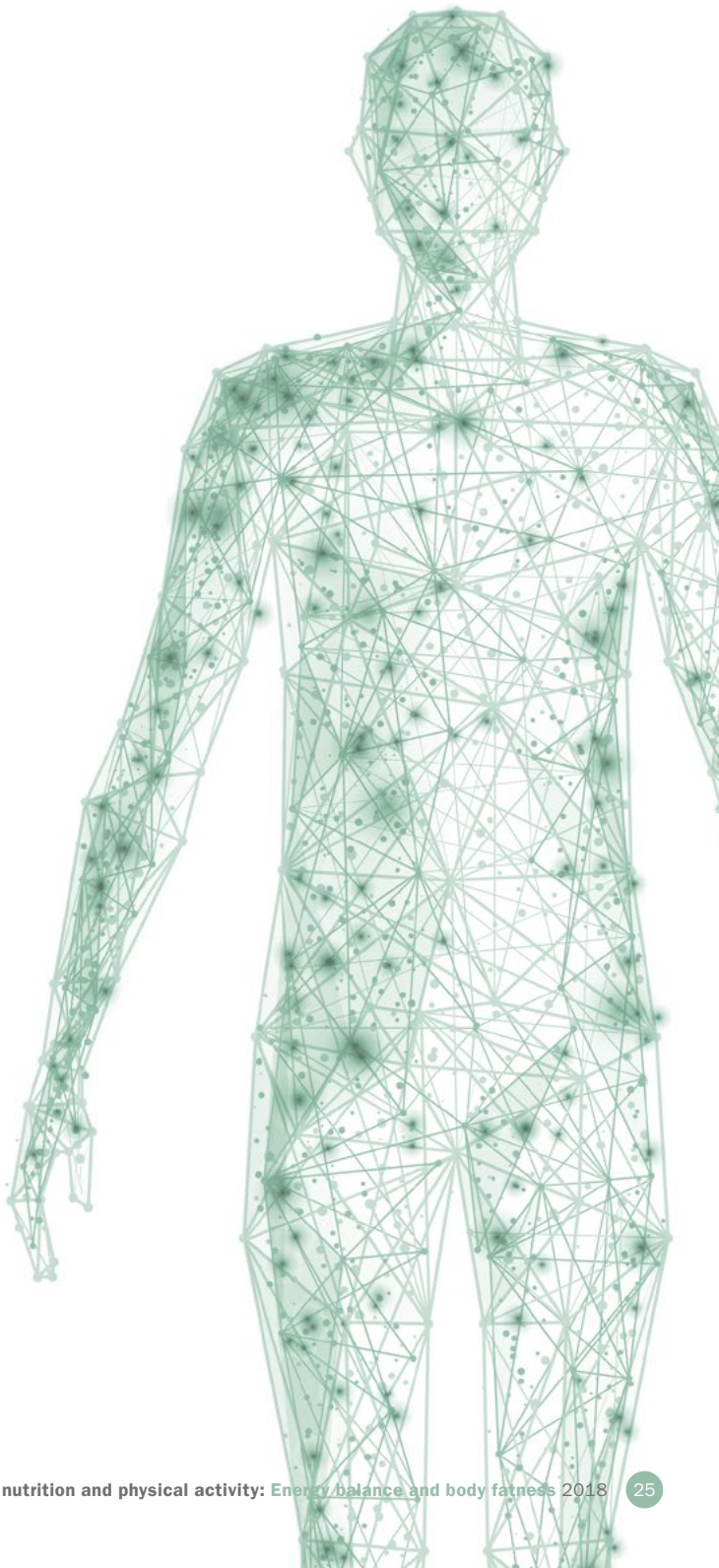
### Approaches to conceptualising diet and activity

- Many studies have focused on associations between weight change and specific components of the diet. However, the overall impact of any dietary intervention will depend not only on effects intended by the intervention but also on any consequent changes to diet or lifestyle.

- Studies of diet, nutrition and physical activity frequently attempt to isolate effects of single factors, for instance particular foods, food constituents or nutrients, rather than broader patterns. This could be considered a 'reductionist' approach. However, many exposures correlate with each other and interact physiologically. A more 'synthetic' approach, conceptualising overall patterns, is likely to better represent the true relationships but is less commonly used in studies investigating weight gain, overweight and obesity.

### Social and environmental determinants

- Social (including economic and political) and environmental factors are important determinants of behaviours, including those affecting body composition. Choices about diet and physical activity occur within a broader environment that differs between communities, populations and places. The role of the *policy* environment is the subject of Section 4 of Recommendations and public health and policy implications.



# 6. Methodology

## 6.1 Standardised process and terminology

Throughout the CUP, a standardised process has been used, assessing the likelihood of observed relationships being causal. To achieve this, standardised criteria for grading the evidence and standardised terminology for describing the strength of the evidence have been used. As in the rest of the CUP, these have been applied in this report as well.

A description of the definitions of, and criteria for, the terminology of 'convincing' and 'probable' (referring to the likelihood of causality), and 'limited – suggestive', 'limited – no conclusion' and 'substantial effect on risk unlikely' is in **Appendix 1**. For more information on the process, see Judging the evidence.

## 6.2 Epidemiological data

Because of the large number of studies covering a wide range of *exposures*, and because there are published reviews addressing relevant research questions, the Panel decided to take a pragmatic approach based primarily on a '*review of published reviews*'. The main sources of evidence were:

- A systematic evidence review published in 2014 by the UK's National Institute of Health and Care Excellence (NICE) [101];
- A systematic literature search conducted by the CUP team at Imperial College London for *meta-analyses* published after the cut-off date for the NICE (2014) report (see the Diet, nutrition and physical activity: Energy balance and body fatness literature review 2017[1]);
- The United States Department of Agriculture Dietary Guidelines Advisory Committee (USDA DGAC) 2015 scientific report [102].

Quality assessments were carried out for identified published reviews (for the quality assessment process, see the protocol in the Energy balance and body fatness literature review 2017). Results from meta-analyses and individual studies not included in meta-analyses relevant to the exposures of interest were extracted and are presented in full in the Energy balance and body fatness literature review 2017. The CUP Panel reviewed the epidemiological and mechanistic data and made judgements according to the WCRF/AICR criteria for grading the evidence (see **Appendix 1**).

Where available, quantification of exposures in relation to outcomes has been reported as in the published reviews. However, owing to the methods used (a 'review of published reviews'), reliable summary estimates of quantified thresholds were not able to be calculated in this report.

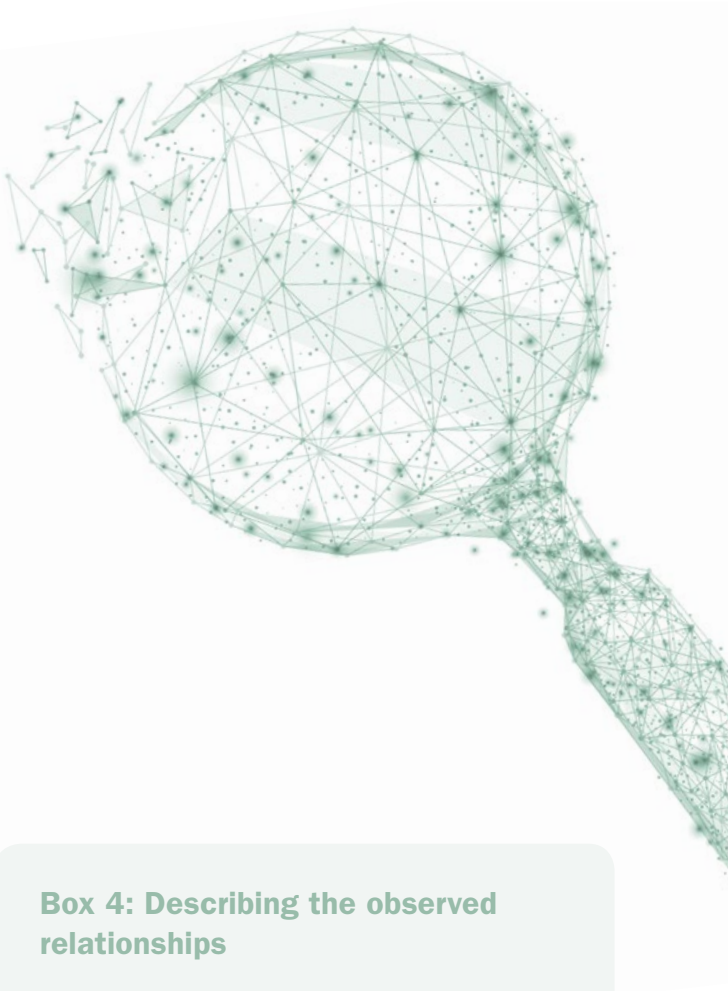
The Energy balance and body fatness literature review 2017 included reviews published up to 21 August 2016. For more information on the methodology, see the full literature review at dietandcancerreport.org.

## 6.3 Evidence of biological plausibility

To complement the epidemiological evidence, evidence was sought of biological plausibility linking an observed association between an exposure and an outcome. This process did not use the same systematic criteria for sourcing epidemiological and intervention data. The mechanisms included in this report were sourced from the WCRF/AICR 2007 Second Expert Report [103], published reviews identified through the process for epidemiological data that included a review

[1] Hereafter referred to as the 'Energy balance and body fatness literature review 2017'.

of biological plausibility, and primary studies; they have undergone review by the CUP Panel members and the Secretariat. A brief summary is given of possible mechanisms for wholegrains, fruit and vegetables, foods containing dietary fibre, a '*Mediterranean type' dietary pattern*, refined grains, sugar sweetened drinks, 'fast foods', a 'Western type' diet, *aerobic physical activity* (including walking), sedentary behaviours, screen time, having been breastfed and lactation (mothers).



## 7. Evidence and judgements

The following sections summarise the evidence identified in the Energy balance and body fatness literature review 2017. Each section also includes a brief description of potential biological mechanisms for each *exposure*.

Dietary exposures that were judged to decrease the risk of weight gain, overweight and obesity are presented first, followed by dietary exposures that increase the risk. This is followed by activity related exposures that decrease risk, followed by activity related exposures that increase risk. Exposures relevant to specific populations – lactation and having been breastfed – are presented last.

For each exposure, evidence is presented for adults and children separately where available. No evidence was identified for children for the following exposures: wholegrains, a '*Mediterranean type' dietary pattern*, refined grains, meat (part of a 'Western type' diet) and walking.

For information on the criteria for grading the epidemiological evidence used by the CUP Panel, see **Appendix 1** of this report. The terminology used to describe observed relationships is set out in **Box 4**.

### Box 4: Describing the observed relationships

***Use of 'effect' or 'association'.*** 'Effect' is used to describe relationships observed in trials; 'association' is used to describe relationships observed in cohort studies.

***Positive effect or association.*** Describes when the exposure of interest and the outcome are observed to change together in the same direction; an increase in the exposure is associated with an increase in the outcome measure, and a decrease in the exposure is associated with a decrease in the outcome measure.

***Inverse effect or association.*** Describes when the exposure of interest and the outcome are observed to change in opposite directions; an increase in the exposure is associated with a decrease in the outcome measure, and a decrease in the exposure is associated with an increase in the outcome measure.

## 7.1 Wholegrains

*(Also see Energy balance and body fatness literature review 2017: Section 2.1)*

Five published reviews were identified: Bautista-Castano and Serra-Majem (2012) [104], Pol *et al.* (2013) [105], Summerbell *et al.* (2009)[1] [106], Fardet and Boirie (2014)[2] [107] and Ye *et al.* (2012) [108].

Four published reviews [104–106, 108] were assessed as high quality. One '*review of reviews*' was identified [107] and was assessed as moderate quality. (For the quality assessment process, please see the protocol in the Energy balance and body fatness literature review 2017.)

### Meta-analyses – randomised controlled trials

Two published reviews [105, 108] conducted *meta-analyses* of *randomised controlled trials* investigating intake of wholegrains and *adiposity* in adults. When comparing the effect on weight change of interventions to increase wholegrain intake (versus no intervention), one published review reported a positive (adverse) effect [105] and one reported a protective effect [108]; neither was *statistically significant*. Pol *et al.* (2013) [105] also conducted a meta-regression and found no difference in body weight change by wholegrain dose. The results are shown in **Table 1**; see also Table 18 in the Energy balance and body fatness literature review 2017. The durations of trials included in both published reviews were relatively short, ranging from 2 to 16 weeks. Stratification within the weight change meta-analysis from Pol *et al.* (2013) [105] showed no clear differences by type of wholegrains. Seven trials were included in both meta-analyses investigating body weight.

Pol *et al.* (2013) [105] also reported on change in percentage body fat, which showed a statistically significant inverse effect (WMD -0.48 [95% CI -0.95, -0.01] %); however, removal of one influential study [109] from this analysis led to a loss of significance. A meta-analysis reporting on waist circumference [105] was not significant (see Table 18 in the Energy balance and body fatness literature review 2017).

### Studies not included in meta-analyses – prospective cohort studies

Four prospective *cohort studies* (five publications [110–114]) investigating wholegrain intake and adiposity in adults were identified through three published reviews [104, 106, 108] providing eight results. Six results showed lower adiposity with increasing wholegrain intake, of which two were statistically significant. Two results reported non-significant increased risks. See Table 19 in the Energy balance and body fatness literature review 2017.

Results from the Health Professionals' Follow-up Study reported a significant inverse trend when comparing the highest and lowest categories of wholegrain intake [110] and a non-significant decreased *relative risk* of overweight when comparing intakes of more than one serving per day of wholegrain breakfast cereal to rarely or never eating wholegrain breakfast cereal [114]. The Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA1) Study [112] and the Danish Diet, Cancer and Health Study [111], both reporting on waist circumference, reported inverse associations for men and women when measuring quintiles of wholegrain bread intake at baseline [112] and positive (adverse) associations for men and women when measuring megajoules per day of wholegrain products at baseline [111]. Results from the Nurses' Health Study (NHS) I [113], reporting on both odds of weight gain and

[1] The published review identified in NICE (2014) [101] was the WCRF/AICR 2005 systematic literature review for the determinants of weight gain, overweight and obesity, now available as a published review [106].

[2] This published review is a 'review of reviews' in itself. One published review was identified: Ye *et al.* (2012) [108].

**Table 1: Summary of meta-analyses of randomised controlled trials from published reviews investigating intake of wholegrains and adiposity in adults**

| Published review | Outcome | Increment/ contrast | Result (95% CI) | $I^2$ (%) | No. of studies | Participants |
|---|---|---|---|---|---|---|
| **Pol *et al.* (2013) [105]** | Weight change | Interventions to increase wholegrain intake vs control | **WMD** 0.06 (-0.09, 0.20) kg | 0 | 26 | 2,060 |
| **Ye *et al.* (2012) [108]** | | Wholegrain intake, g/day | **Beta coefficient** -0.0013 (-0.011, 0.009) kg | NR | NR | NR |
| | | Interventions to increase wholegrain intake vs control | **WMD** -0.18 (-0.54, 0.18) kg | 82 | 9 | 629 |
| **Pol *et al.* (2013) [105]** | Percentage body fat | Interventions to increase wholegrain intake vs control | **WMD** -0.48 (-0.95, -0.01) % | 0 | 7 | 1,087 |

**Abbreviations used:** g = grams; kg = kilogram; WMD = weighted mean difference; NR = not reported.

odds of obesity, reported significant inverse trends when comparing the highest and lowest categories of wholegrain intake.

## MECHANISMS

Consumption of wholegrains may promote *energy balance* and thus decrease risk of weight gain over time, by a number of mechanisms (see [115] for a review).

- **Satiation:** Increased *satiation* – the termination of a current meal due to a feeling of fullness – when eating wholegrains may be due to the additional chewing required, related to their fibre content, particle size and structural integrity. This may be modified by the degree of processing.
- **Gastrointestinal hormones:** Eating a meal of barley kernels (relative to white bread) led to increased release of glucagon-like peptide 1 (GLP-1), as well as depressing energy intake and hunger over two subsequent meals [116]. However, these results may not be applicable to all wholegrains in general.
- **Improved glycaemic response:** Some limited evidence in human trials has shown that consumption of wholegrains can favourably modulate glycaemic response to both the current and subsequent meal. For example, a favourable (depressed) glycaemic response was observed following a standardised breakfast when barley kernels were consumed the previous evening when compared with an equivalent amount of refined grain wheat bread [117, 118]. However, these results may be specific to barley kernels and not wholegrains in general.
- **Fermentation in the bowel:** It is hypothesised that fermentation in the bowel of undigested carbohydrates from wholegrains influences appetite. Gut microbiota can ferment certain carbohydrates to produce *short chain fatty acids*. These can influence glucose and lipid metabolism and stimulate the secretion of gut *hormones* implicated in appetite regulation, gastrointestinal transit and glucose metabolism, such as peptide-tyrosine-tyrosine (PYY) and GLP-1 [119].

- **Source of dietary fibre:** Wholegrains are a source of *dietary fibre*, primarily contained in the bran of the grain; see **Section 7.3**.

### CUP PANEL'S CONCLUSION

The evidence for wholegrains was limited but generally consistent. Meta-analyses of randomised controlled trials showed no statistically significant effect for weight change and a significant but modest inverse relationship for percentage body fat. However, the durations of included trials were relatively short, ranging from 2 to 16 weeks. Two of the eight analyses from cohort studies not included in any meta-analyses reported statistically significant decreased risk of adiposity with increasing intake of wholegrains. The effect size was generally modest. There is evidence of biological plausibility for mechanisms of action.

**The CUP Panel concluded:**

- **The evidence suggesting that consumption of wholegrains decreases the risk of weight gain, overweight and obesity is limited.**

## 7.2 Fruit and vegetables

*(Also see Energy balance and body fatness literature review 2017: Section 2.3)*

Ten published reviews were identified: Summerbell *et al.* (2009) [106], USDA (2010) [120, 121], Bertoia *et al.* (2015) [122], Bertoia *et al.* (2016) [123], Kaiser *et al.* (2016) [124], Mytton *et al.* (2014) [125], Schwingshackl *et al.* (2015) [126], Fardet and Boirie (2014)[1] [107], and Tohill *et al.* (2004) [127].

Four published reviews [106, 124–126] were assessed as high quality, and five published reviews [120–123, 127] were assessed as moderate quality. One '*review of reviews*' was identified [107] and was assessed as moderate quality. (For the quality assessment process, please see the protocol in the Energy balance and body fatness literature review 2017.)

Dietary patterns, such as vegetarianism and veganism, were investigated as part of this review. With respect to vegetarian and vegan diets, the evidence was judged to be limited, with no conclusions possible (see **Matrix** on page 8 and Section 7.1 in the Energy balance and body fatness literature review 2017).

### ADULTS

Four published reviews [122, 124–126] conducted meta-analyses investigating intake of fruit and vegetables and *adiposity* in adults. The meta-analyses are categorised by study type (*randomised controlled trials* or prospective *cohort studies*) and by *exposure* (fruit and vegetables combined, fruit alone, or vegetables alone). One published review [123] conducted a meta-analysis investigating intake of dietary flavonoids, which can be interpreted as a marker of fruit and vegetable intake.

[1] This published review is a 'review of reviews' in itself. One published review was identified: Tohill *et al.* (2004) [127].

### Meta-analyses – randomised controlled trials

***Fruit and vegetables combined.*** Two published reviews [124, 125] conducted meta-analyses of randomised controlled trials investigating weight change and intake of fruit and vegetables combined (**Table 2**). One meta-analysis [124] of seven trials reported a non-significant positive (adverse) association and the other meta-analysis [125], also of seven trials, reported significantly less weight gain in individuals following 'high fruit and vegetable' interventions relative to the control arms. One meta-analysis [125] reported high *heterogeneity* ($I^2$ = 73%). One trial was included in both meta-analyses. The duration of trials included ranged from 8 weeks to 6 months.

### Meta-analyses – prospective cohort studies

***Fruit and vegetables combined.*** One published review [126] reported significantly lower odds of weight gain or overweight at follow-up when comparing highest with lowest categories of fruit and vegetable intake; see **Table 3**. High heterogeneity was reported ($I^2$ = 53%). Exposure measurement and outcome varied between included studies.

### Table 2: Summary of meta-analyses of randomised controlled trials from published reviews investigating intake of fruit and vegetables combined and adiposity in adults

| Published review | Outcome | Increment/contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Kaiser *et al.* (2016) [124]** | Weight change | Increased fruit and vegetable intake (varied interventions) vs control | **SMD** 0.04 (-0.10, 0.17) | 5 | 7 | 1,149 |
| **Mytton *et al.* (2014) [125]** | Weight change | Increased fruit and vegetable intake (50–465 g/day; varied interventions) vs control | **MD** -0.54 (-1.05, -0.04) kg | 73 | 7 | 1,026 |

**Abbreviations used:** g = grams; kg = kilograms; MD = mean difference; SMD = standardised mean difference.

### Table 3: Summary of meta-analyses of prospective cohort studies from published reviews investigating intake of fruit and vegetables combined and adiposity in adults

| Published review | Outcome | Increment/contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Schwingshackl *et al.* (2015) [126]** | Odds of weight gain or overweight | Highest vs lowest categories of fruit and vegetable intake | **OR** 0.91 (0.84, 0.99) | 53 | 5 | 327,492 |

**Abbreviations used:** OR = odds ratio.

***Fruit.*** One published review [122] combined data from the NHS I, NHS II and Health Professionals' Follow-up Study (HPFS) and reported that each daily serving of fruit was associated with a weight change of -0.53 pounds (-0.24 kilograms) (95% CI -0.61, -0.44) over 4 years. Significant protective associations, with increased fruit intake being associated with lower adiposity at follow-up, were also reported by one published review [126] for weight change, waist circumference, and odds of weight gain or overweight. High heterogeneity was reported for one analysis of weight change ($I^2$ = 96% [126]). In general, effect sizes were modest. See **Table 4**.

***Vegetables.*** When combining data from the NHS I, NHS II and HPFS, each daily serving of vegetables was associated with a *statistically significant* but modest weight change of -0.25 pounds (-0.11 kilograms) (95% CI -0.35, -0.14) over a 4-year period [122]. Another published review [126] reported both a non-significant positive (adverse) association (increased intake of vegetables was associated with increased weight at follow-up) and a significant protective association (lower odds of weight gain or overweight at follow-up when comparing highest with lowest categories of intake). High heterogeneity was observed. See **Table 5**.

***Dietary flavonoids.*** One published review [123] investigated dietary *flavonoid* intake and weight change in adults, using the NHS I, NHS II and HPFS (124,086 participants in total). The meta-analysis result reported a protective association between flavonoid intake and weight change over a 4-year period: MD -0.20 pounds (0.09 kilograms) (95% CI -0.31, -0.09). Flavonoids are *bioactive compounds* that are found naturally in fruits and vegetables, as well as other dietary sources such as tea (*Camellia sinensis*). After *adjustment* for *dietary fibre* intake, associations remained significant for three flavonoid subclasses: anthocyanins, proanthocyanidins and total flavonoid polymers.

### Studies not included in meta-analyses – randomised controlled trials

***Fruit and vegetables combined.*** Three randomised controlled trials in adults were identified [128–130]. One reported no significant difference [128], and one did not report level of significance [130]. The third study [129] reported an adverse effect of an intervention diet high in fruit and vegetables but a protective effect when this was combined with a low-fat intervention diet; statistical significance was not reported. See Table 33 in the Energy balance and body fatness literature review 2017.

### Studies not included in meta-analyses – prospective cohort studies

***Fruit and vegetables combined.*** Five prospective cohort studies were identified investigating fruit and vegetable intake and adiposity in adults [112, 131–134]. Four out of six results reported protective associations, of which one was statistically significant [132]. See Table 34 in the Energy balance and body fatness literature review 2017.

***Fruit.*** Four prospective cohort studies were identified [135–138]. No significant associations were reported. See Table 28 in the Energy balance and body fatness literature review 2017.

***Vegetables.*** Five prospective cohort studies were identified [135, 136, 138–140]. Twelve out of 15 results reported protective associations, of which half were statistically significant. See Table 30 in the Energy balance and body fatness literature review 2017.

## Table 4: Summary of meta-analyses of prospective cohort studies from published reviews investigating intake of fruit and adiposity in adults

| Published review | Outcome | Increment/ contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Bertoia *et al.* (2015) [122]** | Weight change | Per daily serving of fruit over a 4-year period | **MD** -0.53 (-0.61, -0.44) lb | NR | 3 | 117,918 |
| **Schwingshackl *et al.* (2015) [126]** | Weight change | Per additional 100 g/day intake of fruit over 1-year period | **Regression coefficient** -13.68 (-22.97, -4.40) g | 96 | 5 | 354,880 |
| | Waist circumference | Increased fruit consumption over 1-year period | **Regression coefficient** -0.04 (-0.05, -0.02) cm | 29 | 2 | 48,879 |
| | Odds of weight gain or overweight | Highest vs lowest categories of fruit intake | **OR** 0.83 (0.71, 0.99) | 28 | 4 | 93,266 |

**Abbreviations used:** cm = centimetres; g = grams; lb = pounds; MD = mean difference; NR = not reported; OR = odds ratio.

## Table 5: Summary of meta-analyses of prospective cohort studies from published reviews investigating intake of vegetables and adiposity in adults

| Published review | Outcome | Increment/ contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Bertoia *et al.* (2015) [122]** | Weight change | Per daily serving of vegetables over a 4-year period | **MD** -0.25 (-0.35, -0.14) lb | NR | 3 | 117,918 |
| **Schwingshackl *et al.* (2015) [126]** | Weight change | Per additional 100 g/day intake of vegetables over 1-year period | **Regression coefficient** 1.69 (-10.37, 13.74) g | 97 | 4 | 354,632 |
| | Odds of weight gain or overweight | Highest vs lowest categories of vegetable intake | **OR** 0.83 (0.70, 0.99) | 75 | 5 | 172,502 |

**Abbreviations used:** g =grams; lb = pounds; MD = mean difference; NR = not reported; OR = odds ratio.

## CHILDREN

Four individual prospective cohort studies [141–144] were identified, through three published reviews [106, 120, 126], investigating fruit and vegetable intake and adiposity in children. Results reported both protective and adverse relationships with no clear pattern, generally with small effect sizes. See Tables 24, 25 and 26 in the Energy balance and body fatness literature review 2017.

## MECHANISMS

Consumption of fruit and vegetables may promote *energy balance*, and thus decrease risk of weight gain over time, by several mechanisms:

- **Energy density:** Many fruits and most non-starchy vegetables are typically low in energy density. Eating foods with lower energy density reduces the likelihood of passive overconsumption. In general, people tend to consume roughly the same amount of food from day to day, measured by bulk and weight, indicating that appetite is more influenced by mass of food (weight and volume) than intrinsic amount of energy, at least in the short to medium term [67, 145].
- **Low glycaemic index:** Most non-starchy vegetables tend to have a low *glycaemic index*; foods with lower glycaemic indices tend to promote favourable *insulin* responses and post-prandial blood glucose profiles, enhancing appropriate appetite regulation [146].
- **Source of dietary fibre:** Fruit and non-starchy vegetables are sources of dietary fibre; see **Section 7.3**.
- **Micronutrient content:** Fruit and vegetables contain high concentrations of a range of *micronutrients* and other *phytochemicals*, including *antioxidants* and phytoestrogens, that may also have a beneficial influence on energy homeostatic pathways [147, 148]. In particular, several flavonoid subclasses have been shown to decrease energy intake, increase glucose uptake in muscle in vivo and decrease glucose uptake in *adipose tissue* in vivo (animal models and short-term human studies) (for a summary, see Bertoia *et al.* (2016) [123]).

## CUP PANEL'S CONCLUSION

The evidence for fruit and vegetables was limited. Meta-analyses of interventions to increase intake of fruit and vegetables reported mixed results: one reported an increased risk of weight gain (not statistically significant) and one reported a decreased risk of weight gain. Meta-analyses of prospective cohort studies measuring intake of fruit, vegetables, or fruit and vegetables, generally reported modest inverse associations across several outcomes. High heterogeneity was observed. Individual randomised controlled trials reported mixed effects. The direction of effect for prospective cohort studies not included in the meta-analyses was not consistent. There is evidence of biological plausibility.

For children, the evidence for an association was considered to be limited and no seperate conclusion was possible.

### The CUP Panel concluded:

- **The evidence suggesting that consumption of fruit and vegetables decreases the risk of weight gain, overweight and obesity is limited.**

## 7.3 Foods containing dietary fibre

*(Also see Energy balance and body fatness literature review 2017: Section 3.1)*

Four published reviews were identified: Summerbell *et al.* (2009) [106], Wanders *et al.* (2011) [149], Ye *et al.* (2012) [108], and USDA (2010) [121].

Two reviews [106, 121] were assessed as high quality, and two reviews [108, 149] were assessed as moderate quality (for the quality assessment process, please see the protocol in the Energy balance and body fatness literature review 2017).

### ADULTS

#### Meta-analyses – randomised controlled trials

One published review [149] conducted a *meta-analysis* of *randomised controlled trials* investigating increased consumption of *dietary fibre* and weight change in adults (**Table 6**). A decrease in body weight was reported for individuals in the intervention arms over a mean study duration of 11.1 weeks (WMD -0.7 kilograms [95% CI not reported]). In addition, a *dose–response* result was reported of 0.014 per cent decrease in body weight over 4 weeks per gram of dietary fibre per day (regression coefficient -0.014% [95% CI not reported]; see **Figure 4**).

The format of the increased dietary fibre intake varied between trials; for example, foods versus supplement, or solid versus liquid. The 61 trials included encompassed 11 fibre types: dextrin, marine polysaccharide, chitosan, fructan, arabinoxylan, mannan, arabinoxylan-rich (wheat bran and psyllium gum), beta-glucan-rich, glucan, resistant starch and pectin.

#### Studies not included in meta-analyses – prospective cohort studies

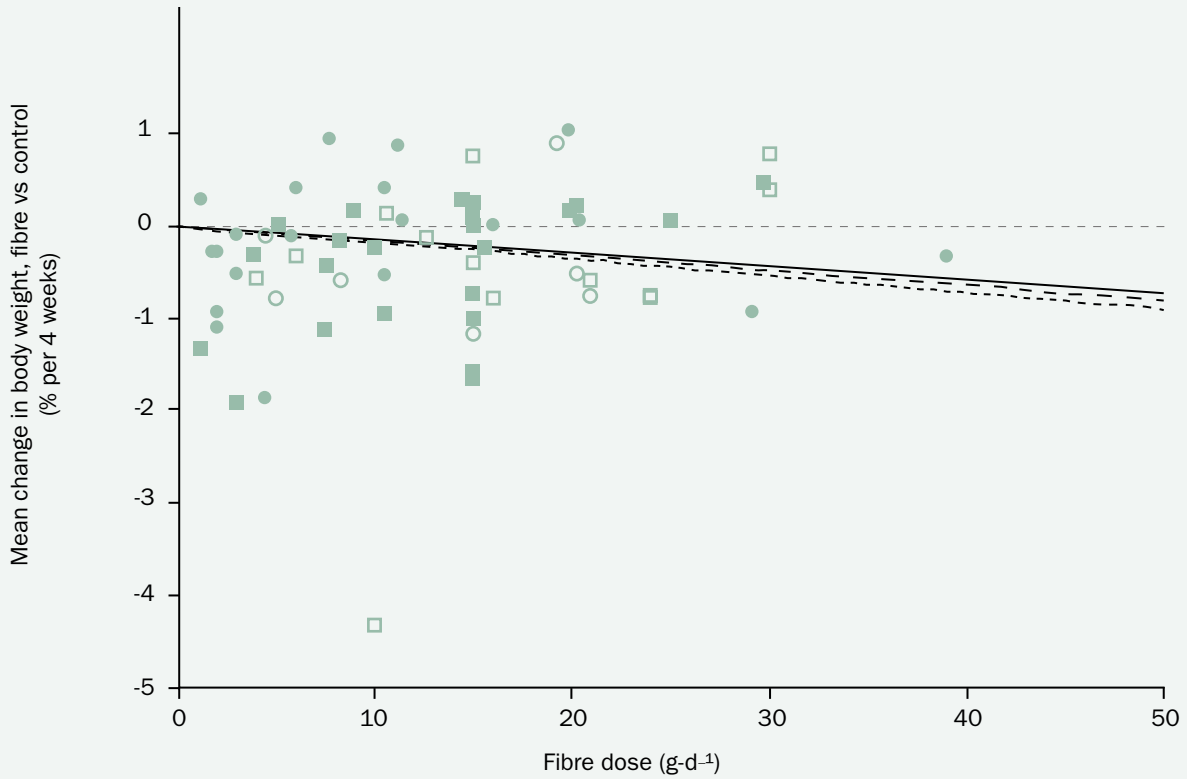
Three prospective *cohort studies* (four publications [110, 113, 150, 151]) investigating consumption of foods containing dietary fibre and *adiposity* in adults were identified through two published reviews [106, 108] providing nine results. Adiposity was marked by weight change, weight attained, *waist-hip ratio*, odds of *BMI* above 25 kg/m$^2$ and odds of BMI above 30 kg/m$^2$. Seven of nine results reported protective associations, with the highest intakes of foods containing dietary fibre being associated with lower adiposity at follow-up; six were *statistically significant*.

### Table 6: Summary of meta-analyses of randomised controlled trials from published reviews investigating intake of dietary fibre and weight change in adults

| Published review | Outcome | Increment/contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Wanders *et al.* (2011) [149]** | Weight change | Increased fibre intake (mean dose 11.1 g/day) vs no intervention | **WMD** -0.7 kg (95% CI NR) | NR | 61 | 2,486 |
| | | Per gram increase in fibre intake per day | **Regression coefficient** -0.014% (95% CI NR) per 4 weeks | NR | 61 | 2,486 |

**Abbreviations used:** CI = confidence interval; NR = not reported; WMD = weighted mean difference.

**Figure 4: Dose-response regression [149] of randomised controlled trials of percentage weight change and dietary fibre intake in adults**




*Mean changes in body weight by fibre dose, viscosity and fermentability. Filled symbols, more viscous fibres; open symbols, less viscous fibres. Squares, more fermentable fibres; circles, less fermentable fibres. Regression lines: —, overall; - - - -, more viscous fibres; ·····, more fermentable fibres. Regression lines were forced through the origin because a zero change in diet should produce a zero change in appetite or body weight. Regression lines were weighted for number of subjects per study. Mean change in body weight per 4 weeks for all comparisons (n = 66). The slope of the overall regression line is -0.014X; the slope of the more viscous fibres regression line is -0.016X; the slope of the more fermentable fibres regression line is -0.018X [149].*

Results from the Coronary Artery Risk Development in Young Adults (CARDIA) study [151] were stratified by ethnicity (black and white men and women). Significant protective associations between the highest quintiles of dietary fibre intake and attained weight and waist-hip ratio were observed for both groups, although they were borderline significant for waist-hip ratio in black men and women (p = 0.05). Two results from the NHS [150] reported significant positive (adverse) associations. All studies were adjusted for potentially *confounding variables*. See Table 63 in the Energy balance and body fatness literature review 2017.

## CHILDREN

Four prospective cohort studies [143, 152-154] investigating intake of dietary fibre and adiposity in children were identified through two published reviews [106, 121]. Both positive (adverse) and inverse associations were reported; none were statistically significant. See Table 61 in the Energy balance and body fatness literature review 2017.

### MECHANISMS

Consumption of foods containing dietary fibre may promote *energy balance*, and thus decrease risk of weight gain over time, by a number of mechanisms:

- **Energy density:** Foods containing dietary fibre tend to be low in energy density. Eating foods with lower energy density reduces the likelihood of passive overconsumption. In general, people tend to consume roughly the same amount of food from day to day, measured by bulk and weight, indicating that appetite is more influenced by mass of food (weight and volume) than intrinsic amount of energy, at least in the short to medium term [67, 145].
- **Satiation:** Fibre may increase *satiation* – the termination of a current meal owing to a feeling of fullness – by increasing chewing, slowing gastric emptying and elevating stomach distension, and stimulating cholecystokinin release [155–158].
- **Slowed rate of digestion:** The increased viscosity of soluble fibre can reduce the overall rate and extent of digestion, which may also result in a blunted post-prandial glycaemic and insulinaemic response to carbohydrates [158].
- **Delayed absorption:** Fibre-induced delayed *absorption* and the resultant presence of *macronutrients* in the distal small intestine, known as the ileal brake, mediate the release of several gut *hormones* such as PYY and GLP-1 [159].
- **Fermentation in the bowel:** *Short chain fatty acids* are produced by gut microbiota during fermentation of certain types of dietary fibre. These can influence glucose and lipid metabolism and stimulate the secretion of gut hormones implicated in appetite regulation, gastrointestinal transit and glucose metabolism [119].

### CUP PANEL'S CONCLUSION

The evidence consistently reported decreased risk of adiposity with increased consumption of foods containing dietary fibre. One meta-analysis of randomised controlled trials reported protective effects and demonstrated a dose–response relationship. This was supported by several large prospective cohort studies showing a mostly consistent direction of effect across a range of adiposity measures. There is evidence of biological plausibility with studies demonstrating the effects in humans.

For children, the evidence for an association was considered to be limited and no separate conclusion was possible.

**The CUP Panel concluded:**

- **Consumption of foods containing dietary fibre probably protects against weight gain, overweight and obesity.**

## 7.4 'Mediterranean type' dietary pattern

*(Also see Energy balance and body fatness literature review 2017: Section 1.1)*

Four published reviews were identified: Fogelholm *et al.* (2012) [160], Kastorini *et al.* (2011) [161], USDA DGAC 2015 [102], and Garcia *et al.* (2016) [162].

Two reviews [102, 162] were assessed as high quality, and two reviews [160, 161] were assessed as moderate quality (for the quality assessment process, please see the protocol in the Energy balance and body fatness literature review 2017).

### Box 5: Defining a 'Mediterranean type' dietary pattern

There are recognised scores for quantifying adherence to a so-called 'Mediterranean type' dietary pattern, though there is variation in how the scores are constructed [136, 163, 164]. The term generally describes a diet rich in fruits and vegetables, with modest amounts of meat and dairy, some fish and wine, and rich in unrefined olive oil. Traditionally it is also associated with moderate to high levels of physical activity. Currently most countries around the Mediterranean do not consume such a diet.

Other dietary patterns, such as vegetarianism and veganism, were investigated as part of this review. With respect to vegetarian and vegan diets, the evidence was judged to be limited, with no conclusions possible (see **Matrix** and Section 7.1 in the Energy balance and body fatness literature review 2017).

### Meta-analyses – randomised controlled trials

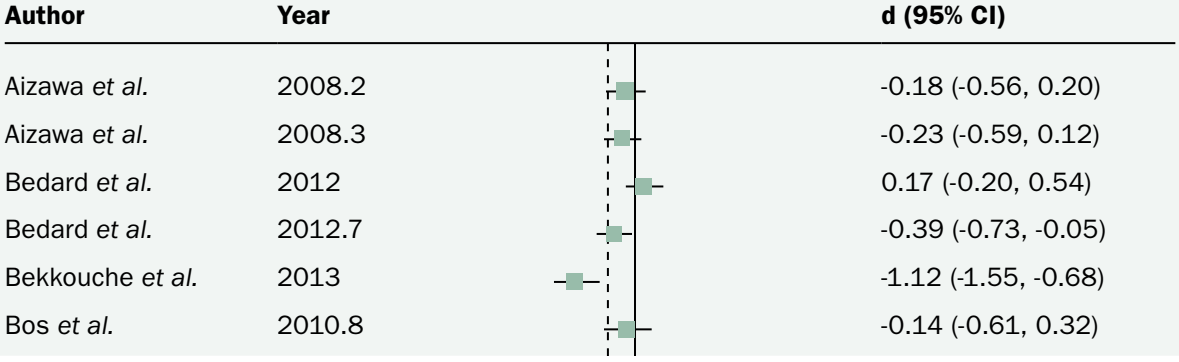
Two published reviews [161, 162] conducted *meta-analyses* of *randomised controlled trials* investigating consumption of a *'Mediterranean type' dietary pattern* and *adiposity* in adults. Both reported significant beneficial effects of adherence to a 'Mediterranean type' dietary pattern on change in waist circumference; see **Table 7** and **Figure 5**. There was overlap of five trials between the two meta-analyses.

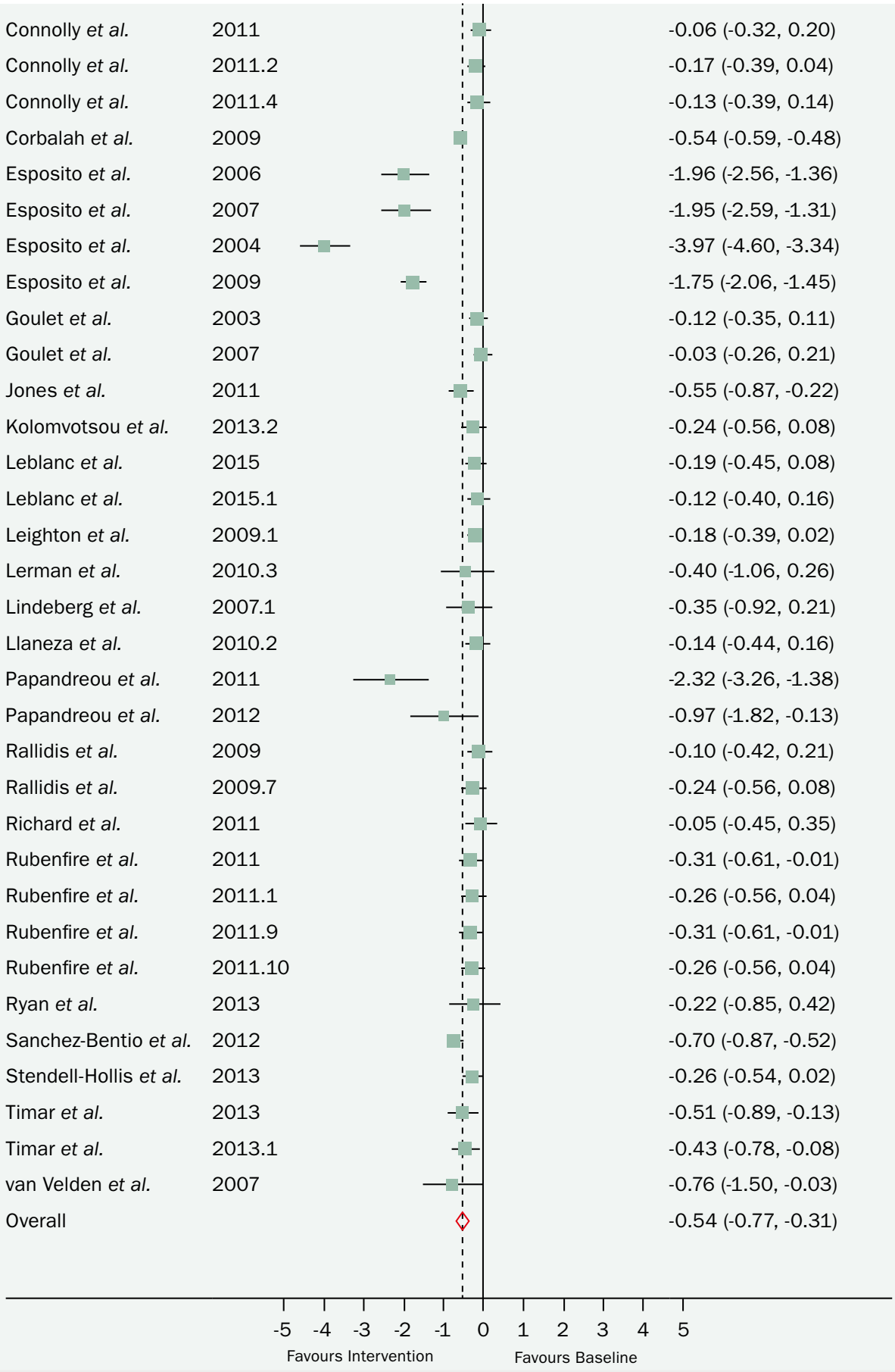
### Table 7: Summary of meta-analyses of randomised controlled trials from published reviews investigating consumption of a 'Mediterranean type' dietary pattern and adiposity in adults

| Published review | Outcome | Increment/contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Garcia *et al.* (2016) [162]** | Waist circumference | 'Mediterranean type' dietary pattern intervention vs control | ***d+*** -0.54 (-0.77, -0.31) | 96 | 29 | 4,133 |
| **Kastorini *et al.* (2011) [161]** | | 'Mediterranean type' dietary pattern intervention vs control | **MD** -0.42 (-0.82, -0.02) cm | ~0 | 11 | 1,646 |

**Abbreviations used:** cm = centimetres; d+ = overall effect size; MD = mean difference.

### Figure 5: Meta-analysis [162] of randomised controlled trials of waist circumference and adherence to a 'Mediterranean type' dietary pattern in adults






**Forest Plot** *for waist circumference. Note: Squares represent* **point estimates** *for each individual study; extended line shows 95%* **confidence intervals** *(CIs); dotted line represents the null value of zero; diamond represents the weighted mean effect size for the outcome [162].*

*For references to studies included in the meta-analysis and other details about the forest plot, please consult the published review [162].*

*Moderator analysis* in one published review [162] of study design, region, 'impact per paper' metric, study duration, proportion of female participants, use of a behavioural technique and level of supervision did not alter the direction of effect. High *heterogeneity* was observed for the overall result ($I^2$ = 96%), which was attributed to study location and duration and the impact factor of the journal in which the studies were published [162].

The result of the other meta-analysis [161] was strongly influenced by a single study [165], although no significant heterogeneity of the effect measured was reported.

### Studies not included in meta-analyses – prospective cohort studies

Four prospective *cohort studies* (six publications [136, 163, 164, 166–168]) investigating consumption of a 'Mediterranean type' dietary pattern and adiposity in adults were identified through three published reviews [102, 160, 161] providing eight results. All eight results reported decreased risks, with higher adherence to the study-defined 'Mediterranean type' dietary pattern being associated with lower adiposity at follow-up; five were *statistically significant*. Adiposity was marked by body weight, *BMI*, waist circumference and odds of obesity. Study size ranged from 2,563 to 373,803 participants. See Table 6 in the Energy balance and body fatness literature review 2017.

In a sensitivity analysis, one study [163] applied five additional scoring systems, including those used by two other studies [136, 164]. The observed inverse association was unchanged by the particular scoring system applied.

## MECHANISMS

Following a 'Mediterranean type' dietary pattern may promote *energy balance* and thus decrease risk of weight gain over time, by several mechanisms:

- **Source of dietary fibre:** The 'Mediterranean type' dietary pattern is rich in plant foods, which provide a high amount and wide variety of both soluble and insoluble *dietary fibres*; see **Section 7.3**.
- **Dietary fat composition:** Typically, the 'Mediterranean type' dietary pattern is high in unsaturated fatty acids relative to saturated fatty acids. Experimental studies in humans have demonstrated that dietary fatty acid composition can influence fat oxidation and daily energy expenditure; in particular oleic acid, a mono-unsaturated fatty acid, may increase oxidation and energy expenditure [169, 170]. This is consistent with results from the PREDIMED trial, which showed no adverse effect on body weight from long-term adherence to a 'Mediterranean type' dietary pattern, supplemented with either olive oil or nuts, compared with the control group [171].
- **Low glycaemic load:** 'Mediterranean type' dietary patterns tend to have a low *glycaemic load* [172]; foods with lower glycaemic indices tend to promote favourable *insulin* responses and post-prandial blood glucose profiles, enhancing appropriate appetite regulation [146].
- **Available energy:** Some foods common in the 'Mediterranean type' dietary pattern, for example, nuts and seeds, resist digestion and *absorption*, leading to lower bioavailability of energy [173–175].
- **Dietary polyphenol content:** A cross-sectional study within the PREDIMED trial reported a significant inverse association between urinary polyphenol concentrations and body weight [176]. It is suggested that the diversity in structure and function of polyphenols means they could influence

a variety of metabolic pathways, such as inhibition of lipogenesis, stimulation of catabolic pathways, reduction of chronic *inflammation* and upregulation of uncoupling proteins. However, further studies are required to confirm the roles and interactions of the polyphenol group; for a review of existing studies, see Guo *et al.* (2017) [176].

- **Increased physical activity:** Traditional lifestyles in the Mediterranean region, similar to other traditional lifestyles around the world, are associated with higher levels of habitual physical activity. Increased physical activity leads to favourable shifts in body composition, appetite regulation and insulin sensitivity (see **Section 7.9** on physical activity and **Section 3** on fundamental concepts).

### CUP PANEL'S CONCLUSION

The evidence for consumption of a 'Mediterranean type' dietary pattern and decreased risk of adiposity was consistent across study designs and analyses. Two meta-analyses of randomised controlled trials reported modest but statistically significant protective effects, with adherence to a 'Mediterranean type' dietary pattern associated with lower risk of adiposity. Results from prospective cohort studies consistently reported protective associations across various measures of adiposity. When different scoring systems based on the 'Mediterranean type' dietary pattern were applied, the direction of effect was unchanged. There is evidence of biological plausibility.

### The CUP Panel concluded:

- **Consumption of a 'Mediterranean type' dietary pattern probably protects against weight gain, overweight and obesity.**

## 7.5 Refined grains

*(Also see Energy balance and body fatness literature review 2017: Section 2.2)*

Three published reviews were identified: Bautista-Castano and Serra-Majem (2012) [104], Fogelholm *et al.* (2012) [160], and Summerbell *et al.* (2009) [106].

Two reviews [104, 106] were assessed as high quality, and one review [160] was assessed as moderate quality (for the quality assessment process, please see the protocol in the Energy balance and body fatness literature review 2017).

### Box 6: Defining refined grains

**The term 'refined grains' refers to the grains themselves, or products of such grains, that have been modified from their original composition. Mechanical processing is used to remove one or more of the bran, germ or endosperm. This results in a product with an altered nutritional profile, often lower in fibre and other nutrients. Examples include white rice, white flour and products made from white flour such as white bread. This is in contrast to wholegrains (or the products of such grains), which contain the bran, germ and endosperm.**

### Studies not included in meta-analyses – prospective cohort studies

Seven prospective *cohort studies* (eight publications [110–114, 177–179]) investigating consumption of *refined grains* and *adiposity* in adults were identified through three published reviews [104, 106, 160] providing 13 results. Ten out of 13 results reported positive (adverse) associations, of which seven were *statistically significant*, with higher intake of refined grains being associated with higher adiposity at follow-up. Adiposity was

marked by weight change, *BMI* change, waist circumference, waist circumference for a given BMI, odds of weight gain, *relative risk* of overweight and odds of obesity. See **Table 8**; see also Table 21 in the Energy balance and body fatness literature review 2017.

Studies used varied definitions of the *exposure*, including specific refined grain products [110, 112, 114, 179], refined grains in general [177], refined grain products alongside other food items [111] and dietary patterns defined by refined grain foods [178]. The largest study [177], pooling data from three cohorts (120,887 participants), reported significantly more weight gain in individuals who increased their intake of refined grains over a 4-year period. Two studies [112, 114] reported non-significant protective associations, with intake of refined grains being associated with lower adiposity at follow-up; both results were for men. Multivariate adjusted models were used in all studies.

## MECHANISMS

Consumption of refined grains may promote positive *energy balance*, and thus increase risk of weight gain over time, by three key mechanisms:

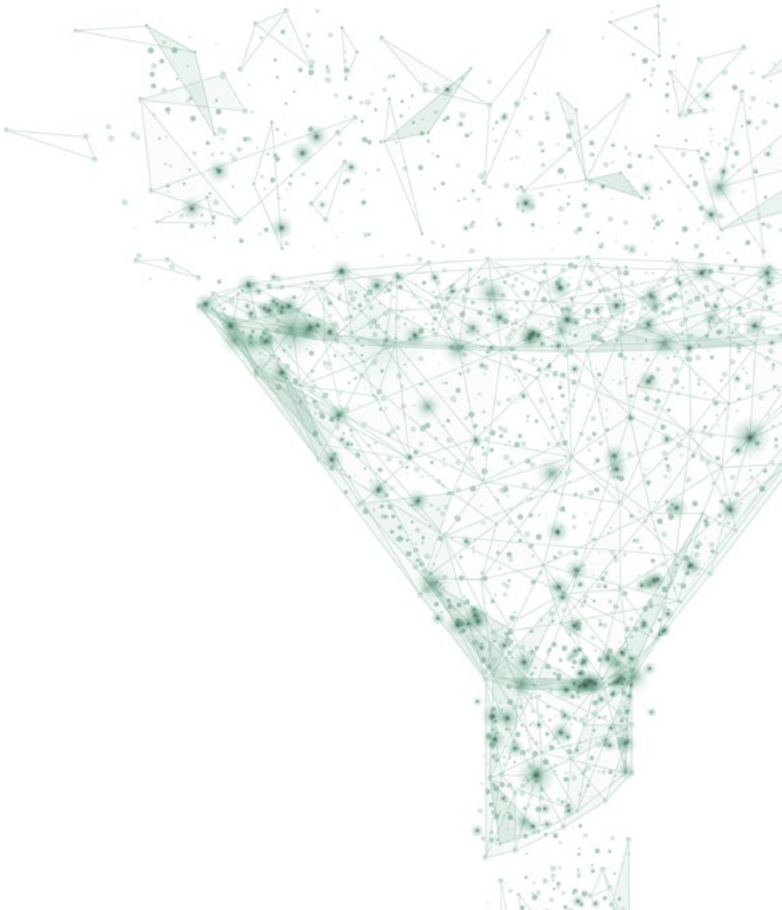
- **High glycaemic index:** Refined grain products often have a high glycaemic index, provoking high insulin responses and a fast glucose decline [151]. It is hypothesised that these properties could increase hunger and enhance lipogenesis (see next point), thereby promoting obesity. (For a summary, see Fogelholm *et al.* (2012) [160].)
- **Fat tissue synthesis:** Animal feeding studies suggest that consumption of refined grain products can promote fat synthesis even when total energy intake is unchanged [180].
- **Displacement:** It is possible that higher intakes of refined grains reflect lower consumption of other dietary factors that might promote energy balance and protect against weight gain (see also **Section 5.2**).

## CUP PANEL'S CONCLUSION

Evidence was generally consistent but of variable quality. Evidence from prospective cohort studies reported increased risk of adiposity with increased consumption of refined grains; more than half of the results reported significant adverse associations. Three results reported non-significant protective associations. Studies varied in their definition of refined grains and so a consistent exposure is not reported. There is evidence of biological plausibility.

### The CUP Panel concluded:

- **The evidence suggesting that consumption of refined grains increases the risk of weight gain, overweight and obesity is limited.**



## Table 8: Summary of prospective cohort studies from published reviews investigating consumption of refined grains and adiposity in adults

| Study [publication] | Outcome | Increment/ contrast | Results | No. participants Follow-up |
|---|---|---|---|---|
| **Health Professionals' Follow-up Study (HPFS) [110]** | Weight change | Servings per day of refined grain cereal | Positive association, p for trend < 0.001 | M: 27,082<br>8 years |
| | | Categories of refined grain intake | No association | |
| **Nurses' Health Study (NHS) I, NHS II, HPFS (pooled) [177]** | Weight change | Increased servings per day of refined grains over a 4-year period | MD 0.39 (0.21, 0.58) lb<br>p < 0.001 | M&W: 120,887<br>20 years |
| **Baltimore Longitudinal Study of Aging [178]** | BMI change | 'White bread'-defined dietary pattern vs 'healthy' dietary pattern at baseline | Beta coefficient 0.05 (-0.10, 0.23) kg/m$^2$ | M&W: 459<br>1 year |
| | Waist circumference | | Beta coefficient 0.90 (0.12, 1.68) cm | |
| **Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA1) [112]** | Waist circumference | Per quintile intake of refined bread | **M:** beta coefficient -0.06 (-0.22, 0.09) cm<br>**W:** beta coefficient 0.29 (0.07, 0.51) cm | M: 1,127<br>W: 1,073<br>6 years |
| **Danish Diet, Cancer and Health study [111]** | Waist circumference | Per MJ per day of refined grain products and potatoes | **M:** beta coefficient 0.06 (-0.12, 0.25) cm<br>**W:** beta coefficient 0.48 (0.18, 0.78) cm | M: 20,126<br>W: 22,570<br>5.3 years |
| **European Prospective Investigation into Cancer (EPIC) (5 centres) [179]** | $\Delta WC_{BMI}$ | 100 kcal increments of white bread consumption over 1 year | Beta coefficient 0.01 (0.01, 0.02) cm | M&W: 48,361<br>5.5 years |
| **NHS I [113]** | Odds of weight gain | Highest vs lowest quintile intake of refined grains | OR 1.26 (0.97, 1.64), p for trend = 0.04 | W: 74,091<br>12 years |
| | Odds of obesity | | OR 1.18 (1.08, 1.28), p for trend < 0.0001 | |
| **HPFS [114]** | Risk of overweight | Intake of > 1 serving of refined grain breakfast cereal per day vs rarely/never eat | RR 0.81 (0.65, 1.01), p for trend = 0.08 | M: 17,881<br>13 years |

**Abbreviations used:** $\Delta WC_{BMI}$ = waist circumference for a given BMI; cm = centimetre; kcal = kilocalories; lb = pounds; MD = mean difference; MJ = mega joules; OR = odds ratio; RR = relative risk.

## 7.6 Sugar sweetened drinks

*(Also see Energy balance and body fatness literature review 2017: Section 2.7)*

Twelve published reviews were identified: Mattes *et al.* (2011)[1] [181], Malik *et al.* (2013) [182], Kaiser *et al.* (2013) [183], Te Morenga *et al.* (2013) [184], USDA (2010) [121], Pan *et al.* (2013) [185], Fardet and Boirie (2014)[2] [107], Olsen and Heitmann (2009) [186], Malik *et al.* (2006) [187], Perez-Morales *et al.* (2013) [188], Gibson (2008) [189] and Vartanian *et al.* (2007) [190].

Six published reviews [121, 181–184, 186] were assessed as high quality, and five published reviews [185, 187–190] were assessed as moderate quality. One '*review of reviews*' was identified [107] and was assessed as moderate quality. (For the quality assessment process, please see the protocol in the Energy balance and body fatness literature review 2017.)

Two published reviews reported receiving industry funding [183, 189].

### Box 7: Defining sugar sweetened drinks

**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.**

Low calorie or non-caloric drinks sweetened with artificial sweeteners, such as sucralose or aspartame, are becoming increasingly available. This *exposure* was considered as part of the evidence review. The evidence was judged to be limited, with no conclusions possible (see **Matrix** and Section 8.6 in the Energy balance and body fatness literature review 2017).

### ADULTS

Three published reviews [182, 183, 185] conducted *meta-analyses* investigating consumption of sugar sweetened drinks and *adiposity* in adults. Results from meta-analyses both of *randomised controlled trials* and prospective *cohort studies* reported significant positive (adverse) relationships of sugar sweetened drink consumption on change in weight; see **Tables 9** and **10**.

#### Meta-analyses – randomised controlled trials

Two meta-analyses of randomised controlled trials in adults were identified [182, 183]. The interventions varied between included trials with respect to volume, energy content and type of sugar sweetened drink provided but all sought to increase intake relative to the control arms. The intervention arms were associated with significant increases in weight over the study periods (see **Table 9**). Intervention duration ranged from 3 weeks to 6 months, although the shorter durations are inadequate to observe meaningful weight change or avoidance of weight gain. Neither meta-analysis reported high *heterogeneity*. When one meta-analysis [182] was stratified by baseline weight status there was greater, but not significant, weight gain observed in the studies conducted in non-overweight populations. The other meta-analysis [183] included one trial conducted in children, which also had the most participants.

[1] The published review was updated by Kaiser *et al.* (2013) [183].
[2] This published review is a 'review of reviews' in itself. Five published reviews were identified: Olsen and Heitmann (2009) [186], Malik *et al.* (2006) [187], Perez-Morales *et al.* (2013) [188], Gibson (2008) [189] and Vartanian *et al.* (2007) [190].

### Table 9: Summary of meta-analyses of randomised controlled trials from published reviews investigating consumption of sugar sweetened drinks and adiposity in adults

| Published review | Outcome | Increment/ contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Malik *et al.* (2013) [182]** | Weight change | Increased SSB intake vs control | **WMD** 0.85 (0.50, 1.20) kg | 0 | 5 | 292 |
| **Kaiser *et al.* (2013) [183]** | Weight change | Increased SSB intake vs control | **SMD** 0.28 (0.12, 0.44) | 48 | 7 | 665 |

**Abbreviations used:** kg = kilograms; SSB = sugar sweetened beverage; SMD = standardised mean difference; WMD = weighted mean difference.

### Table 10: Summary of meta-analyses of prospective cohort studies from published reviews investigating consumption of sugar sweetened drinks and adiposity in adults

| Published review | Outcome | Increment/ contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Malik *et al.* (2013) [182]** | Annual weight change | Per 12 oz serving of SSB per day | **WMD** 0.22 (0.09, 0.34) kg | 70 | 7 | 170,141 |
| **Pan *et al.* (2013) [185]** | Weight change | Per standard serving of SSB per day over 4-year period | **MD** 0.36 (0.24, 0.48) kg | NR | 3 | 124,988 |

**Abbreviations used:** kg = kilograms; MD = mean difference; NR = not reported; oz = ounce; SSB = sugar sweetened beverage; WMD = weighted mean difference.

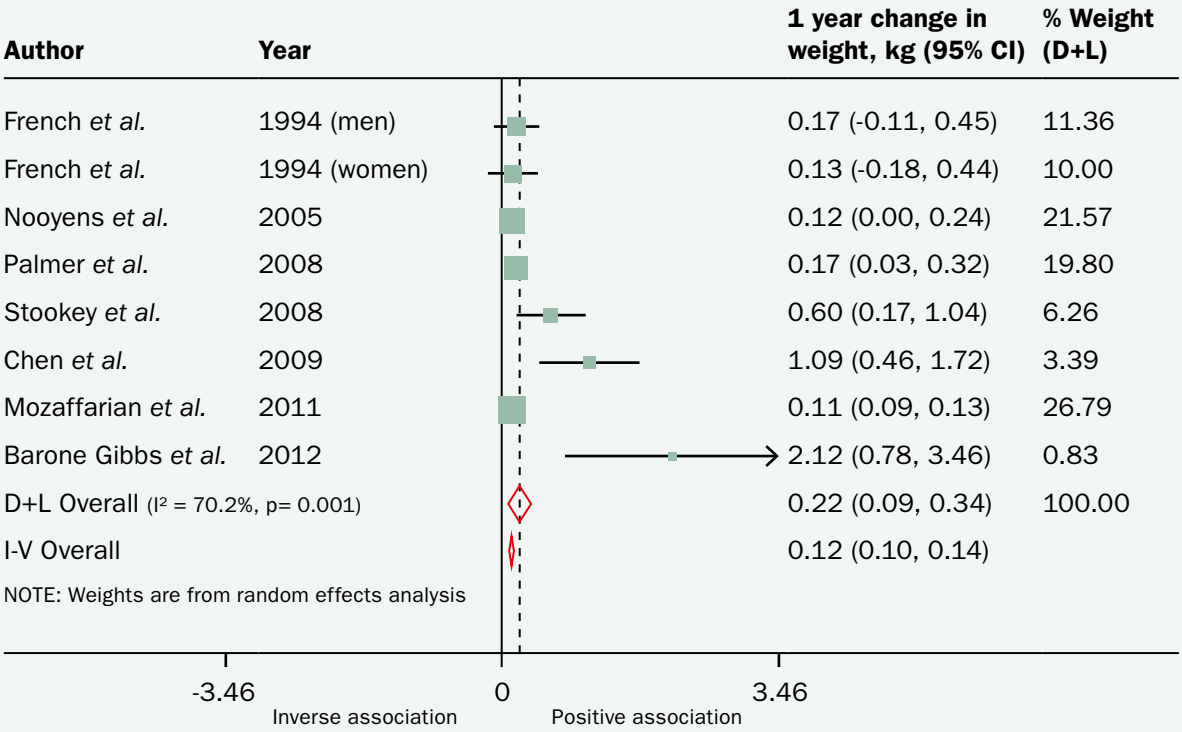
#### Meta-analyses – prospective cohort studies

Two meta-analyses of prospective cohort studies in adults were conducted [182, 185] (**Table 10**); significant positive (adverse) associations were reported in both, with higher intake of sugar sweetened drinks associated with increased adiposity. One meta-analysis reported a significant 0.22 kilogram weight gain over 1 year per 12 ounce serving of sugar sweetened drinks per day (WMD 0.22 [95% CI 0.09, 0.34] kilograms; see **Figure 6**). The other meta-analysis [185] combined data from the NHS I, the NHS II and the HPFS and reported a 0.36 kilogram weight increase per standard serving of sugar sweetened drinks per day over a 4-year period. The first meta-analysis [182] included one study which used data from the NHS I, NHS II and HPFS cohorts; exclusion of this study from the meta-analysis increased the summary estimate (WMD 0.31 [95% CI 0.11, 0.50] kg) but did not affect heterogeneity ($I^2$ = 71%).

#### Studies not included in meta-analyses – prospective cohort studies

Six prospective cohort studies [191–196] investigating consumption of sugar sweetened drinks in adults were identified through six published reviews [121, 182, 186, 187, 189, 190] providing 12 results. Ten out of 12 results reported positive (adverse) associations, with higher intake of sugar sweetened drinks being associated with higher adiposity at follow-up; six were significant. Adiposity was marked by weight change, *BMI* change, and odds of weight gain, overweight, obesity and unhealthy waist circumference. See Table 59 in the Energy balance and body fatness literature review 2017.

**Figure 6: Meta-analysis [182] of prospective cohort studies of weight change and increased sugar sweetened drink consumption in adults**




*One-year changes (95% CI) in weight (kg) per 1-serving/d increase in sugar sweetened beverages from prospective cohort studies in adults using a change versus change analysis strategy. Horizontal lines denote 95% CIs; solid diamonds represent the* **point estimate** *of each study. Open diamonds represent pooled estimates, and the dashed line denotes the point estimate of the pooled result from the random-effects model (D+L). Weights are from the random-effects analysis (D+L). Pooled estimates from the random-effects analysis (D+L) and the fixed-effects analysis (I-V) are shown based on 7 cohort studies (n = 174,252). The I² and P values for heterogeneity are shown. D+L, DerSimonian and Laird; I-V, inverse variance [182].*

*For references to studies included in the meta-analysis, please consult the published review [182].*

## CHILDREN

Three published reviews [182–184] conducted meta-analyses investigating consumption of sugar sweetened drinks and adiposity in children. Results from meta-analyses both of randomised controlled trials and prospective cohort studies reported positive (adverse) relationships of sugar sweetened drink consumption on measures of adiposity; see **Tables 11** and **12**.

### Meta-analyses – randomised controlled trials

Two meta-analyses of randomised controlled trials in children were identified [182, 183], and both reported non-significant effects, with interventions to reduce sugar sweetened drink intake leading to reduced adiposity at follow-up (**Table 11**). One meta-analysis [183] standardised several adiposity measures to report the overall outcome measure, including percentage weight change, BMI and BMI z-score. This meta-analysis included two trials in adult populations and six trials in children. Of those six trials, five were also included in the other meta-analysis [182]. Both published reviews noted that the non-significant effects may reflect the difficulty in achieving a reduction in sugar sweetened drink consumption, particularly in interventions which did not provide substitute beverages.

### Meta-analyses – prospective cohort studies

Two meta-analyses of prospective cohort studies in children [182, 184] both reported significant positive (adverse) associations between increased sugar sweetened drink

### Table 11: Summary of meta-analyses of randomised controlled trials from published reviews investigating consumption of sugar sweetened drinks and adiposity in children

| Published review | Outcome | Increment/ contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Malik *et al.* (2013) [182]** | BMI change | Interventions to reduce SSB intake vs control | **WMD** -0.17 (-0.39, 0.05) kg/m$^2$ | 75 | 5 | 2,772 |
| **Kaiser *et al.* (2013) [183]** | 'Adiposity' change | Interventions to reduce SSB intake vs control | **SMD** -0.06 (-0.13, 0.01) | 59 | 8 | 3,205 |

**Abbreviations used:** SSB = sugar sweetened beverage; SMD = standardised mean difference; WMD = weighted mean difference.

### Table 12: Summary of meta-analyses of prospective cohort studies from published reviews investigating consumption of sugar sweetened drinks and adiposity in children

| Published review | Outcome | Increment/ contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Malik *et al.* (2013) [182]** | Annual BMI change | Per 12 oz serving of SSB per day | **WMD** 0.07 (0.01, 0.12) kg/m$^2$ | 92 | 15 | 25,745 |
| **Te Morenga *et al.* (2013) [184]** | Odds of overweight or obesity | More than one serving of SSB per day vs little/ no intake | **OR** 1.55 (1.32, 1.82) | 0 | 5 | 12,317 |

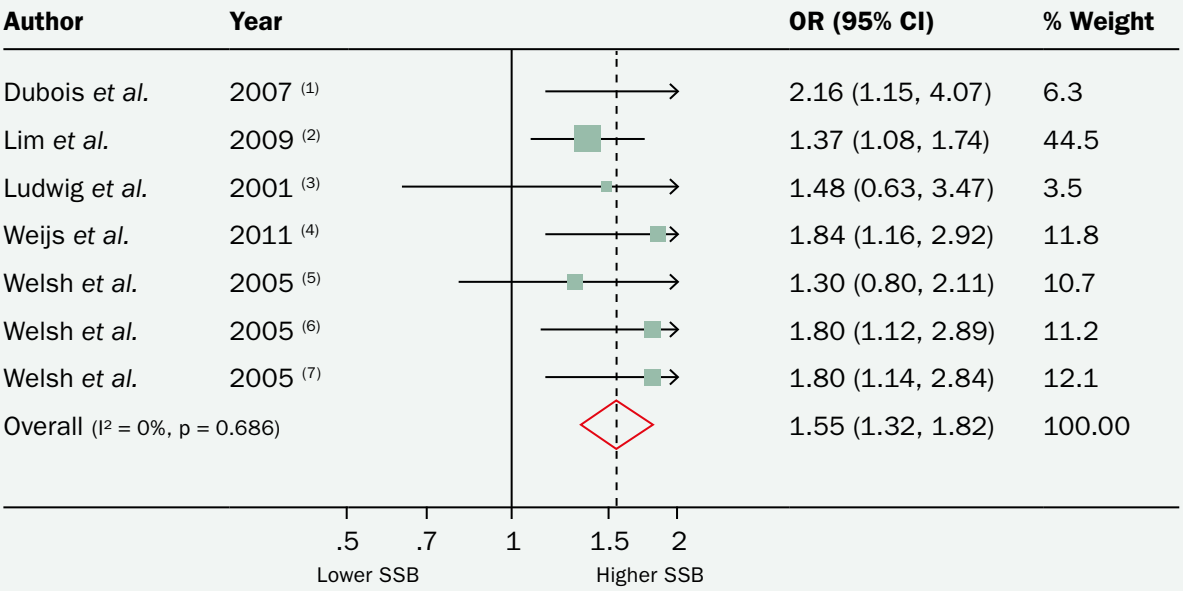
**Abbreviations used:** OR = odds ratio; oz = ounce; SSB = sugar sweetened beverage; WMD = weighted mean difference.

consumption and BMI change [182] and odds of overweight [184] (see **Table 12** and **Figure 7**). No heterogeneity ($I^2$ = 0% [184]) and high heterogeneity ($I^2$ = 92% [182]) were observed. The larger meta-analysis [182] also calculated an estimate for annual BMI change (WMD 0.06 [95% CI 0.02, 0.10] kg/m$^2$). When this meta-analysis was stratified for studies that were adjusted for total energy and those that were not, the estimate was greater in studies that did not make the *adjustment* (adjusted studies WMD 0.04 [95% CI 0.00, 0.07] kg/m$^2$, $I^2$ = 0%, comparisons = 3; unadjusted studies WMD 0.08 [95% CI 0.02, 0.14] kg/m$^2$, $I^2$ = 91%, comparisons = 17).

#### Studies not included in meta-analyses – prospective cohort studies

Nine prospective cohort studies [197–205] investigating consumption of sugar sweetened drinks in children were identified through seven published reviews [121, 182, 184, 186, 188–190] providing 22 results. Fifteen out of 22 results reported positive (adverse) relationships, with higher intake of sugar sweetened drinks being associated with higher adiposity at follow-up; 10 were *statistically significant*. Adiposity was marked by weight change, BMI change, BMI z-score change, fat mass, percentage body fat, percentage trunk fat, waist circumference and odds of overweight. Age at recruitment varied between the studies, ranging from 3 to 18 years. See Table 56 in the Energy balance and body fatness literature review 2017.

**Figure 7: Meta-analysis [184] of prospective cohort studies of odds of overweight and increased sugar sweetened drink consumption in children**




*(1) OR for incident obesity in frequent versus infrequent consumers of SSB between meals*

*(2) OR for incident overweight per daily serve SSB (8 ounces)*

*(3) OR for incident obesity per daily serve SSB*

*(4) OR for incident overweight per approximate daily serve SSB (5% energy from beverage sugar)*

*(5) OR for incident overweight in normal weight children who consumed >1 serve/day SSB versus <1 SSB/day*

*(6) OR for remaining overweight in overweight children who consumed >1 serve/day SSB versus <1 serve SSB/day*

*(7) OR for incident overweight in children at risk of overweight who consumed >1 serve/day SSB versus <1 serve SSB/day*

*OR = odd ratio; SSB = sugar sweetened beverage.*

*Association between free sugars intakes (primarily SSB intake) and measures of body fatness in children. Pooled estimates for odd ratios for incident overweight or obesity in children consuming one or more servings of sugar sweetened beverages per day at baseline compared with children who consumed none or very little at baseline. Overall estimate shows higher odds of overweight or obesity at follow-up in those who consumed one or more servings of sugar sweetened beverages at baseline. Data are expressed as* **odds ratio** *(95%* **confidence interval***), using generic inverse variance models with random effects [184].*

*For references to studies included in the meta-analysis, please consult the published review [184].*

## MECHANISMS

Consumption of sugar sweetened drinks may promote positive *energy balance*, and thus increase risk of weight gain over time, by several mechanisms:

- **Energy density:** Sugar sweetened drinks are typically high in energy density (compared with non-sugar sweetened drinks). Consuming foods and drinks with higher energy densities increases the likelihood of passive overconsumption. In general, people tend to consume roughly the same amount of food from day to day, measured by bulk and weight, indicating that appetite is more influenced by mass of food (weight and volume) than the intrinsic amount of energy, at least in the short to medium term [67, 145].
- **Lack of compensation:** Energy from sugars may not be compensated for in the same way when consumed in a soft drink as when consumed as part of a solid meal: energy in liquid form appears to be less effective in inducing satiation or satiety [71], and so may promote excess energy intake.
- **Modified fat deposition:** It has been hypothesised that high fructose corn syrup or sucrose, the key sweetening agents of many soft drinks, may promote the

deposition of liver, muscle and visceral fat and an increase in serum lipids independently of an effect on body weight (reviewed in Malik and Hu (2015) [206]).

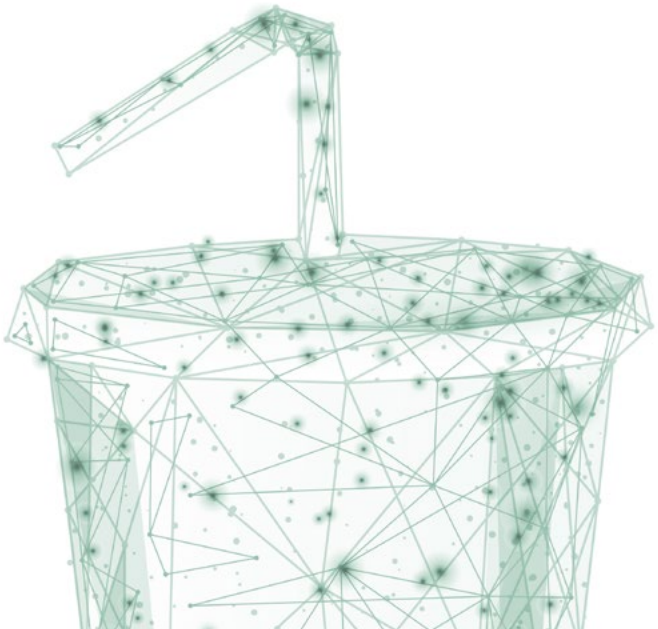
- **Altered hedonics:** Increased intake of high-sugar foods and drinks has been associated with greater reward response and decreased inhibitory response to such foods and drinks [207, 208].

### CUP PANEL'S CONCLUSION

Overall, the evidence for an increased risk of adiposity in both adults and children with increased consumption of sugar sweetened drinks was strong and consistent. All results from meta-analyses of both randomised controlled trials and prospective cohort studies reported increased risks; six out of eight meta-analysis results were statistically significant. Statistically significant dose–response associations were demonstrated. The observed relationships are supported by evidence from multiple individual prospective cohort studies. There is robust evidence of biological plausibility.

### The CUP Panel concluded:

- **Consumption of sugar sweetened drinks is a convincing cause of weight gain, overweight and obesity.**



## 7.7 'Fast foods'

*(Also see Energy balance and body fatness literature review 2017: Section 2.6)*

Six published reviews were identified: Bezerra *et al.* (2012) [209], Mesas *et al.* (2012) [210], USDA (2010) [121], Summerbell *et al.* (2009) [106], Rosenheck *et al.* (2008) [211], and USDA DGAC (2015) [102].

Three reviews [102, 106, 209] were assessed as high quality, and three reviews [121, 210, 211] were assessed as moderate quality (for the quality assessment process, please see the protocol in the Energy balance and body fatness literature review 2017).

### Box 8: Defining 'fast foods'

**'Fast foods' here refer to readily available convenience foods that tend to be energy dense and are often consumed frequently and in large portions. Most of the evidence on 'fast foods' is from studies of foods such as burgers, fried chicken pieces, chips (French fries) and high-calorie drinks (containing sugars, such as cola, or fat, such as shakes), as typically served in international franchise outlets. Many other foods can also be prepared quickly, but the speed of preparation is not the important factor, even though it is characteristic of this group of foods.**

### ADULTS

#### Studies not included in meta-analyses – prospective cohort studies

**Food from 'fast food' establishments.** Seven prospective *cohort studies* (nine publications [194, 212–219]) investigating consumption of 'fast foods' in adults were identified through six published reviews [102, 106, 121, 209–211] providing 23 results. Nineteen of the 23 results reported positive (adverse)

relationships, with higher intake of 'fast foods' being associated with higher *adiposity* at follow-up; 15 were *statistically significant* (**Table 13**). Adiposity was marked by weight change, *BMI* change, waist circumference, odds of weight maintenance, odds of weight gain and risk of obesity. The majority of studies adjusted for potentially *confounding factors*. See Table 51 in the Energy balance and body fatness literature review 2017.

***Food from restaurants and cafeterias.*** Three prospective cohort studies (four publications [213, 214, 220, 221]) investigating eating in restaurants and cafeterias in adults were identified through five published reviews [102, 121, 209–211] providing eight results. Seven out of the eight results reported positive (adverse) associations, with more frequent eating in restaurants and cafeterias being associated with higher adiposity at follow-up; five were statistically significant (**Table 14**). One result reported a non-significant protective association [213]. Adiposity was marked by weight change, BMI change, waist circumference, odds of weight gain and risk of overweight or obesity. Three publications [213, 214, 220] reported using highly adjusted statistical models. See Table 52 in the Energy balance and body fatness literature review 2017.

### Table 13: Summary of prospective cohort studies from published reviews investigating consumption of 'fast food' and adiposity in adults

| Study [publication] | Outcome | Increment/contrast | Results | No. participants Follow-up |
|---|---|---|---|---|
| **Pound of Prevention Study [212]** | Weight change | Per increase of one 'fast foods' meal per week | Beta coefficient 0.72 SE ±0.20 kg<br>p = 0.01 | W: 891<br>3 years |
| **Coronary Artery Risk Development in Young Adults (CARDIA) Study [213–215]** | Weight change | Frequency of 'fast foods' consumption at baseline | **Black participants:** Beta coefficient 2.22 SE ±0.72 kg, p = 0.0014<br>**White participants:** Beta coefficient 1.56 SE ±0.55 kg, p = 0.0064 | Black participants: 1,444<br>White participants: 1,587<br>15 years<br>[215] |
| | | Change in frequency of 'fast foods' consumption over study duration | **Black participants:** Beta coefficient 0.74 SE ±0.45 kg, p = 0.1053<br>**White participants:** Beta coefficient 1.84 SE ±0.44 kg, p < 0.0001 | |
| | Weight change | Frequency of meals at 'fast foods' restaurants per week at baseline | Beta coefficient 0.15 SE ±0.05 kg, p < 0.001 | M&W: 3,643<br>13 years<br>[214] |
| | Waist circumference | | Beta coefficient 0.12 SE ±0.04 cm, p > 0.05 | |
| | BMI change | Increase in frequency of 'fast foods' consumption across study period | Beta coefficient 0.20 (0.005, 0.393) kg/m², p = 0.044 | M&W: 3,394<br>3 years<br>[213] |
| | | Increase in frequency of 'fast foods' and restaurant food consumption across study period | Beta coefficient 0.29 (0.060, 0.509) kg/m², p = 0.013 | |

| Study [publication] | Outcome | Increment/contrast | Results | No. participants Follow-up |
|---|---|---|---|---|
| **Portland Neighborhood Environment and Health Study [216]** | Weight change | More than 1–2 meals at 'fast foods' restaurants per week vs no consumption | Beta coefficient 0.65 SE ±0.32 kg, p < 0.05 | M&W: 1,145<br>1 year |
| | Waist circumference | | Beta coefficient 1.06 SE ±0.41 cm, p < 0.05 | |
| **Supplemental Nutrition Program for Women, Infants and Children 1998 [217]** | BMI change | Frequency per week of eating at 'fast foods' restaurants | **M:** Beta coefficient -0.23 (-0.56, 0.11) kg/m$^2$<br>**W (high income):** Beta coefficient 0.02 (-0.05, 0.09) kg/m$^2$<br>**W (low income):** Beta coefficient -0.06 (-0.20, 0.08) kg/m$^2$ | M: 198<br>W (high income): 529<br>W (low income): 332<br>1 year |
| **Australian Longitudinal Study on Women's Health [218]** | Odds of weight maintenance | Occasional consumption of 'fast foods' relative to never/rarely | OR 0.85 (0.75, 0.96) | W: 8,726<br>4 years |
| | | Frequent consumption of 'fast foods' relative to never/rarely | OR 0.88 (0.76, 1.02) | |
| **The Seguimiento University of Navarra (SUN) Cohort [194]** | Odds of weight gain | Highest vs lowest quintile of 'fast foods' consumption | OR 1.2 (1.02, 1.41) | M&W: 7,194<br>28.5 months |
| **Black Women's Health Study [219]** | Risk of obesity | Consumption of specific type of 'fast foods' more than once per week vs fewer than five times per year | Hamburgers: HR 1.27 (1.14, 1.41)<br>p for trend < 0.001 | W: 19,479<br>14 years |
| | | | Fried chicken: HR 1.08 (0.96, 1.21)<br>p for trend = 0.02 | |
| | | | Pizza: HR 1.08 (0.92, 1.27), p for trend = 0.04 | |
| | | | Chinese food: HR 1.20 (1.05, 1.37)<br>p for trend = 0.05 | |
| | | | Mexican food: HR 0.92 (0.74, 1.14)<br>p for trend = 0.78 | |
| | | | Fried fish: HR 0.92 (0.75, 1.12), p for trend = 0.78 | |

**Abbreviations used:** cm = centimetres; HR = hazard ratio; kg = kilograms; M = men; OR = odds ratio; SE = standard error; W = women.

### Table 14: Summary of prospective cohort studies from published reviews investigating consumption of food from restaurants and cafeterias and adiposity in adults

| Study [publication] | Outcome | Increment/ contrast | Results | No. participants Follow-up |
|---|---|---|---|---|
| **The SUN Cohort [220]** | Weight change | ≥ 2 times per week eating out relative to never/ rarely | Beta coefficient 129 (62, 197) g per year, p < 0.001 | M&W: 9,182 4.4 years |
| | BMI change | | Beta coefficient 0.07 (0.04, 0.10) kg/m2, p < 0.001 | |
| | Odds of weight gain | | OR 1.36 (1.13, 1.63) | |
| | Risk of overweight or obesity | | HR 1.33 (1.13, 1.57) | |
| **The CARDIA Study [213, 214]** | Weight change | Increase of one meal at a restaurant per week at baseline | Beta coefficient 0.09 SE ±0.04 kg, p > 0.05 | M&W: 3,643 13 years [214] |
| | Waist circumference | | Beta coefficient 0.08 SE ±0.03 cm, p > 0.05 | |
| | BMI change | Increase in frequency of restaurant food consumption across study period | Beta coefficient -0.01 (-0.212, 0.187) kg/ $m^2$, p = 0.903 | M&W: 3,394 3 years [213] |
| **Health and Retirement Study [221]** | BMI change | Per $1 decreased individual spending on eating out | Beta coefficient -0.0003 kg/$m^2$, p < 0.05 | M&W: 6,012 10 years |

**Abbreviations used:** cm = centimetres; g = grams; HR = hazard ratio; kg = kilograms; M = men; OR = odds ratio; SE = standard error; W = women.

## CHILDREN

### Studies not included in meta-analyses – prospective cohort studies

Seven prospective cohort studies [222–228] investigating consumption of 'fast foods' in children were identified through five published reviews [102, 106, 121, 210, 211] providing 13 results. Eight out of 13 results reported positive (adverse) associations, with higher intake of 'fast foods' being associated with higher adiposity at follow-up; 6 were statistically significant (**Table 15**). Adiposity was marked by BMI change, BMI z-score change, percentage body fat, risk of overweight and risk of obesity. Number of participants ranged from 101 to 14,355, with larger studies tending to report significant, positive (adverse) associations. Studies varied in *adjustment* for potentially confounding factors; the National Longitudinal Study of Adolescent Health (NLSAH) cohort [224] was the most highly adjusted. Also see Table 50 in the Energy balance and body fatness literature review 2017.

## Table 15: Summary of prospective cohort studies from published reviews investigating consumption of 'fast food' and adiposity in children

| Study [publication] | Outcome | Increment/contrast | Results | No. participants Follow-up |
|---|---|---|---|---|
| **Growing Up Today Study [222]** | BMI change | Increased consumption of fried food away from home from baseline to follow-up | Beta coefficient 0.21 (0.03, 0.39) kg/m$^2$ | 14,355 3 years |
| | | Decreased consumption of fried food away from home from baseline to follow-up | Beta coefficient -0.03 (-0.25, 0.19) kg/m$^2$ | |
| **Identifying Determinants of Eating and Activity (IDEA) and Etiology of Childhood Obesity (ECHO) cohorts [223]** | BMI change | Frequency of 'fast foods' purchases over one month | **B:** No significant association **G:** No significant association | B: 340 G: 353 2 years |
| | Percentage body fat | | **B:** No significant association **G:** No significant association | |
| **National Longitudinal Study of Adolescent Health (NLSAH) cohort [224]** | BMI z-score change | Frequency of 'fast foods' consumption at baseline | Beta coefficient 0.02 SE ±0.01, $p < 0.05$ | 9,919 5 years |
| **Avon Longitudinal Study of Parents and Children (ALSPAC) [225]** | BMI z-score change | Frequency of 'fast foods' consumption at baseline | Beta coefficient 0.0822 SE ±0.028, $p < 0.05$ | 4,022 2 years |
| | Percentage body fat | | Beta coefficient 2.063 SE ±0.3713%, $p < 0.05$ | |
| | Risk of obesity | | OR 1.23 (1.02, 1.49) | |
| **Massachusetts Institute of Technology cohort 1990 [226]** | BMI z-score change | Frequency of 'quick service' foods at baseline | **Never:** 0.28 SE ±0.07 **Once per week:** 0.20 SE ±0.10 **≥2 times per week:** 0.82 SE ±0.15 $F = 6.49$, $p = 0.0023$ | 101 4–7 years |
| **Health, Eating and Play Study (HEAPS) [227]** | BMI z-score change | Frequency of 'fast foods' consumption | No significant association | 293 3 years |
| | Percentage body fat | | No significant association | |
| **Project Eating Among Teens (EAT) Study [228]** | Risk of overweight | Fast food consumption in days per week at baseline | **B:** OR 1.03 (0.90, 1.17) **G:** OR 0.88 (0.79, 0.98) | B: 1,119 G: 1,380 5 years |

**Abbreviations used:** B = boys; G = girls; OR = odds ratio; SE = standard error.

## MECHANISMS

Consumption of 'fast foods' may promote positive *energy balance*, and thus increase risk of weight gain over time, by several mechanisms:

- **Energy density:** 'Fast foods' are typically energy dense. Eating food with higher energy density increases the likelihood of passive overconsumption. In general, people tend to consume roughly the same amount of food from day to day, measured by bulk and weight, indicating that appetite is more influenced by mass of food (weight and volume) than intrinsic amount of energy, at least in the short to medium term [67, 145].
- **Degree of processing:** Highly processed foods, such as those typically served at 'fast foods' outlets (for example, French fries (chips) and nuggets), have generally undergone industrial processing and may be unrecognisable from their original plant or animal source. They are frequently high in energy (see point above). Data from the EPIC cohort reported that high levels of trans fatty acids in the blood were associated with a lower likelihood of weight loss and increased risk of weight gain [229]; plasma trans fatty acids were interpreted as a *biomarker* of dietary *exposures* to industrially processed foods.
- **Cluster of characteristics:** Excess energy intake is also promoted through a cluster of characteristics embodied by 'fast foods', such as being highly palatable, served in large portions, high energy density (see point above), affordable and easy to access.
- **Sugar sweetened drinks:** 'Fast foods' are frequently consumed alongside sugar sweetened drinks, which have their own positive energy balance promoting effects (see **Section 7.6**).
- **Preparation and service:** Increased intake of energy is observed when eating in 'fast food' outlets and restaurants [230-232]. This may be mediated by environmental cues which prompt increased energy intake [233] such as offers to increase portion size or add more food items, or lack of control over initial portion size [234] or ingredients (see **Sections 7.5, 7.6** and **7.8**).

## CUP PANEL'S CONCLUSION

Consumption of 'fast foods' was consistently associated with greater adiposity in prospective cohort studies, many of which were statistically significant. No data from *randomised controlled trials* were identified. The association remained apparent when considering either 'fast foods' as a whole or individual food items, although some individual food items were not significantly associated. There is evidence of biological plausibility.

### The CUP Panel concluded:

- **Consumption of 'fast foods' is probably a cause of weight gain, overweight and obesity.**

## 7.8 'Western type' diet

*(Also see Energy balance and body fatness literature review 2017: Sections 2.4, 3.2 and 3.3)*

### Box 9: Defining a 'Western type' diet

**Three exposures were included in the literature review – free sugars, dietary fat and meat. The Panel initially discussed these separately but noted that these exposures tend to cluster together in a dietary pattern characteristic of 'Western' societies and therefore each can be regarded as a marker of a 'Western type' diet. The Panel took an integrated approach to the interpretation of the evidence for the determinants of weight gain, overweight and obesity (see Section 8) and decided to consider the totality of the evidence for these three exposures together and to draw an overarching conclusion with respect to a 'Western type' diet.**

**As well as being characterised by high intakes of free sugars, dietary fat and meat, such a dietary pattern is usually also low in fruit and vegetables. This pattern of eating is becoming more prevalent in countries characterised by low and middle indices of income and/or development (see also Section 2.2). However, it should be noted that diets of 'Western' countries vary greatly and are not all unhealthy [235].**

Dairy products were considered as part of the evidence review. The evidence was judged to be limited, with no conclusions possible (see **Matrix** and Section 2.5 in the Energy balance and body fatness literature review 2017).

Four published reviews were identified regarding free sugars: Te Morenga *et al.* (2013) [184], Sievenpiper *et al.* (2012) [236], Wiebe *et al.* (2011) [237], and Ma *et al.* (2016) [238]. Three published reviews were identified regarding meat: Fogelholm *et al.* (2012) [160], USDA (2010) [121], and Summerbell *et al.* (2009) [106]. Four published reviews were identified regarding dietary fat: Hooper *et al.* (2012)[7] [239], USDA (2010) [121], Summerbell *et al.* (2009) [106], and Hooper *et al.* (2015) [240].

Eight reviews [106, 121 (with respect to dietary fat), 184, 236–240] were assessed as high quality, and two reviews [121 (with respect to meat), 160] were assessed as moderate quality (for the quality assessment process, please see the protocol in the Energy balance and body fatness literature review 2017).

### ADULTS

Five published reviews [106, 184, 236, 238, 240] conducted 12 *meta-analyses* in total investigating components of the 'Western type' diet and *adiposity* in adults. Nine meta-analyses (three published reviews [184, 236, 238]) investigated intake of free sugars; three meta-analyses (two published reviews [106, 240]) investigated intake of dietary fat; no meta-analyses were identified with respect to consumption of meat. The results generally showed positive (adverse) relationships, with increased consumption of components of the 'Western type' diet being related to higher adiposity. See Tables 67, 68, 74 and 77 in the Energy balance and body fatness literature review 2017.

[7] This published review was updated by Hooper *et al.* (2015) [240].

### Meta-analyses – randomised controlled trials

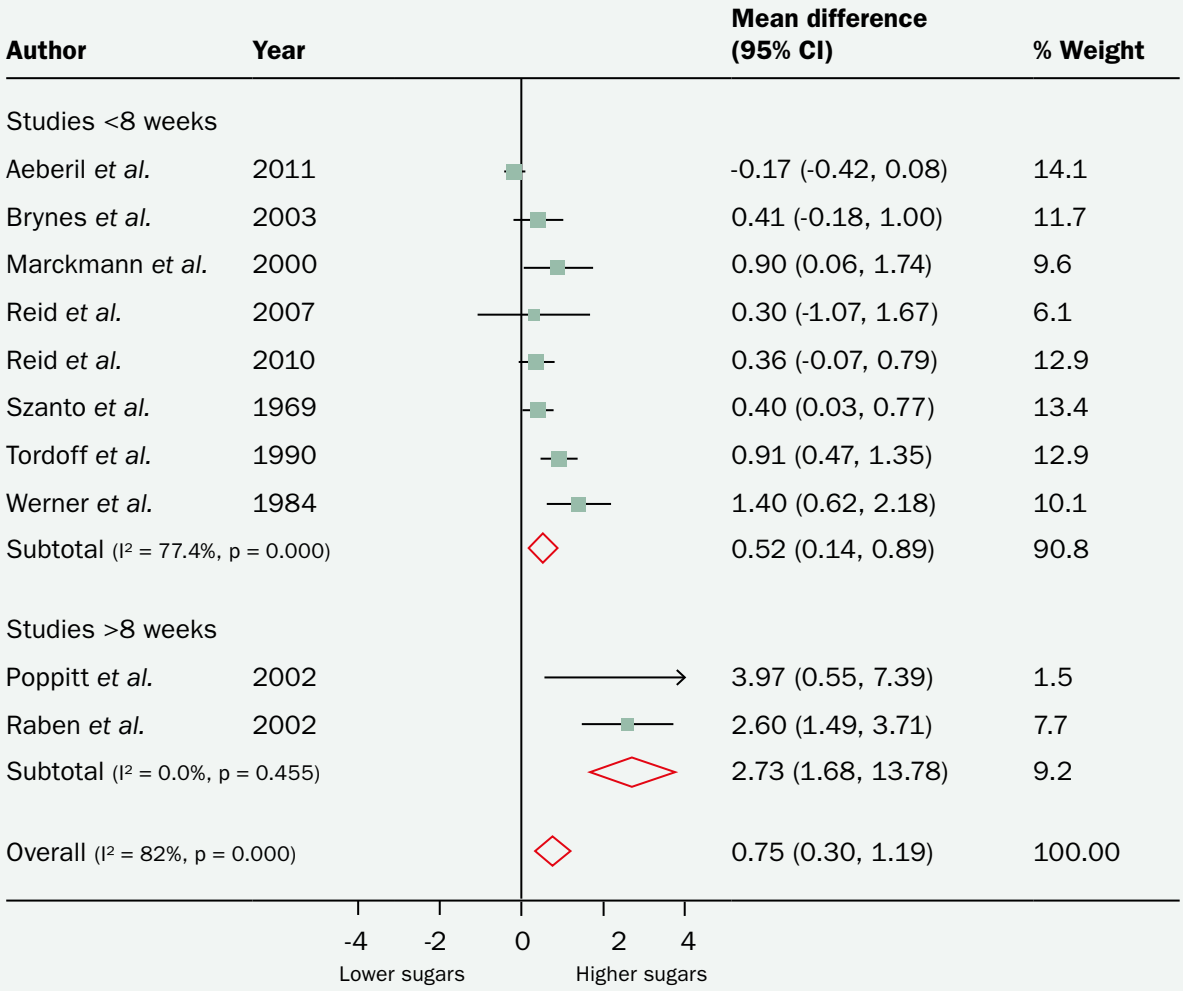
**Free sugars.** With respect to weight change, five meta-analyses of *randomised controlled trials* investigating intake of free sugars were identified (**Table 16**). Three reported significant, positive (adverse) associations: ad libitum diet with reduced sugars intake was associated with less weight gain than habitual diet [184]; hyperenergetic addition of free sugars was associated with higher weight gain than habitual diet [184] (see **Figure 8**); and hyperenergetic addition of fructose was associated with higher weight gain than habitual diet [236]. Meta-analyses of randomised controlled trials exchanging free sugars for other complex carbohydrates reported no significant effects [184, 236]. One published review [238] conducted meta-analyses of randomised controlled trials and hyperenergetic addition of sugars with respect to accumulated ectopic fat in the liver and lower extremity muscles (see Table 67 in the Energy balance and body fatness literature review 2017). The results reported significant positive (adverse) effects with higher sugars intake leading to more accumulated ectopic fat: accumulated liver fat, SMD 0.93 [95% CI 0.64, 1.21] and accumulated lower extremity muscle fat, SMD 0.63 [95% CI 0.23, 1.04]. No *heterogeneity* ($I^2$ = 0%) and moderate heterogeneity ($I^2$ = 42%) were reported, respectively.

**Table 16: Summary of meta-analyses of randomised controlled trials from published reviews investigating components of the 'Western type' diet and weight change in adults**

| Published review | Outcome | Increment/contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Sugars** | | | | | | |
| ***Interventions to reduce sugars intake*** | | | | | | |
| **Te Morenga *et al.* (2013) [184]** | Weight change | Ad libitum diet with reduced free sugars intake vs habitual diet | **WMD** -0.80 (-1.21, -0.39) kg | 17 | 5 | 1,286 |
| ***Interventions to exchange sugars with other macronutrients*** | | | | | | |
| **Te Morenga *et al.* (2013) [184]** | Weight change | Isoenergetic exchange of free sugars vs complex CHO | **WMD** 0.04 (-0.04, 0.13) kg | 32 | 11 | 144 |
| **Sievenpiper *et al.* (2012) [236]** | Weight change | Isoenergetic exchange of fructose vs other dietary CHO | **MD** -0.13 (-0.37, 0.10) kg | 8 | 13 | 417 |
| ***Interventions to increase sugars intake*** | | | | | | |
| **Te Morenga *et al.* (2013) [184]** | Weight change | Hyperenergetic addition of free sugars vs habitual diet | **WMD** 0.75 (0.30, 1.19) kg | 82 | 10 | 382 |
| **Sievenpiper *et al.* (2012) [236]** | Weight change | Hyperenergetic addition of fructose vs habitual diet | **MD** 0.37 (0.15, 0.58) kg | 0 | 8 | 176 |
| **Dietary fat** | | | | | | |
| **Hooper *et al.* (2015) [240]** | Weight change | Reduced proportion of energy as dietary fat vs habitual diet | **MD** -1.54 (-1.97, -1.12) kg | 77 | 24 | 53,647 |

**Abbreviations used:** CHO = carbohydrates; kg = kilograms; MD = mean difference; WMD = weighted mean difference.

## Figure 8: Meta-analysis [184] of randomised controlled trials of weight change and hyperenergetic addition of free sugars in adults

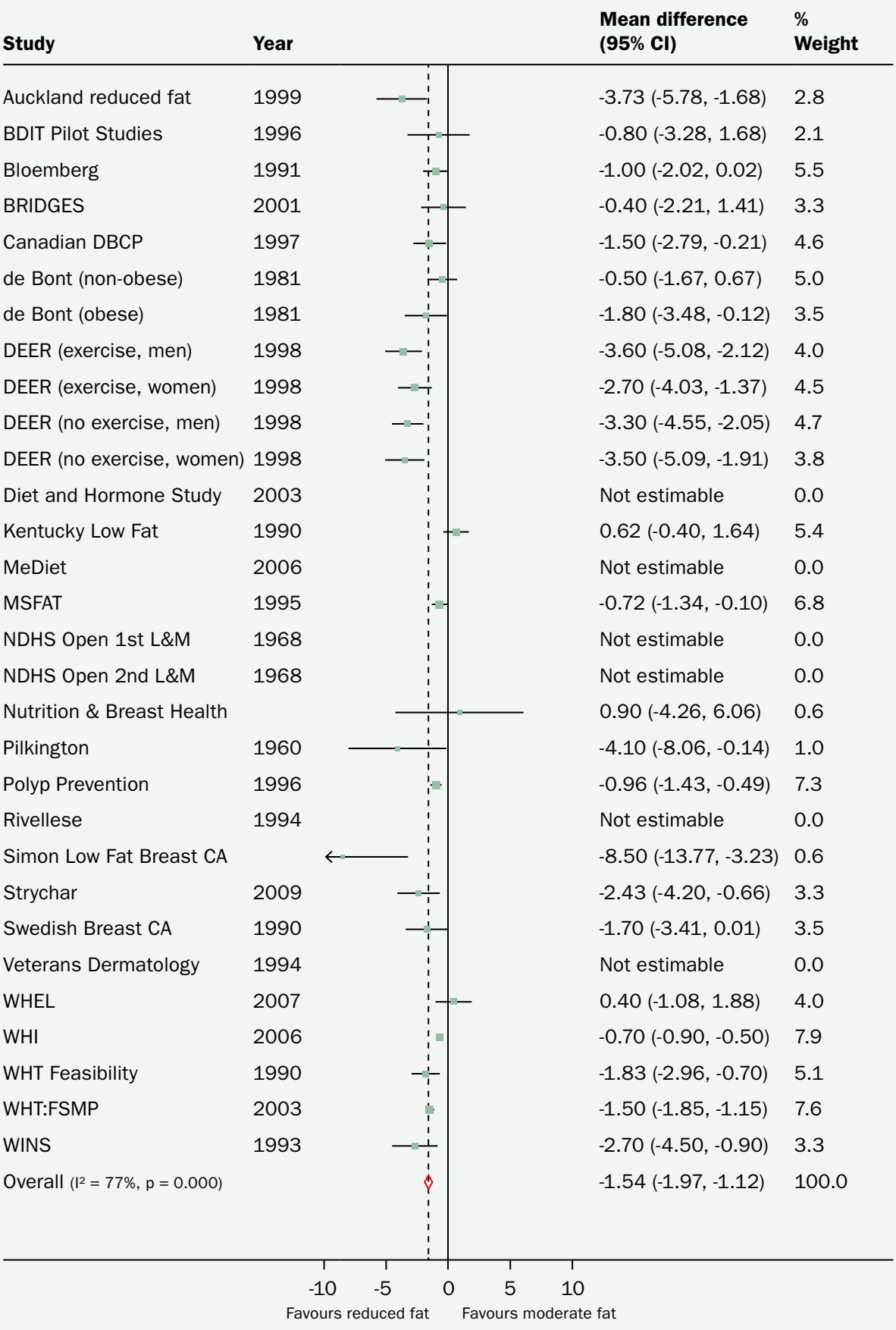



*Effect of increasing free sugars on measures of body fatness in adults. Pooled effects for difference in body weight (kg) shown for studies comparing increased intake (higher sugars) with usual intake (lower sugars). Overall effect shows increased body weight after intervention in the higher sugars groups. Data are expressed as weighted mean difference (95% **confidence interval**), using generic inverse variance models with random effects [184].*

*For references to studies included in the meta-analysis, please consult the published review [184].*

***Dietary fat.*** One meta-analysis of 24 *randomised controlled trials* investigating the proportion of energy from dietary fat was identified (**Table 16**). The result reported significantly lower weight gain in individuals with a reduced proportion of energy from dietary fat compared with habitual diet [240]; see **Figure 9**. A high degree of heterogeneity between trials was observed ($I^2$ = 77%), which the authors attributed to variation in the type and number of participants, the duration and nature of the interventions, the control methods and length of follow-up. The authors also conducted a meta-analysis of randomised controlled trials investigating reduced proportion of energy from fat with respect to *BMI* change (results not shown here, see Table 74 in the Energy balance and body fatness literature review 2017). A significantly lower BMI was reported for individuals in the reduced fat arms relative to controls (MD -0.5 [95% CI -0.7, -0.3] kg/m²); there was evidence of high heterogeneity ($I^2$ = 74%).

## Figure 9: Meta-analysis [240] of randomised controlled trials of weight change and reduced proportion of energy from dietary fat in adults




**Forest plot** *of comparison of fat reduction versus usual fat diet in adult RCTs, outcome = weight, kg [240].*
*For references to studies included in the meta-analysis, please consult the published review [240].*

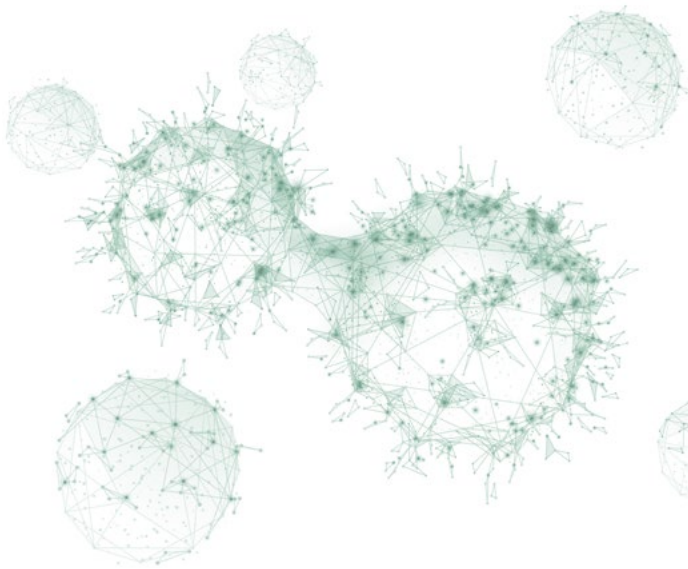
### Meta-analyses – prospective cohort studies

***Sugars in confectionery.*** One published review [184] examining free sugars intake conducted a meta-analysis of prospective *cohort studies* in adults investigating increase in servings of sweets (candy) per day across the course of the studies and reported no significant association (**Table 17**). High heterogeneity was reported between the two included studies ($I^2$ = 91%) which was not explained in the published review. Meta-analysis of four studies investigating daily servings of sweets (candy) at baseline reported no association [184] (regression coefficient 0.00 [95% CI -0.02, 0.03]; $I^2$ = 74%; see Table 68 in the Energy balance and body fatness literature review 2017).

***Dietary fat.*** One published review [106] reported no significant association between change in dietary fat as a percentage of total energy intake and weight change in adults in a meta-analysis of four prospective cohort studies (**Table 17**).

### Studies not included in meta-analyses – randomised controlled trials

***Free sugars.*** Individual trials investigating sugar intake were identified; however, the arms compared types of sugar (for example, sucrose versus glucose) which were not informative to this specific research question. In general, the trials were modest in size and short term; further research is required in this area. See Section 3.2 in the Energy balance and body fatness literature review 2017.



### Table 17: Summary of meta-analyses of prospective cohort studies from published reviews investigating components of the 'Western type' diet and weight change in adults

| Published review | Outcome | Increment/ contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Sugars** | | | | | | |
| **Te Morenga *et al.* (2013) [184]** | Weight change | Additional daily serving of sweets (candy) increase from baseline | **Regression coefficient** 0.02 (-0.02, 0.07) units NR | 91 | 2 | 50,670 |
| **Dietary fat** | | | | | | |
| **Summerbell *et al.* (2009) [106]** | Weight change | Dietary fat as percentage of total energy intake | **Regression coefficient** 0.07 (-0.03, 0.16) units NR | NR | 4 | 9,753 |

**Abbreviations used:** NR = not reported.

### Studies not included in meta-analyses – prospective cohort studies

An overview of results from individual prospective cohort studies not included in meta-analyses of components of the 'Western type' diet is presented in **Table 18**. Overall, the majority of results reported positive (adverse) associations with higher intake of sugars, dietary fat or meat being associated with increased adiposity. While the included studies examined the effect of sugars, meat and dietary fat individually, the Panel considers the 'Western type' diet to be the summary factor responsible for the observed effects on weight (see **Box 9** and **Section 8**). See also tables 37, 38, 39, 40, 70 and 78 in the Energy balance and body fatness literature review 2017.

**Free sugars.** Three prospective cohort studies (four publications [111, 112, 138, 241]) were identified, providing 14 results. Ten results reported positive (adverse) associations, of which three were *statistically significant*. The Danish Diet, Cancer and Healthy Study [111] (20,126 men and 22,570 women) reported higher waist circumferences per mega joule per day of foods with simple or added sugars at baseline, which was significant in women (MD 0.39 [95% CI 0.18, 0.60] centimetres) but not men (MD 0.09 [95% CI -0.06, 0.23] centimetres). One study [138] reported a significantly increased likelihood of a small weight loss per additional 100 grams of sweets (candy) consumed at baseline (OR 1.43 [95% CI 1.07, 1.90]). Proxy markers of sugars intake were used in all studies: intake of sweets (candy) [138], sweet foods [111, 112], and jams, syrups and sugars [241]. Follow-up ranged from just over 2 years [138] to 6 years [112]. See Table 70 in the Energy balance and body fatness literature review 2017.

***Dietary fat.*** Seven prospective cohort studies with more than 1,000 participants [111, 138, 150, 151, 242–244] provided 23 results. Seventeen results reported positive (adverse) associations between dietary fat intake and adiposity, of which seven were statistically significant. Six results reported inverse associations, of which three were statistically significant: one study reported a higher proportion of energy from fat at the expense of protein was associated with weight decreases in both men and women [243], and one study reported increased odds of a small weight loss (less than 2 kilograms) with increased intake of fat in men [138]. Studies on dietary fat intake were challenging to compare because of differences in the way the exposure was reported (modifications to 'total' dietary fat or percentage energy from dietary fat) and the extent of statistical *adjustment* for other potentially *confounding* variables. Type of dietary fat was not investigated. For full results, see Table 78 in the Energy balance and body fatness literature review 2017. For references and results of the six studies with fewer than 1,000 participants, please see Section 3.3 in the Energy balance and body fatness literature review 2017.

***Meat.*** Twelve prospective cohort studies [112, 135, 136, 138, 139, 177, 179, 194, 241, 245–247] were identified from three published reviews [106, 121, 160]. The results are categorised based on reported exposure: total meat intake, red meat intake, *processed meat intake*, or poultry intake (see tables 37, 38, 39 and 40 in the Energy balance and body fatness literature review 2017). In total, 52 out of 59 results reported positive (adverse) associations, with increased meat consumption being related to greater adiposity at follow-up, of which 32 were statistically significant (see **Table 18**). Adiposity was marked by weight change, BMI change, waist circumference and odds of weight gain. **Table 19** presents the results of the eight studies [112, 136, 138, 139, 179, 245–247] with respect to total meat consumption (the four other studies relate to other subcategories within meat as an exposure). Within the 'total meat' subcategory, 17 results reported significantly higher adiposity at follow-up with increased meat intake.

## Table 18: Overview of prospective cohort studies (not included in meta-analyses) from published reviews investigating components of the 'Western type' diet and adiposity in adults

| Exposure (increased intake) | | | Publications | Association with adiposity |
|---|---|---|---|---|
| 'Western type' diet | Free sugars | | [111, 112, 138, 241] | **14 results from 4 publications (3 cohorts):**<br>10 results reported positive (adverse) associations, of which 3 were significant<br>4 results reported inverse associations, of which 1 was significant |
| | Dietary fat | | [111, 138, 150, 151, 242–244] | **23 results from 7 publications:**<br>17 results reported positive (adverse) associations, of which 7 were significant<br>6 results reported inverse associations, of which 3 were significant |
| | Meat | Total meat (Also see **Table 19**) | [112, 136, 138, 139, 179, 245–247] | **27 results from 8 publications:**<br>25 results reported positive (adverse) associations, of which 17 were significant<br>1 result reported an inverse association (not significant)<br>1 result reported no association |
| | | Red meat | [135, 177, 179, 194, 241, 245, 247] | **11 results from 7 publications:**<br>9 results reported positive (adverse) associations, of which 4 were significant<br>2 results reported inverse associations, of which 2 were significant |
| | | Processed meat | [138, 177, 179, 241, 245, 247] | **17 results from 6 publications:**<br>15 results reported positive (adverse) associations, of which 9 were significant<br>2 results reported inverse associations, of which 1 was significant |
| | | Poultry | [179, 241, 245] | **4 results from 3 publications:**<br>3 results reported positive (adverse) associations, of which 2 were significant<br>1 result reported an inverse association (not significant) |

For dietary fat, only studies with more than 1,000 participants are reported; please see the Energy balance and body fatness literature review 2017.

## Table 19: Summary of prospective cohort studies from published reviews investigating total meat consumption and adiposity in adults

| Study [publication] | Outcome | Increment/contrast | Results | No. participants Follow-up |
|---|---|---|---|---|
| **EPIC-PANACEA [245]** | Weight change | Per 100 kcal increase in total meat intake | Beta coefficient 65 (39, 90) g/year, p < 0.00001 | M&W: 373,803 5 years |
| **The SUN Cohort [136]** | Weight change | Tertiles of meat intake | **Low:** 0.41 (0.26, 0.56) kg<br>**Mid:** 0.62 (0.40, 0.84) kg<br>**High:** 0.79 (0.56, 1.02) kg<br>p for trend = 0.001 | M&W: 6,319 28 months |
| **EPIC-Oxford [246]** | Weight change | 'Meat eater' dietary pattern vs 'fish eater' dietary pattern over one year | **M:** No significant difference<br>**W:** Significantly greater weight gain in 'meat eater' dietary pattern, p < 0.05 | M: 5,373<br>W: 16,593<br>5.3 years |
| | | 'Meat eater' dietary pattern vs 'vegetarian' dietary pattern over one year | **M:** No significant difference<br>**W:** No significant difference | |
| | | 'Meat eater' dietary pattern vs 'vegan' dietary pattern over one year | **M:** Significantly greater weight gain in 'meat eater' dietary pattern, p < 0.05<br>**W:** Significantly greater weight gain in 'meat eater' dietary pattern, p < 0.05 | |
| **Cancer Prevention Study II [139]** | BMI change | Highest vs lowest quintile of meat intake | **M:** MD 0.34 kg/m² SE ±0.05, p < 0.001<br>**W:** MD 0.19 kg/m² SE ±0.05, p < 0.001 | M: 35,156<br>W: 44,080<br>10 years |
| | Odds of 'gaining weight at the waist' | | **M:** OR 1.46 (1.25, 1.71)<br>**W:** OR 1.50 (1.20, 1.87) | |
| **Medical Research Council National Survey of Health and Development (MRC NSHD) 1964 birth cohort [247]** | BMI change | Per 10 g increase in total meat intake at baseline | **M:** Beta coefficient 0.013 SE±0.003 kg/m², p < 0.001<br>**W:** Beta coefficient 0.013 SE±0.005 kg/m², p = 0.008 | M: 517<br>W: 635<br>10 years |
| | Waist circumference | | **M:** Beta coefficient 0.034 SE±0.009 cm, p < 0.001<br>**W:** Beta coefficient 0.035 SE±0.012 cm, p = 0.003 | |
| **MONICA1 [112]** | Waist circumference | Per quintile increase of meat product intake | **M:** Beta coefficient 0.11 (-0.06, 0.28) cm<br>**W:** Beta coefficient 0.20 (-0.05, 0.44) cm | M: 1,166<br>W: 1,120<br>6 years |
| **EPIC-Diet, Obesity and Genes (DiOGenes) [179]** | $\Delta WC_{BMI}$ | 100 kcal increments of meat product intake over one year | Beta coefficient 0.02 (0.00, 0.03) cm, p = 0.036 | M&W: 48,631 5.5 years |

| Study [publication] | Outcome | Increment/contrast | Results | No. participants Follow-up |
|---|---|---|---|---|
| **EPIC-Potsdam [138]** | Odds of weight gain (>2kg) | Per 100 g of meat intake | **M:** OR 1.06 (0.85, 1.32)<br>**W:** OR 1.36 (1.04, 1.79) | M: 6,364<br>W: 11,005<br>2.2 years |
| | Odds of weight gain (<2kg) | | **M:** OR 1.00 (0.83, 1.20)<br>**W:** OR 1.21 (0.98, 1.50) | |
| | Odds of weight loss (<2kg) | | **M:** OR 1.01 (0.85, 1.21)<br>**W:** OR 0.79 (0.64, 0.97) | |
| | Odds of weight loss (>2kg) | | **M:** OR 0.79 (0.63, 1.00), p <0.05<br>**W:** OR 0.81 (0.64, 1.03) | |

**Abbreviations used:** $\Delta WC_{BMI}$ = waist circumference for a given BMI; cm = centimetres; g = grams; kcal = kilocalories; M = men; MD = mean difference; OR = odds ratio; PANACEA = Physical Activity, Nutrition, Alcohol, Cessation of Smoking, and Eating out of Home in Relation to Anthropometry; SE = standard error; W = women.

## CHILDREN

Three published reviews [121, 184, 240] provided evidence on two components of the 'Western type' diet (free sugars and dietary fat) and adiposity in children. Please see tables 65, 66, 72 and 73 in the Energy balance and body fatness literature review 2017.

***Free sugars.*** One published review [184] conducted a meta-analysis of five randomised controlled trials investigating the effect of interventions to reduce intake of free sugars on BMI or BMI z-score in children. Children following their habitual diet had a higher BMI or BMI z-score at follow-up relative to children in the intervention groups, although this was not significant (SMD 0.09 [95% CI -0.14, 0.32]). *Compliance* with the intervention was reported as 'poor' in three of the five trials. Six prospective cohort studies [198, 200, 248–251] reported 14 results, of which 10 were inverse associations (two significant), 2 were non-significant positive (adverse) associations and 2 were no association. See Tables 65 and 66 in the Energy balance and body fatness literature review 2017.

***Dietary fat.*** No meta-analyses were identified. Three randomised controlled trials [252–254] investigated the effect of interventions to reduce dietary fat intake on adiposity in children; no significant effects were reported. Three prospective cohort studies [143, 153, 255] with more than 1,000 participants investigated intake of dietary fat and weight or BMI change at follow-up. Mixed results were reported with small effect sizes. See tables 72 and 73 in the Energy balance and body fatness literature review 2017. For references and results of the 26 studies with fewer than 1,000 participants, please see Section 3.3 in the Energy balance and body fatness literature review 2017.

***Meat.*** No evidence was identified.

## MECHANISMS

The mechanisms linking consumption of a 'Western type' diet to increased risk of weight gain, overweight and obesity relate to the constituent components, sugars, dietary fat and meat, both individually and jointly.

- **Energy density:** One characteristic of the 'Western type' diet is its high energy density.
    - Eating a higher energy density diet increases the likelihood of passive overconsumption. In general, people tend to consume roughly the same amount of food from day to day, measured by bulk and weight, indicating that appetite is more influenced by mass of food (weight and volume) than intrinsic amount of energy, at least in the short to medium term [67, 145].
    - Meat, and some meat products in particular, may be energy dense, especially if high in fat, and thereby may increase total energy intake [256].
- **Influence on appetite:** Specific properties of the 'Western type' diet may influence appetite.
    - Prolonged consumption of a high-fat diet may desensitise individuals to a number of appetite signals, such as release of gastrointestinal *hormones* [257].
    - Increased intake of foods high in fat or sugars has been associated with greater reward response and decreased inhibitory responses to such foods [207, 208].
    - The orosensory properties of fat, and foods high in fat, improve palatability [207, 258, 259] which might plausibly lead to voluntary overconsumption [260]. Similar preferences have been observed for palatable foods high in sugars [207, 261]. However, replication of these results in human studies is limited.
    - Dietary protein has a stronger satiating effect than other *macronutrients* (fats and carbohydrates) [262]; as meat is high in protein it is possible that diets containing meat low in fat may have a beneficial impact on appetite cues. However, some small human trials suggest that meat- and vegetarian-based sources of protein do not differ in their satiating effects [263–265].

## CUP PANEL'S CONCLUSION

The evidence relating to a 'Western type' diet is amalgamated from three individual exposures characteristic of such a dietary pattern: free sugars, meat and dietary fat (see **Box 9**). Results from meta-analyses of randomised controlled trials demonstrate consistent increased risk of adiposity for intake of both sugars and dietary fat. The observed relationships are supported by evidence from meta-analyses of prospective cohort studies and multiple individual studies. Prospective cohort studies consistently report increased risk of adiposity with increased consumption of meat, after adjusting for potentially confounding factors. There is evidence of biological plausibility.

For children, the evidence for an association for free sugars or dietary fat was considered to be limited and no separate conclusions were possible. There was no evidence identified in children for meat.

### The CUP Panel concluded:

- **Consumption of a 'Western type' diet is probably a cause of weight gain, overweight and obesity.**

## 7.9 Physical activity

*(Also see Energy balance and body fatness literature review 2017: Section 4)*

Sixteen published reviews were identified: USDA DGAC (2015) [102], Hespanhol *et al.* (2016) [266], Kelley and Kelley (2006) [267], van 't Riet *et al.* (2014) [268], Oja *et al.* (2015) [269], Ismail *et al.* (2012) [270], Summerbell *et al.* (2009) [106], Oja *et al.* (2011) [271], Bochner *et al.* (2015) [272], Costigan *et al.* (2015) [273], Te Velde *et al.* (2012) [274], Murphy *et al.* (2007) [275], Gao *et al.* (2016) [276], Murtagh *et al.* (2015) [277], Hanson and Jones (2015) [278] and Laframboise *et al.* (2011) [279].

Thirteen reviews [102, 106, 266-270, 272, 273, 275–278] were assessed as high quality, and three reviews [271, 274, 279] were assessed as moderate quality (for the quality assessment process, please see the protocol in the Energy balance and body fatness literature review 2017).

*Physical activity* is any movement using skeletal muscles and may be aerobic, strength (resistance) based or a combination. The evidence for strength (resistance) physical activity specifically was updated as part of the Energy balance and body fatness literature review 2017 but did not support a conclusion (see Section 4 in the Energy balance and body fatness literature review 2017).

### 7.9.1 Aerobic physical activity

#### ADULTS

#### Meta-analyses – randomised controlled trials

Five published reviews [266–270] conducted *meta-analyses* of *randomised controlled trials* investigating *aerobic physical activity* and *adiposity* in adults. Out of eight meta-analysis results, seven reported lower adiposity with the aerobic physical activity intervention, compared with the control arms; five were *statistically significant* (see **Table 20**). A meta-analysis of 21 studies from one published review [266] reported a 2.74 kilogram lower body weight in individuals in the intervention arm after up to 52 weeks or more of running training (WMD -2.74 [95% CI -3.43, -2.06] kilograms; $I^2$ = 0%); the greatest difference in body weight was observed with the longest intervention period, see **Figure 10**. One study [268] reported significantly higher *BMI* in the intervention arm of active video gaming, compared with no intervention, in an elderly population. A range of adiposity measures were used as outcomes between the meta-analyses.

The trials included across the published reviews comprised a variety of aerobic physical activities, including running, cycling, participation in football and active video gaming. In general, these trials were small, increasing the risk of *publication bias*; results of *Egger's test* were not reported in the published reviews for these estimates. See also Table 86 in the Energy balance and body fatness literature review 2017.

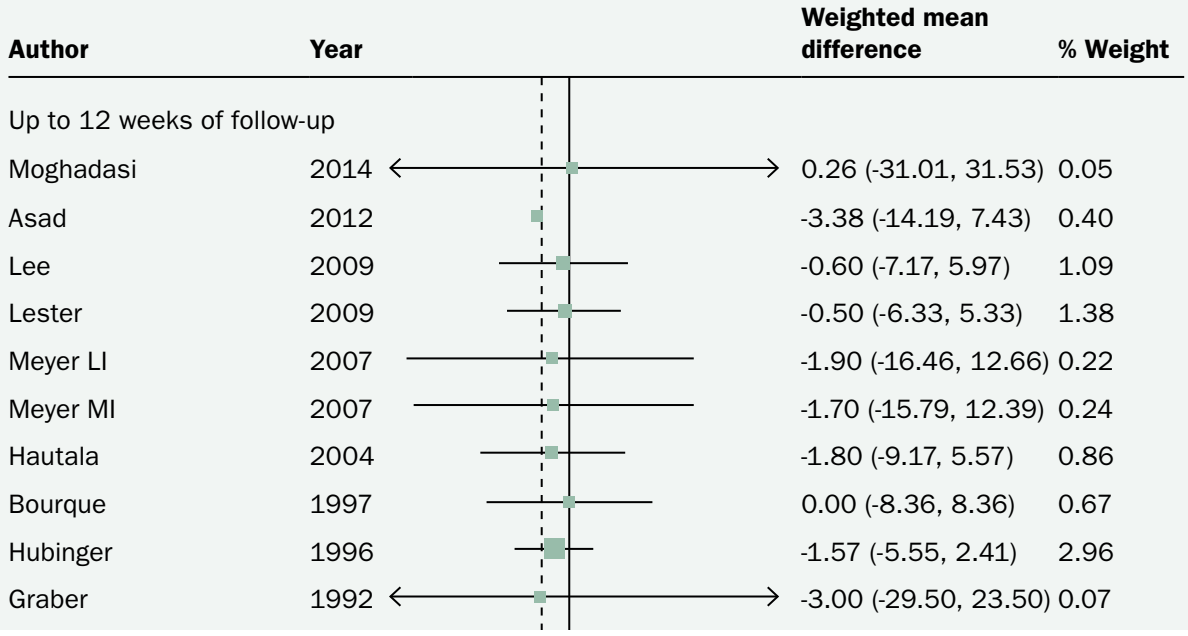
## Table 20: Summary of meta-analyses of randomised controlled trials from published reviews investigating aerobic physical activity and adiposity in adults

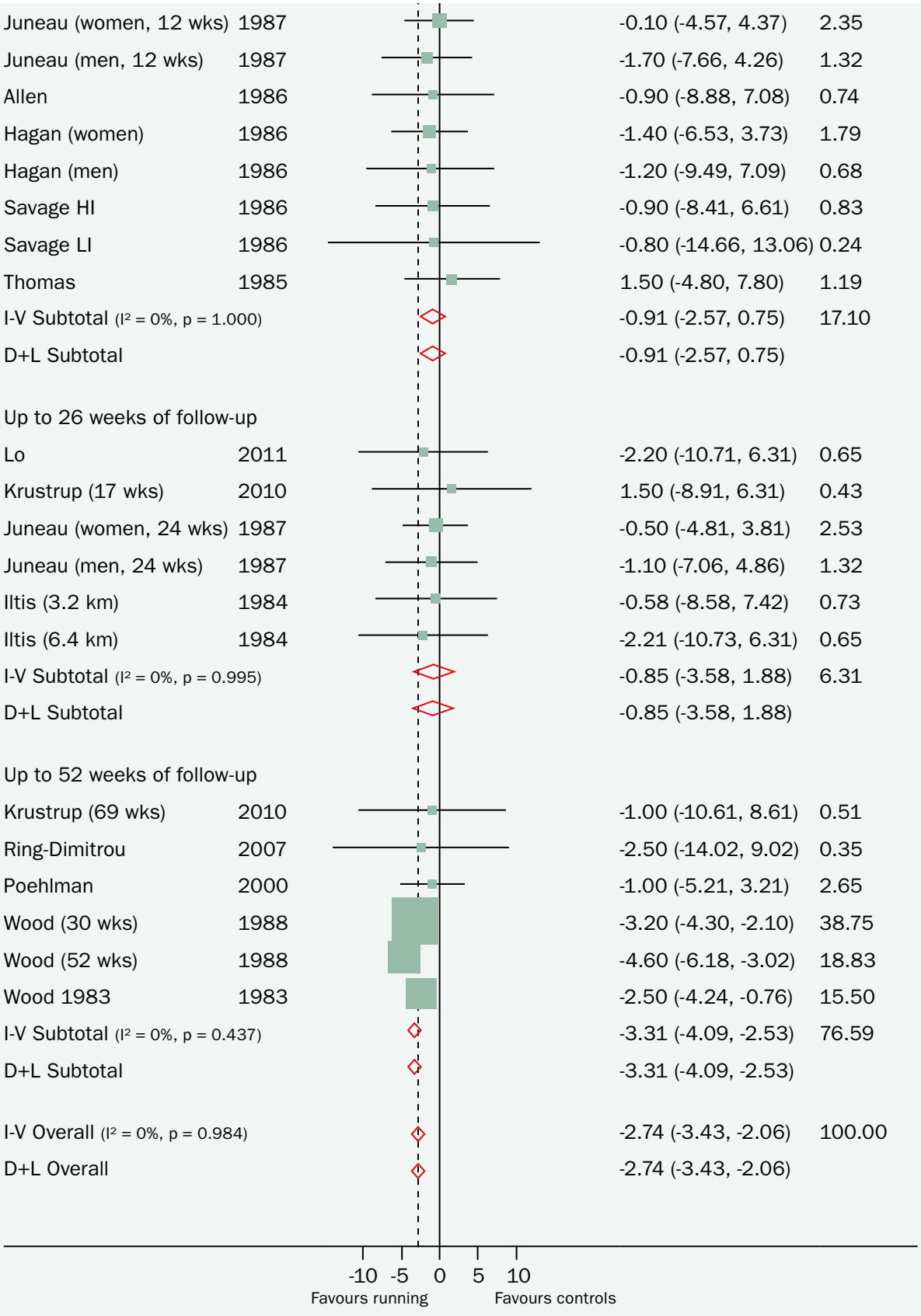
| Published review | Outcome | Increment/contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Hespanhol *et al.* (2016) [266]** | Weight change | Running programme vs no intervention | **WMD** -2.74 (-3.43, -2.06) kg | 0 | 21 | 979 |
| **Kelley and Kelley (2006) [267]** | | Varied aerobic exercise vs control | **MD** -3.4 (-5.3, -1.5) kg | NR* | 3 | NR |
| **van 't Riet *et al.* (2014) [268]** | BMI change | Active video gaming vs no intervention | **SMD** 0.68 (0.13, 1.24) | 68 | 6 | 142 |
| **Hespanhol *et al.* (2016) [266]** | | Running programme vs no intervention | **WMD** -0.23 (-0.61, 0.15) $kg/m^2$ | 0 | 10 | 256 |
| **Hespanhol *et al.* (2016) [266]** | Percentage body fat change | Running programme vs no intervention | **WMD** -1.63 (-2.15, -1.12) % | 0 | 11 | 657 |
| **Kelley and Kelley (2006) [267]** | | Varied aerobic exercise vs control | **MD** -1.4 (-2.3, -0.6) % | NR* | 3 | NR |
| **Oja *et al.* (2015) [269]** | Fat mass change | Interventions to participate in football (soccer) vs no intervention | **MD** -2.64 (-6.06, 0.78) kg | 16 | 5 | NR |
| **Ismail *et al.* (2012) [270]** | VAT change | Varied aerobic exercise interventions vs control | **SMD** -0.23 (-0.35, -0.12) | 71 | 27 | 1,409 |

*$I^2$ statistic not reported; Q statistic for weight change meta-analysis, Q = 2.8, p = 0.25; Q statistic for percentage body fat change meta-analysis, Q = 1.7, p = 0.43.

**Abbreviations used:** kg = kilograms; MD = mean difference; NR = not reported; SMD = standardised mean difference; VAT = visceral adipose tissue; WMD = weighted mean difference.

## Figure 10: Meta-analysis [266] of randomised controlled trials of weight change and running (aerobic physical activity) in adults






*Overall and length of training subgroups meta-analyses for body weight (kg). 'I-V Overall' represents the overall fixed-effect model weighted by the inverse-variance. 'I-V Subtotal' represents the fixed-effect model weighted by the inverse-variance by length of training. 'D+L Overall' represents the overall random-effects model weighted by the inverse of the variance within and between (tau-squared) studies. 'D+L Subtotal' represents the random-effects model weighted by the inverse of the variance within and between (tau-squared) studies by length of training. I-V: inverse-variance. D+L: DerSimonian and Laird method with the estimate of heterogeneity being taken from the inverse-variance fixed-effect model. HI: high intensity. MI: moderate intensity. LI: low intensity. Wks: weeks [266].*

*For references to studies included in the meta-analysis, please consult the published review [266].*

### Studies not included in meta-analyses – prospective cohort studies

Eleven prospective *cohort studies* (12 publications [280–291]), with more than 500 participants, investigating aerobic physical activity in adults were identified through three published reviews [106, 269, 271] providing 24 results. Twenty out of 24 results reported inverse relationships, with increased aerobic physical activity being associated with lower adiposity at follow-up; 14 were statistically significant. Adiposity was marked by weight change, BMI change, waist circumference, odds or risk of weight gain, and odds of obesity. Most studies adjusted for several potentially *confounding factors*. See Table 87 in the Energy balance and body fatness literature review 2017.

For references and results of the eight randomised controlled trials and six prospective cohort studies with fewer than 500 participants, please see Section 4 in the Energy balance and body fatness literature review 2017.

## CHILDREN

### Meta-analyses – randomised controlled trials

Three published reviews [268, 272, 273] conducted meta-analyses of randomised controlled trials investigating aerobic physical activity and adiposity in children (**Table 21**). Three out of five results reported significant protective effects of aerobic physical activity in the form of high-intensity interval training across sports (sprints, walking, swimming and cycling) in adolescents [273]; **Figure 11** shows the *forest plot* for BMI change. Two published reviews [268, 272] investigating aerobic activity led by on-screen videos reported non-significant effects. There was overlap of five trials between these two meta-analyses, and the studies were generally of low quality. See also Table 83 in the Energy balance and body fatness literature review 2017.

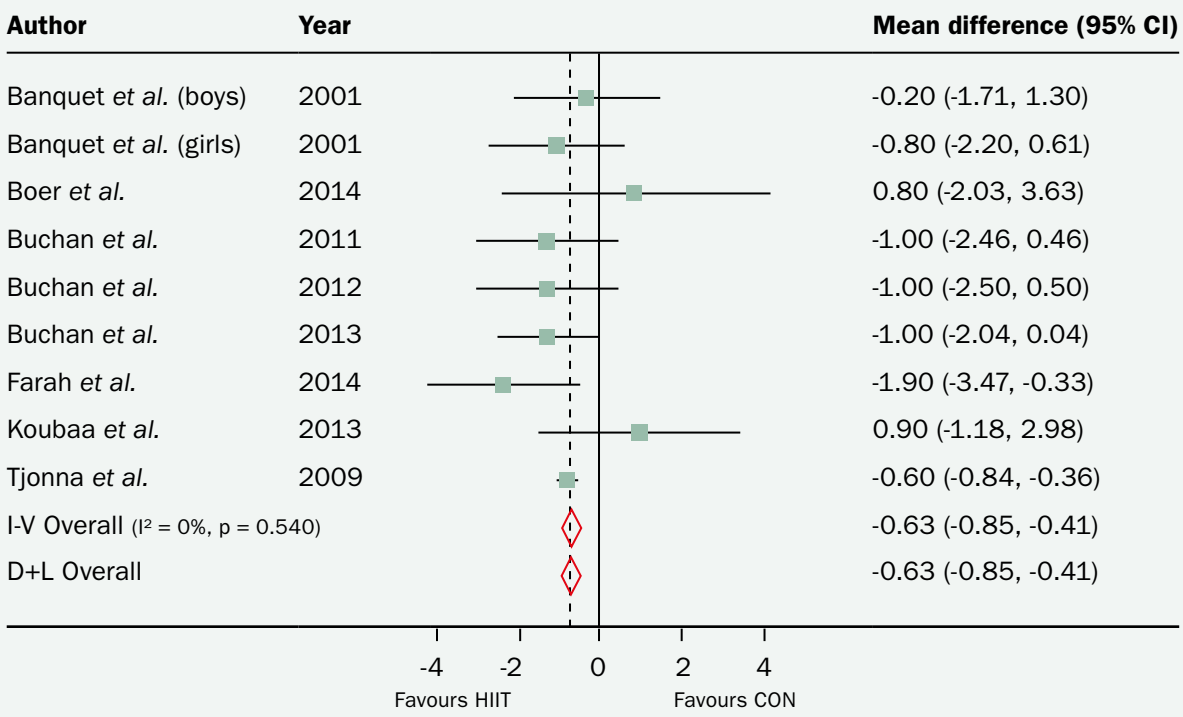
### Table 21: Summary of meta-analyses of randomised controlled trials from published reviews investigating aerobic physical activity and adiposity in children

| Published review | Outcome | Increment/ contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Bochner *et al.* (2015) [272]** | Weight change | Active video gaming vs no intervention | **SMD** -0.08 (-0.25, 0.08) kg | NR* | 7 | 588 |
| **van 't Riet *et al.* (2014) [268]** | BMI change | Active video gaming vs no intervention | **SMD** 0.20 (-0.08, 0.48) | 46 | 5 | 561 |
| **Costigan *et al.* (2015) [273]** | BMI change | High-intensity interval training programme vs control | **MD** -0.6 (-0.9, -0.4) $kg/m^2$ | 0 | 8 | 870 |
| | Percentage body fat change | High-intensity interval training programme vs control | **MD** -1.6 (-2.9, -0.5) % | 63 | 7 | 786 |
| | Waist circumference | High-intensity interval training programme vs control | **MD** -1.5 (-4.1, -1.1) cm | 68 | 6 | NR |

*$I^2$ value not reported; test for heterogeneity $\chi^2 = 0.69$, degrees of freedom = 6, P = 1.0.

**Abbreviations used:** cm = centimetres; kg = kilograms; MD = mean difference; NR = not reported; SMD = standardised mean difference.

**Figure 11: Meta-analysis [273] of randomised controlled trials of BMI change and high-intensity interval training (aerobic physical activity) in children**




*Forest plot of high-intensity interval training (HIIT) effect on body mass index [273].*
*For references to studies included in the meta-analysis, please consult the published review [273].*

### Studies not included in meta-analyses – prospective cohort studies

Four prospective cohort studies [292–295] investigating aerobic physical activity in children, with more than 500 participants, were identified through two published reviews [106, 274] providing nine results. Seven of nine results reported inverse associations, with increased aerobic physical activity being associated with lower adiposity at follow-up; four were statistically significant. Adiposity was marked by risk or odds of overweight and obesity and odds of 'excess weight gain'. See Table 84 in the Energy balance and body fatness literature review 2017. For references and results of the nine studies with fewer than 500 participants, please see Section 4 in the Energy balance and body fatness literature review 2017.

## MECHANISMS

Increasing levels of aerobic physical activity may promote *energy balance*, and thus decrease risk of weight gain over time through several key mechanisms:

- **Increased total energy expenditure:** *Physical activity* is a major contributor to total energy expenditure; as total energy expenditure increases, this can promote energy balance (assuming energy expenditure is equalled by energy intake through foods and drinks), or negative energy balance (assuming insufficient compensation by energy intake).
- **Sensitivity to appetite controls:** Higher levels of physical activity sensitise individuals to appetite signals, directly potentiating *satiety* signals via the gastrointestinal tract (reviewed in Blundell *et al.* (2012) [65] and MacLean *et al.* (2017) [66]). This promotes energy balance

at a higher level of total energy intake (and expenditure). In addition, habitually active people are able to better compensate for higher energy density diets [296].

- **Body composition and biological feedback:** Increased physical activity is also associated with shifts in body composition, favouring lean mass over fat mass [297]; increased lean mass relative to fat mass alters *resting metabolic rate*, energy demand and drive to eat [66]; also see **Section 3** on fundamental concepts.

- **Lipid metabolism and insulin sensitivity:** Endurance aerobic activity, such as long distance running, promotes fat oxidation, which may explain the favourable effects of such activities on changes to body fat (for a summary, see Hespanhol *et al.* (2015) [266]). In addition, increased physical activity has beneficial effects for *insulin* sensitivity [298].

### CUP PANEL'S CONCLUSION

Overall the evidence that increased aerobic physical activity reduces the risk of adiposity is consistent both in adults and children. Results from meta-analyses of randomised controlled trials generally reported decreased risk of adiposity with interventions to increase aerobic physical activity, across a variety of *anthropometric measures*; of these, five results in adults and three results in children reported statistically significant results. This was supported by evidence from individual prospective cohort studies. There is robust evidence of biological plausibility.

**The CUP Panel concluded:**

- **Aerobic physical activity probably protects against weight gain, overweight and obesity.**

#### 7.9.1.1 Walking

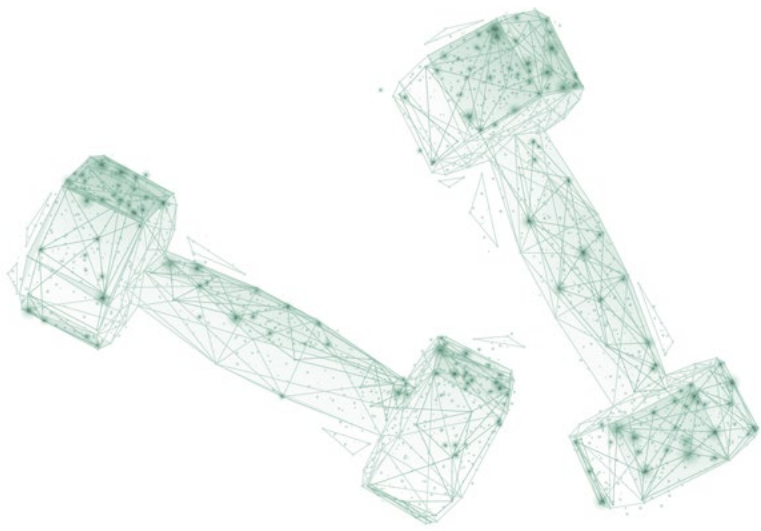
Walking is considered a type of *aerobic physical activity*. The evidence search for this *exposure* yielded published reviews of trials only, so no individual prospective *cohort studies* are presented here; please see Section 4 of the Energy balance and body fatness literature review 2017.

### ADULTS

#### Meta-analyses – randomised controlled trials

Four published reviews [275–278] conducted *meta-analyses* of *randomised controlled trials* investigating walking and *adiposity* in adults (**Table 22**). All 14 results reported protective effects, with lower adiposity reported for the intervention arms compared to the control arms; 12 results were *statistically significant*. This effect was observed across a variety of *anthropometric measures*. The *forest plot* for one meta-analysis [278] for *BMI* change is shown in **Figure 12**. The interventions across all studies included ranged from 20 to 65 minutes per session, taking place two to seven times per week, for 8 to 52 weeks. See also Table 88 in the Energy balance and body fatness literature review 2017.

There is some overlap of trials between the meta-analyses; the meta-analysis by Hanson and Jones (2015) [278] contains the most unique trials, with none overlapping. For details, please see Table 81 in the Energy balance and body fatness literature review 2017.



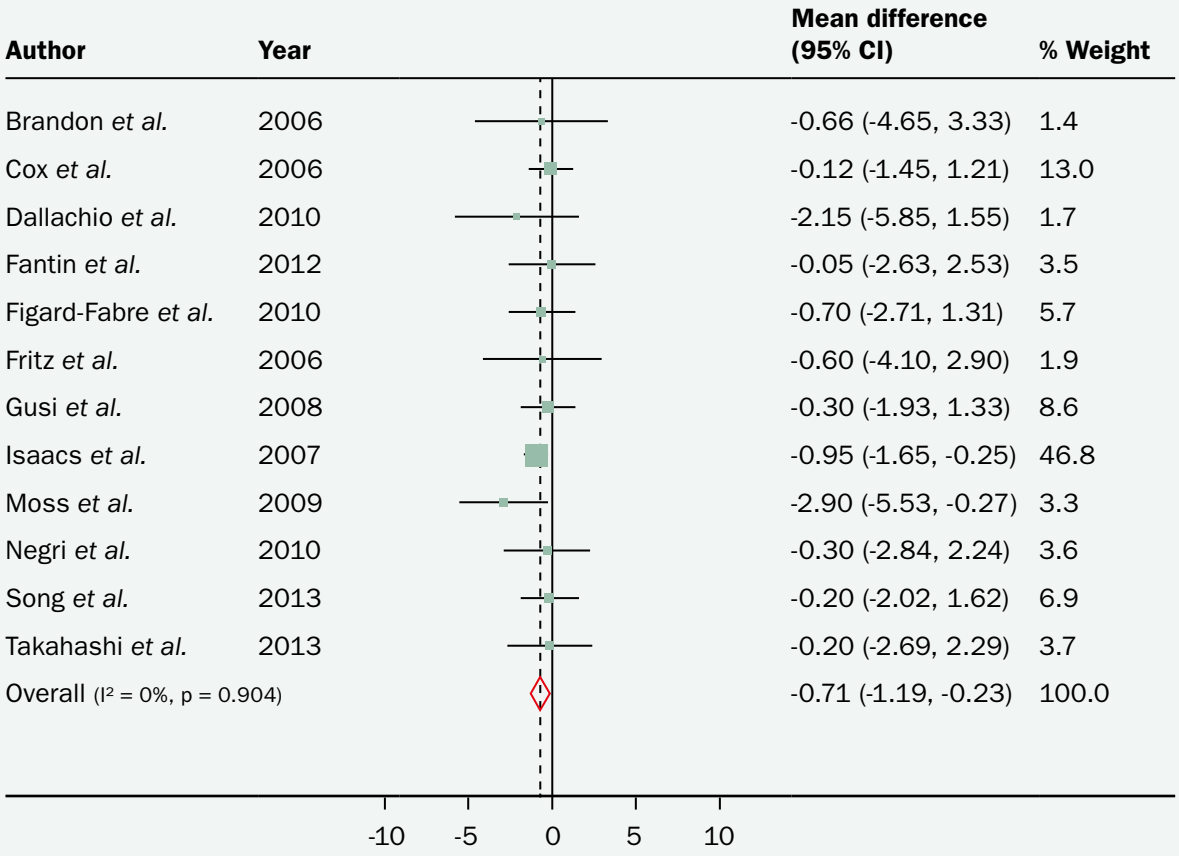
## Table 22: Summary of meta-analyses of randomised controlled trials from published reviews investigating walking and adiposity in adults

| Published review | Outcome | Increment/contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Murphy *et al.* (2007) [275]** | Weight* | Walking intervention vs habitual lifestyle | **WMD** -0.95 SD ±0.61 kg, p < 0.001 | NR | 18 | 738 |
| **Gao *et al.* (2016) [276]** | Weight change | Walking intervention vs habitual lifestyle | **WMD** -1.14 (-1.86, -0.42) kg | 20 | 8 | 853 *women only* |
| **Murtagh *et al.* (2015) [277]** | | Walking intervention vs habitual lifestyle | **WMD** -1.37 (-1.75, -1.00) kg | 66 | 25 | 1,275 |
| **Murphy *et al.* (2007) [275]** | BMI* | Walking intervention vs habitual lifestyle | **WMD** -0.28 SD ±0.20 kg/m$^2$ p = 0.015 | NR | 16 | 836 |
| **Gao *et al.* (2016) [276]** | BMI change | Walking intervention vs habitual lifestyle | **WMD** -0.33 (-0.62, -0.04) kg/m$^2$ | 11 | 6 | 701 *women only* |
| **Hanson and Jones (2015) [278]** | | Walking intervention vs habitual lifestyle | **MD** -0.71 (-1.19, -0.23) kg/m$^2$ | 0 | 12 | 451 |
| **Murtagh *et al.* (2015) [277]** | | Walking intervention vs habitual lifestyle | **MD** -0.53 (-0.72, -0.35) kg/m$^2$ | 70 | 23 | 1,201 |
| **Murphy *et al.* (2007) [275]** | Percentage body fat* | Walking intervention vs habitual lifestyle | **WMD** -0.63 SD ±0.66%, p = 0.035 | NR | 12 | 604 |
| **Gao *et al.* (2016) [276]** | Percentage body fat change | Walking intervention vs habitual lifestyle | **WMD** -2.36 (-3.21, -1.52) % | 0 | 3 | 444 *women only* |
| **Hanson and Jones (2015) [278]** | | Walking intervention vs habitual lifestyle | **MD** -1.31 (-2.10, -0.52) % | 0 | 7 | 328 |
| **Murtagh *et al.* (2015) [277]** | | Walking intervention vs habitual lifestyle | **WMD** -1.22 (-1.70, -0.73) % | 68 | 14 | 719 |
| **Hanson and Jones (2015) [278]** | Waist circumference | Walking intervention vs habitual lifestyle | **MD** -3.55 (-8.08, 0.98) cm | 0 | 2 | 35 |
| | | Walking intervention vs habitual lifestyle | **WMD** -1.51 (-2.34, -0.68) cm | 38 | 11 | 574 |
| **Murtagh *et al.* (2015) [277]** | Waist-hip ratio | Walking intervention vs habitual lifestyle | **WMD** -0.01 (-0.02, 0.00) | 60 | 14 | 706 |

*Unclear if result is difference in change between groups or difference in attained measure between groups.

**Abbreviations used:** cm = centimetres; kg = kilogram; MD = mean difference; NR = not reported; WMD = weighted mean difference.

## Figure 12: Meta-analysis [278] of randomised trials of BMI change and walking



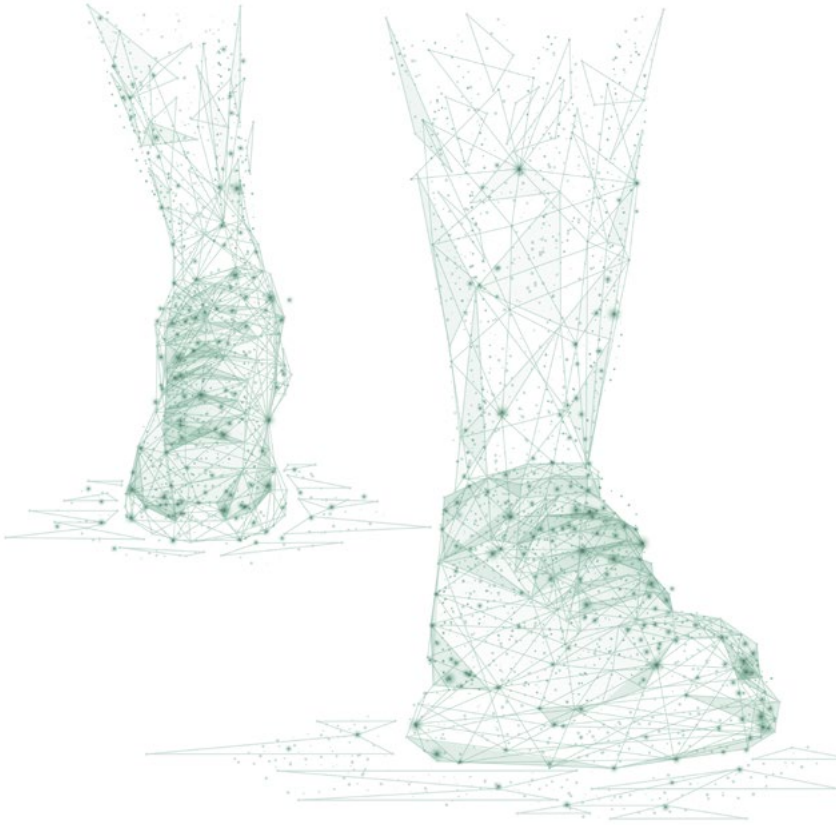

*For references to studies included in the meta-analysis, please consult the published review [278].*

### MECHANISMS

See **Section 7.9.1** on aerobic physical activity.

### CUP PANEL'S CONCLUSION

The evidence was consistent in direction of effect. All meta-analyses of randomised controlled trials reported lower adiposity in participants in the intervention arms; the majority were statistically significant. This effect was observed across a range of anthropometric measures. There is robust evidence of biological plausibility.



### The CUP Panel concluded:

- **Walking protects convincingly against weight gain, overweight and obesity.**

## 7.10 Sedentary behaviours

*(Also see Energy balance and body fatness literature review 2017: Section 5.1)*

Four published reviews were identified: Van Uffelen *et al.* (2010a) [299], Summerbell *et al.* (2009) [106], USDA DGAC (2015) [102], and Azevedo *et al.* (2016) [300].

Three reviews [102, 106, 300] were assessed as high quality, and one review [299] was assessed as moderate quality (for the quality assessment process, please see the protocol in the Energy balance and body fatness literature review 2017).

### Box 10: Defining sedentary behaviours

**Sedentary behaviours involve both a high level of inactivity and a low level of activity; they include viewing television, sitting at a desk, driving vehicles and reading. The outcome of a recent consensus project defined sedentary behaviour as any waking behaviour characterised by an energy expenditure less than or equal to 1.5 metabolic equivalents (METs), while in a sitting, reclining or lying posture [301, 302].**

**Studies tend to measure physical inactivity, which is only one component of sedentary behaviours. For example, someone may be inactive for considerable periods of time but may also engage in regular moderate or vigorous physical activity and thus is not sedentary.**

**Screen time is a specific type of sedentary behaviour that has other behaviours associated with it (see Box 11).**

### ADULTS

#### Studies not included in meta-analyses – prospective cohort studies

Ten prospective *cohort studies* [218, 289, 303–310] investigating sedentary behaviours in adults were identified through three published reviews [102, 106, 299] providing 20 results. Twelve out of the 20 results reported positive (adverse) relationships, with increased time spent sedentary associated with higher *adiposity* at follow-up; four were *statistically significant* (**Table 23**). Adiposity was marked by weight change, percentage weight change, attained *BMI*, BMI change, odds of weight gain and risk of obesity. See Table 92 in the Energy balance and body fatness literature review 2017.

The measurement of the *exposure* varied between studies but broadly included time spent sitting at work, at home or in a motor vehicle. Data from all studies on time spent sedentary were self reported by participants. The majority of studies used multivariate adjusted models. For references and results of the four studies with fewer than 1,000 participants, please see Section 5.1 in the Energy balance and body fatness literature review 2017.

## Table 23: Summary of prospective cohort studies with more than 1,000 participants from published reviews investigating sedentary behaviours and adiposity in adults

| Study [publication] | Outcome | Increment/contrast | Results | No. participants Follow-up |
|---|---|---|---|---|
| **Australian Longitudinal Study on Women's Health [218, 303, 304]** | Weight change | Hours per weekday spent sitting down at baseline | Beta coefficient<br>0.030 (-0.051, 0.112)<br>Units of weight unclear | W: 5,562<br>6 years<br>[303] |
| | Percentage weight change | Hours per day spent sitting down over 3 years (2001–2004) | Beta coefficient<br>0.64 (-0.20, 1.48) % | W: 8,233<br>6 years<br>[304] |
| | | Hours per day spent sitting down over 3 years (2004–2007) | Beta coefficient<br>-0.51 (-1.35, 0.33) % | |
| | Odds of weight gain | > 52 hours per week sitting time vs < 33 hours | OR 0.80 (0.70, 0.91) | W: 8,726<br>4 years<br>[218] |
| **Copenhagen City Heart Study [305]** | BMI (attained) | Quartiles of leisure time physical activity at baseline relative to Q1 ('sedentary') | **Q2** 25.9 SD ±3.8, p > 0.05<br>**Q3** 26.0 SD ±3.9, p > 0.05<br>**Q4** 25.8 SD ±3.6, p > 0.05 | M: 6,506<br>15 years |
| | | | **Q2** 24.9 SD ±4.6, p > 0.05<br>**Q3** 24.9 SD ±4.5, p > 0.05<br>**Q4** 24.6 SD ±4.1, p > 0.05 | W: 7,708<br>15 years |
| | | Transition between quartiles of leisure time physical activity (Q1 = 'sedentary') across study period relative to no change | **Becoming more sedentary:**<br>27.0 kg/m² SD ±4.4, p > 0.05<br>**Becoming less sedentary:**<br>26.5 kg/m² SD ±3.7, p > 0.05 | M: 2,946<br>15 years |
| | | | **Becoming more sedentary:**<br>26.0 SD ±5.0, p > 0.05<br>**Becoming less sedentary:**<br>25.5 SD ±4.4, p > 0.05 | W: 4,124<br>15 years |
| **University of North Carolina Alumni Heart Study [306]** | BMI change | Categorised as sedentary at baseline and follow-up vs non-sedentary at baseline and follow-up | Beta coefficient<br>0.09 (0.05, 0.13) kg/m² | M&W: 2,070<br>8 years |
| | | Categorised as becoming non-sedentary across study period vs non-sedentary at baseline and follow-up | Beta coefficient<br>-0.04 (-0.08, 0.00) kg/m² per year | |
| | | Categorised as becoming sedentary across study period vs non-sedentary at baseline and follow-up | Beta coefficient<br>0.06 (0.03, 0.09) kg/m² per year | |
| **1958 British Birth Cohort [307]** | BMI change | Per hour per day increase in sitting at work | MD<br>-0.01 (-0.04, 0.02) kg/m² | M&W: 6,562<br>5 years |
| **Cancer Prevention Study II [289]** | Odds of weight gain | > 6 hours per day of non-occupational sedentary behaviour vs < 3 hours | OR 1.06 (0.87, 1.30) | W: 18,583<br>7 years |
| **NHS [308]** | Risk of obesity | Number of hours per week sitting at work or away from home vs 0–1 hours | **2–5 hours:**<br>RR 1.02 (0.89, 1.18)<br>**>40 hours:**<br>RR 1.25 (1.02, 1.54) | W: 50,277<br>6 years |
| | | Number of hours per week sitting at home vs 0–1 hours | **2–5 hours:**<br>RR 0.99 (0.83, 1.18)<br>**>40 hours:**<br>RR 1.11 (0.85, 1.45) | |

| Study [publication] | Outcome | Increment/contrast | Results | No. participants Follow-up |
|---|---|---|---|---|
| **The SUN Cohort [309]** | Risk of obesity | Annual distance travelled in motor vehicles > 20,000 km vs < 10,000 km | HR 1.00 (0.85, 1.17) | M&W: 6,808 6.4 years |
| **Whitehall II Cohort [310]** | Risk of obesity | > 40 hours sedentary time at work per week vs 0–6 hours | OR 1.10 (0.59, 1.96) | M&W: 10,308 6 years |
| | | > 17 hours non-TV leisure time per week vs 0–6 hours | OR 0.88 (0.40, 1.95) | |

**Abbreviations used:** HR = hazard ratio; M = men; OR = odds ratio; Q = quartile; RR = relative risk; SD = standard deviation; W = women.

## CHILDREN

### Meta-analyses – randomised controlled trials

One published review [300] conducted two *meta-analyses* of *randomised controlled trials* investigating interventions to reduce sedentary behaviours and adiposity in children (**Table 24**). Children in the intervention groups had significantly lower BMI z-scores and BMIs than those in the control groups at follow-up; also see **Figure 13**. Moderate to high *heterogeneity* was observed: $I^2$ = 50% for the BMI or BMI z-score meta-analysis and $I^2$ = 88% for the BMI meta-analysis.

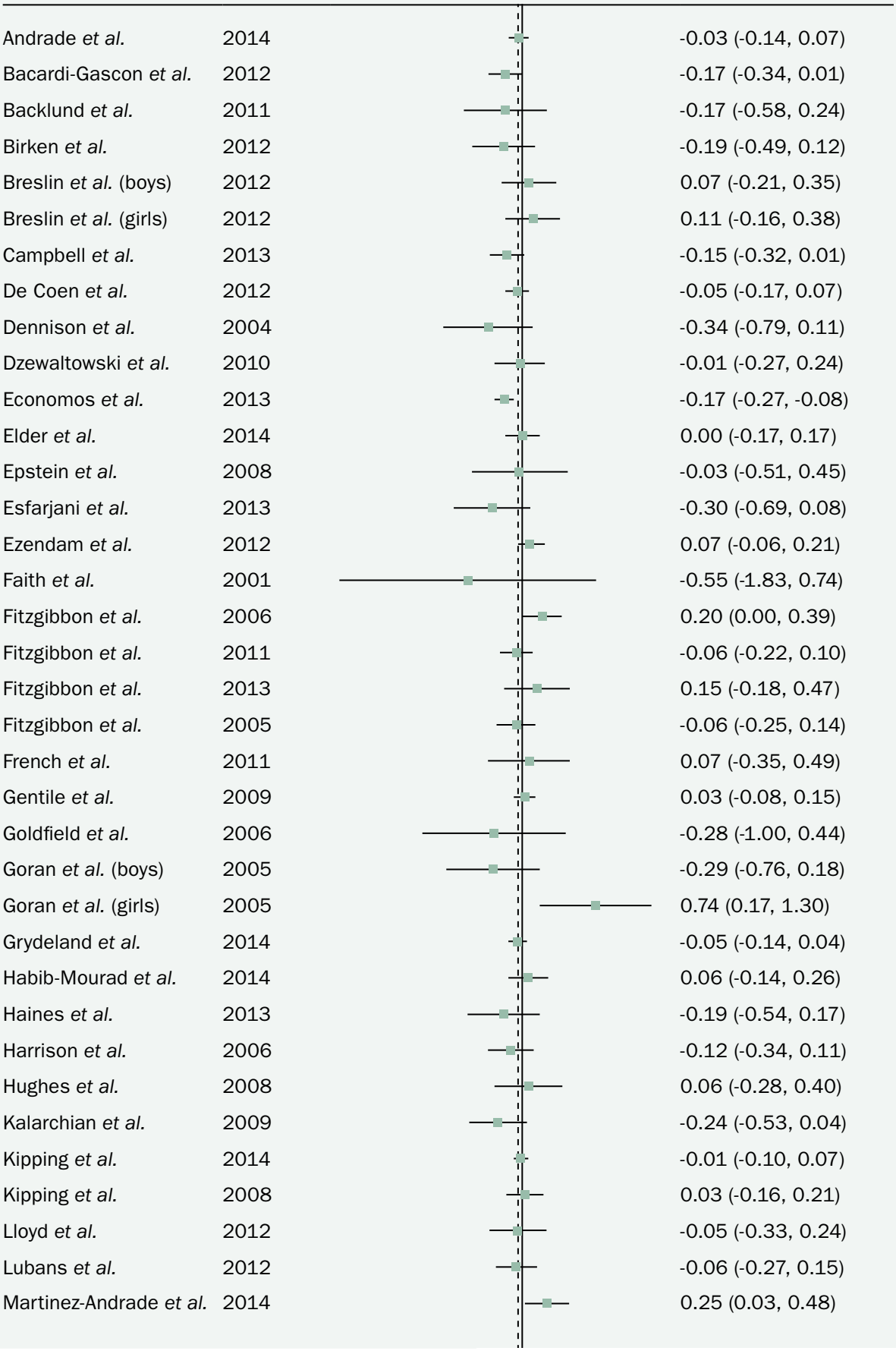
The majority of the included studies were conducted in children aged 5 to 12 years old and lasted less than 6 months. Eight of the 71 studies were in children who had overweight or obesity at baseline. Stratifying by age group, weight status of participants at baseline, intervention type, setting, duration, or risk of *bias* did not affect the direction of the overall effect but some results did lose significance. The authors noted that the corresponding funnel plot was asymmetric and results from *Egger's test* indicated there was *publication bias*.

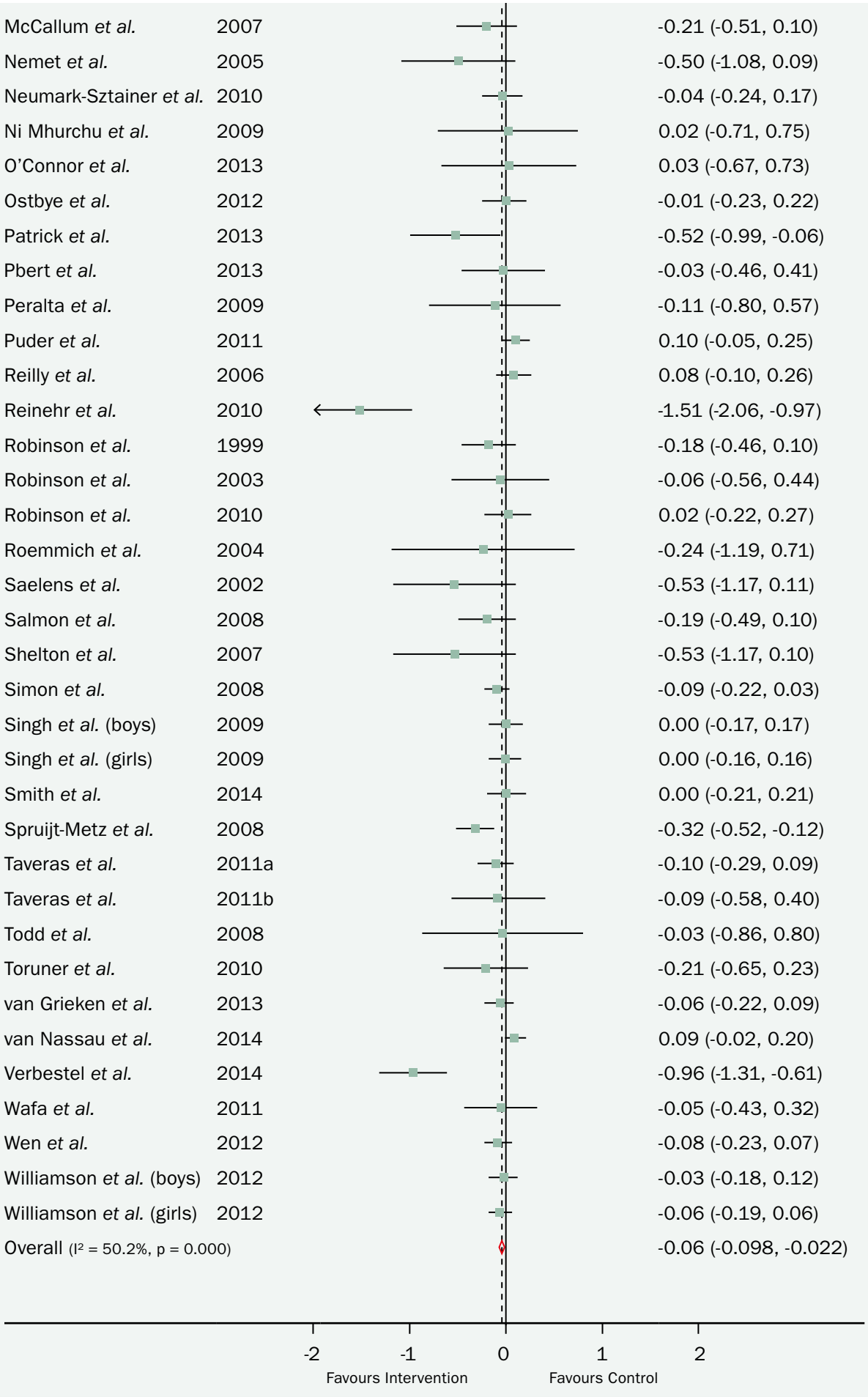
### Table 24: Summary of meta-analyses of randomised controlled trials from published reviews investigating sedentary behaviours and adiposity in children

| Published review | Outcome | Increment/ contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Azevedo *et al.* (2016) [300]** | BMI or BMI z-score change | Interventions to reduce sedentary behaviours vs no intervention | SMD -0.060 (-0.098, -0.022) | 50 | 71 | 29,650 |
| | BMI change | | MD -0.158 (-0.238, -0.077) kg/m$^2$ | 88 | 51 | 18,012 |

**Abbreviations used:** MD = mean difference; SMD = standardised mean difference.

**Figure 13: Meta-analysis [300] of randomised controlled trials of BMI or BMI z score change and reduced sedentary behaviours in children**






*For references to studies included in the meta-analysis, please consult the published review [300].*

### MECHANISMS

Greater time spent being sedentary may promote positive *energy balance*, and thus increase risk of weight gain over time:

- **Decreased total energy expenditure:** Physical activity is the main variable contributor to total energy expenditure. If physical activity is low (through increased sedentary time) then total energy expenditure will decrease; this can lead to positive (adverse) energy balance (assuming insufficient compensation by decreased energy intake).
- **Appetite dysregulation:** Physical inactivity (through increased time spent sedentary) impairs *satiety* sensitivity and appetite signals [65]. At low levels of energy expenditure (and when food and drink are freely available), adequate suppression of appetite to maintain energy balance may be compromised [66, 296] (also see **Section 3** on fundamental concepts).

### CUP PANEL'S CONCLUSION

The evidence was limited but generally consistent. Results from one meta-analysis in children reported a decreased risk of adiposity when sedentary behaviours were reduced through interventions. Results from prospective cohort studies in adults supported this relationship, with increased sedentary behaviours being associated with an increased risk of adiposity. The definition of the exposure varied between studies. There is evidence of biological plausibility.

**The CUP Panel concluded:**

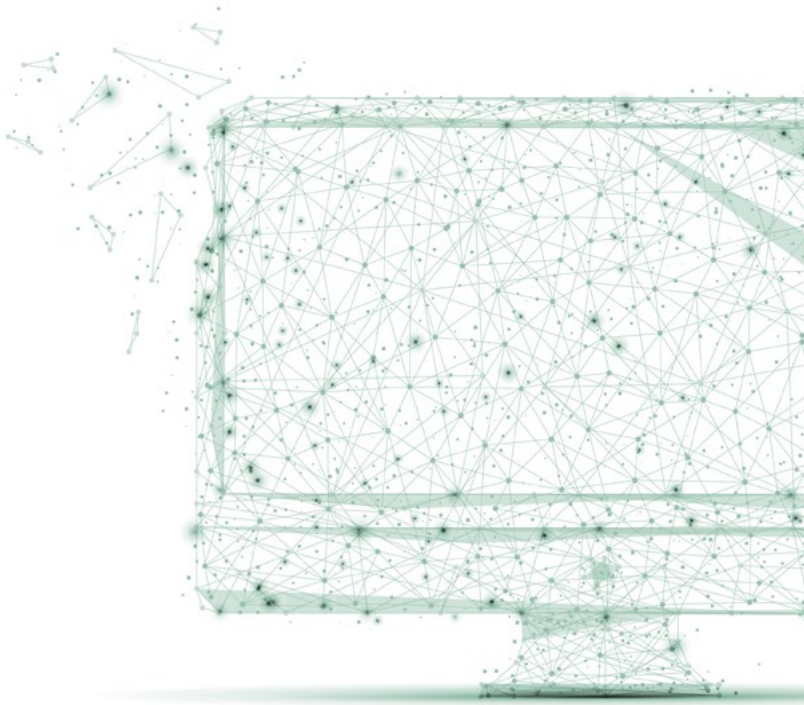
- **The evidence suggesting that sedentary behaviours increase the risk of weight gain, overweight and obesity is limited.**

## 7.11 Screen time

*(Also see Energy balance and body fatness literature review 2017: Section 5.2)*

Nine published reviews were identified: USDA DGAC (2015) [102], Summerbell *et al.* (2009) [106], Van Uffelen *et al.* (2010a) [299], Tremblay *et al.* (2011) [311], Wahi *et al.* (2011) [312], Marshall *et al.* (2004) [313], Costigan *et al.* (2013) [314], Le Blanc *et al.* (2012) [315] and USDA (2010) [121].

Seven published reviews [102, 106, 121, 311, 312, 314, 315] were assessed as high quality, and two published reviews [299, 313] were assessed as moderate quality (for the quality assessment process, please see the protocol in the Energy balance and body fatness literature review 2017).



## Box 11: Defining screen time

Time spent watching television or using other electronic devices, such as computers (including occupational screen time), tablets and mobile phones, is a discrete and measurable activity. Such activities can be recalled with relative precision, and it is straightforward to measure the number of hours someone spends, for example, watching television.

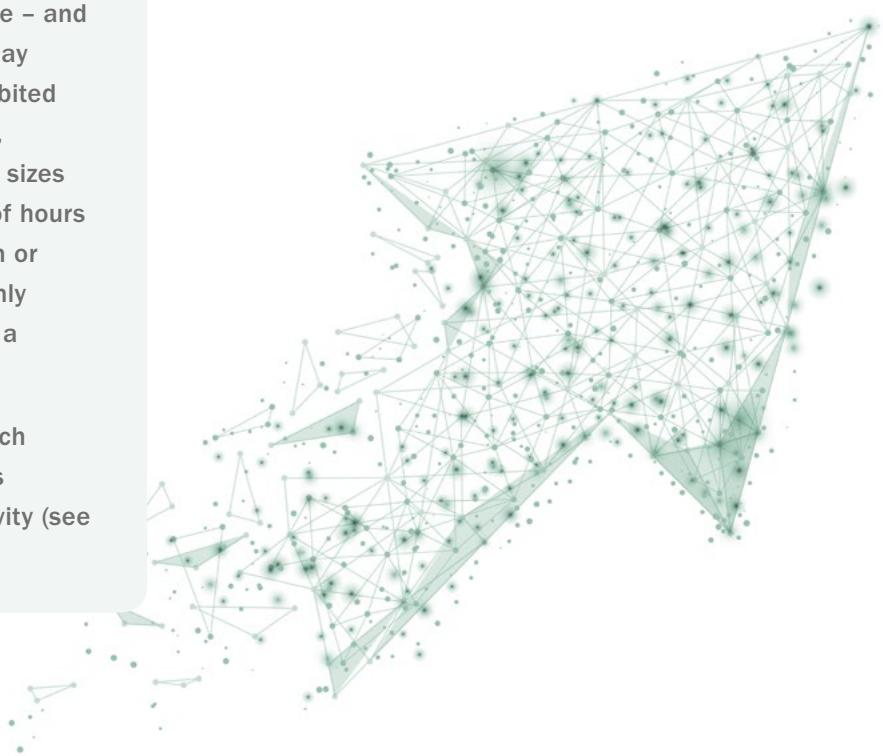
The adverse effects associated with increased screen time are unlikely to be caused simply by the act of viewing a screen. Screen time is a sedentary behaviour and the degree of physical inactivity while watching television or using a tablet appears to be profound compared with other sedentary activities, such as sitting and talking. Screen time may also displace opportunities for other more active pursuits [316, 317] and increases the likelihood of being exposed to promotion of foods that may promote weight gain, particularly to children and adolescents [318, 319]. Furthermore, screen time – and television watching in particular – may be accompanied by relatively uninhibited consumption of energy-dense foods, which may be eaten in large portion sizes [320–322]. Measuring the number of hours someone spends watching television or using other electronic devices not only captures physical inactivity but also a collection of related behaviours.

Please note, 'active' screen time, such as exercise led by on-screen cues, is considered here under physical activity (see **Section 7.9**).

## ADULTS

### Studies not included in meta-analyses – prospective cohort studies

Eight prospective *cohort studies* (eight publications [177, 307, 308, 310, 323–326]) investigating screen time in adults were identified through three published reviews [102, 106, 299] providing 15 results. Twelve out of the 15 results reported positive (adverse) associations, with increased screen time being associated with higher *adiposity* at follow-up; nine were *statistically significant* (**Table 25**). Adiposity was marked by weight change, *BMI* change, waist circumference and odds or risk of overweight or obesity. The majority of studies adjusted for multiple potential *confounders*. Also see Table 97 in the Energy balance and body fatness literature review 2017. For references and results of the two studies with fewer than 1,000 participants, please see Section 5.2 in the Energy balance and body fatness literature review 2017.



### Table 25: Summary of prospective cohort studies with more than 1,000 participants from published reviews investigating screen time and adiposity in adults

| Study [publication] | Outcome | Increment/contrast | Results | No. participants Follow-up |
|---|---|---|---|---|
| **NHS I, NHS II, HPFS (pooled) [177]** | Weight change | Per hour per day increase in TV viewing | Beta coefficient 0.31 (0.20, 0.42) lb | M&W: 120,877 20 years |
| **NHS [308]** | Risk of obesity | Number of hours per week watching TV vs 0–1 hours | **2–5 hours per week:** RR 1.22 (1.06, 1.42) **>40 hours per week:** RR 1.94 (1.51, 2.49) | W: 50,277 6 years |
| **National Weight Control Register [323]** | Weight change | Frequency of TV viewing at baseline | Beta coefficient 0.081 kg t = 2.532, p = 0.011 | M&W: 1,422 1 year |
| | | Increase in frequency of TV viewing from baseline | Beta coefficient 0.123 kg t = 3.885, p = 0.000 | |
| **1958 British Birth Cohort [307, 324]** | BMI change | Per hour per day increase in TV viewing | MD 0.06 (0.01, 0.12) kg/m$^2$ | M&W: 6,562 5 years [307] |
| | Waist circumference | Watching TV 3–4 times per week vs < 2 times at baseline | Beta coefficient 0.351 (-0.659, 1.361) cm | M&W: 5,972 21 years [324] |
| | | Watching TV > 5 times per week vs < 2 times at baseline | Beta coefficient 1.166 (0.325, 2.008) cm | |
| **AusDiab [325]** | Waist circumference | Per 10 hours per week of TV viewing at baseline | **M:** Beta coefficient -0.25 (-0.56, 0.06) cm **W:** Beta coefficient 0.04 (-0.31, 0.39) cm | M: 1,703 W: 2,143 5 years |
| | | Increase in TV viewing (hours per week) | **M:** Beta coefficient 0.43 (0.08, 0.78) cm **W:** Beta coefficient 0.68 (0.30, 1.05) cm | |
| **Atherosclerosis Risk in Communities (ARIC) [326]** | Odds of overweight or obesity | Level of TV exposure at baseline | **High:** OR 0.93 (0.83, 1.04) **Medium:** OR 1.03 (0.92, 1.15) | M&W: 12,678 6 years |
| **Whitehall II Cohort [310]** | Risk of obesity | > 19 hours TV viewing per week vs 0–6 hours | OR 0.97 (0.41, 2.29) | M&W: 1,071 6 years |

**Abbreviations used:** cm = centimetres; kg = kilograms; lb = pounds; M = men; MD = mean difference; OR = odds ratio; RR = relative risk; TV = television; W = women.

## CHILDREN

### Meta-analyses – randomised controlled trials

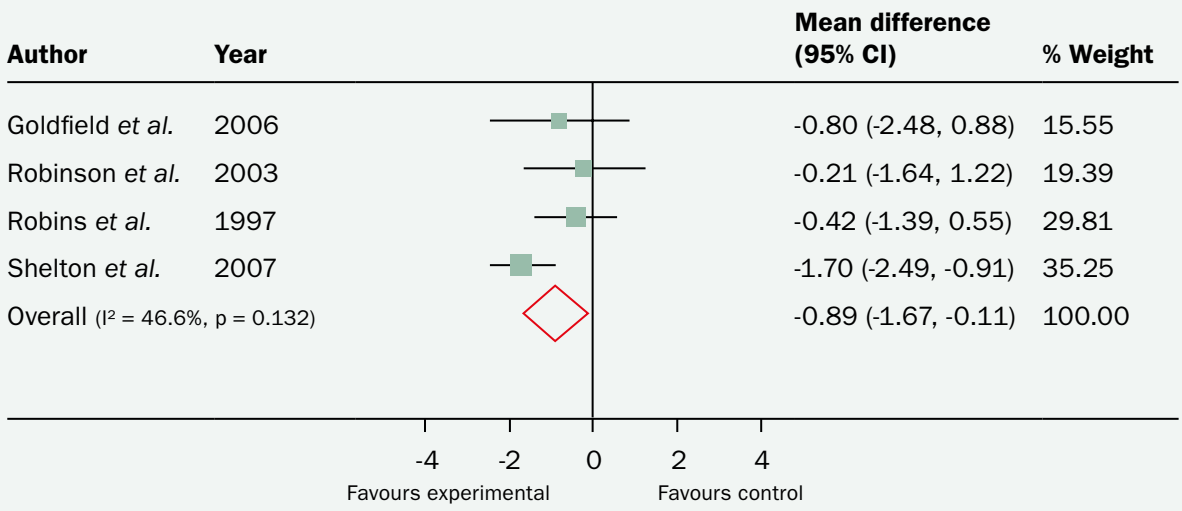
Two published reviews [311, 312] conducted *meta-analyses* of *randomised controlled trials* investigating interventions to decrease screen time and the effects on adiposity in children (**Table 26**). Both reported lower BMI values in the intervention arms than in the controls, with one [311] reaching statistical significance; see **Figure 14**. Mean age at baseline across both meta-analyses ranged from 4 to 11 years old, with the majority of interventions taking place within a school setting.

## Table 26: Summary of meta-analyses of randomised controlled trials from published reviews investigating screen time and BMI in children

| Published review | Outcome | Increment/contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Tremblay *et al.* (2011) [311]** | BMI change | Intervention to decrease screen time vs no intervention | **MD** -0.89 (-1.67, -0.11) kg/m$^2$ | 46 | 4 | 326 |
| **Wahi *et al.* (2011) [312]** | BMI change | Intervention to decrease screen time vs no intervention | **MD** -0.10 (-0.28, 0.09) kg/m$^2$ | 38 | 6 | 708 |

**Abbreviations used:** MD = mean difference.

## Figure 14: Meta-analysis [311] of randomised controlled trials of BMI change and reduced screen time in children




*Meta-analysis of randomised controlled studies examining decreases in sedentary behaviour and effect on body mass index [311].*

*For references to studies included in the meta-analysis, please consult the published review [311].*

### Meta-analyses – prospective cohort studies

One published review [313] conducted a meta-analysis of prospective cohort studies investigating screen time and adiposity in children (**Table 27**). The result reported a small but significant association between more time spent watching television and increases in combined measures of body fatness (including BMI and skinfold thickness). Two of the included studies are cross-sectional analyses reported 2 years apart.

### Table 27: Summary of meta-analyses of prospective cohort studies from published reviews investigating screen time and combined measures of adiposity in children

| Published review | Outcome | Increment/ contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Marshall *et al.* (2004) [313]** | Combined measures of body fatness | Increased time spent watching TV | $r_c$ 0.053 (0.030, 0.052) Units NR | NR | 6 | 15,797 |

**Abbreviations used:** NR = not reported; $r_c$ = fully corrected sample-weighted mean effect size.

#### Studies not included in meta-analyses – prospective cohort studies

Fifteen prospective cohort studies (18 publications [293, 295, 327–342]) investigating screen time and adiposity in children were identified through five published reviews [102, 106, 311, 314, 315] providing 41 results. Thirty-two out of the 41 results reported positive (adverse) relationships, with increased screen time being associated with higher adiposity at follow-up; 23 were statistically significant. Adiposity was marked by BMI z-score (change and attained), BMI percentile change, BMI acceleration, BMI (change and attained), odds of excess weight gain and overweight and/or obesity, probability of being overweight and incident obesity. See Table 96 in the Energy balance and body fatness literature review 2017. For references and results of the 4 randomised controlled trials and 18 prospective cohort studies with fewer than 1,000 participants, please see Section 5.2 in the Energy balance and body fatness literature review 2017.

### MECHANISMS

Increased time spent in front of a screen may promote positive *energy balance*, and thus increase risk of weight gain over time, by a number of mechanisms:

- **Decreased total energy expenditure:** *Physical activity* is the main variable contributor to total energy expenditure. If physical activity level is low (through increased sedentary time) then total energy expenditure will decrease; this can lead to positive energy balance (assuming insufficient compensation by energy intake).
- **Appetite dysregulation:** Physical inactivity (through increased time spent sedentary) impairs *satiety* sensitivity and appetite signals, leading to passive overconsumption [65] (see Section 7.10 on sedentary behaviours and Section 3 on fundamental concepts).
- **Exposure to marketing and promotions:** Time spent watching television or using other devices may increase exposure to marketing of foods and drinks that promote weight gain, leading to increased preference for, purchasing of and intake of such foods, at least in children and adolescents [318, 319].
- **Pattern of behaviours:** Time spent watching television or using other devices may be accompanied by relatively uninhibited consumption of energy-dense foods, for example, through distraction, which may be eaten in large portion sizes [320-322] and can occur in the absence of advertising or marketing [343].
- **Displacement:** Time spent watching television or using other devices displaces opportunities for more active pursuits [316, 317, 344].

### CUP PANEL'S CONCLUSION

***Adults.*** The evidence was generally consistent. No randomised controlled trials were identified. Results of prospective cohort studies consistently reported an increased risk of adiposity with increased screen time; this relationship was observed across a variety of *anthropometric measures* of body fatness. Most studies adjusted for potentially confounding variables. There is robust evidence of biological plausibility operating in humans.

**The CUP Panel concluded:**

- **Greater screen time is probably a cause of weight gain, overweight and obesity in adults.**

***Children.*** The evidence was strong and consistent. Two meta-analyses of randomised controlled trials reported decreased risk of adiposity with interventions to decrease screen time, of which one was statistically significant. This was supported by evidence from a statistically significant meta-analysis of prospective cohort studies and multiple individual prospective cohort studies. This relationship was observed across a range of body fatness outcomes. There is robust evidence of biologically plausible mechanisms operating in humans.

**The CUP Panel concluded:**

- **Greater screen time is a convincing cause of excess weight gain, overweight and obesity in children.**

## 7.12 Having been breastfed

*(Also see Energy balance and body fatness literature review 2017: Section 1.3)*

Twelve published reviews were identified: Victora *et al.* (2016)[1] [345], Beyerlein and von Kries (2011)[2] [346], Giugliani *et al.* (2015) [347], Owen *et al.* (2005a) [348], Horta *et al.* (2015) [349], Yan *et al.* (2014) [350], Weng *et al.* (2012) [351], Arenz *et al.* (2004) [352], Owen *et al.* (2005b) [353], Harder *et al.* (2005) [354], Ryan (2007) [355] and Pearce *et al.* (2013) [356].

Seven published reviews [347, 349–353, 356] were assessed as high quality, two published reviews [348, 354] were assessed as moderate quality and one published review [355] was assessed as low quality. Two 'reviews of reviews' were identified: one was assessed as high quality [345], and one was assessed as low quality [346]. (For the quality assessment process, please see the protocol in the Energy balance and body fatness literature review 2017.)

The time at which the outcome was measured varied between the studies included in the *meta-analyses*. The majority of studies followed up participants into infancy or childhood with a few following up into adulthood. Body fatness tends to track into adult life, with the majority of children with obesity becoming adults with obesity [357].

[1] This published review is a 'review of reviews' in itself. Two published reviews were identified: Giugliani *et al.* (2015) [347] and Horta *et al.* (2015) [349].

[2] This published review is a 'review of reviews' in itself. Four published reviews were identified: Harder *et al.* (2005), [354], Arenz *et al.* (2004) [352], Owen *et al.* (2005a) [348] and Owen *et al.* (2005b) [353].

### Meta-analyses – randomised controlled trials

One published review [347] conducted two meta-analyses of *randomised controlled trials* investigating the relationship between interventions to increase breastfeeding duration and *adiposity* in infants. A non-significant effect was reported for weight z-score and a borderline significant protective effect was reported for *BMI* or weight-for-height z-score; see **Table 28** and **Figure 15**.

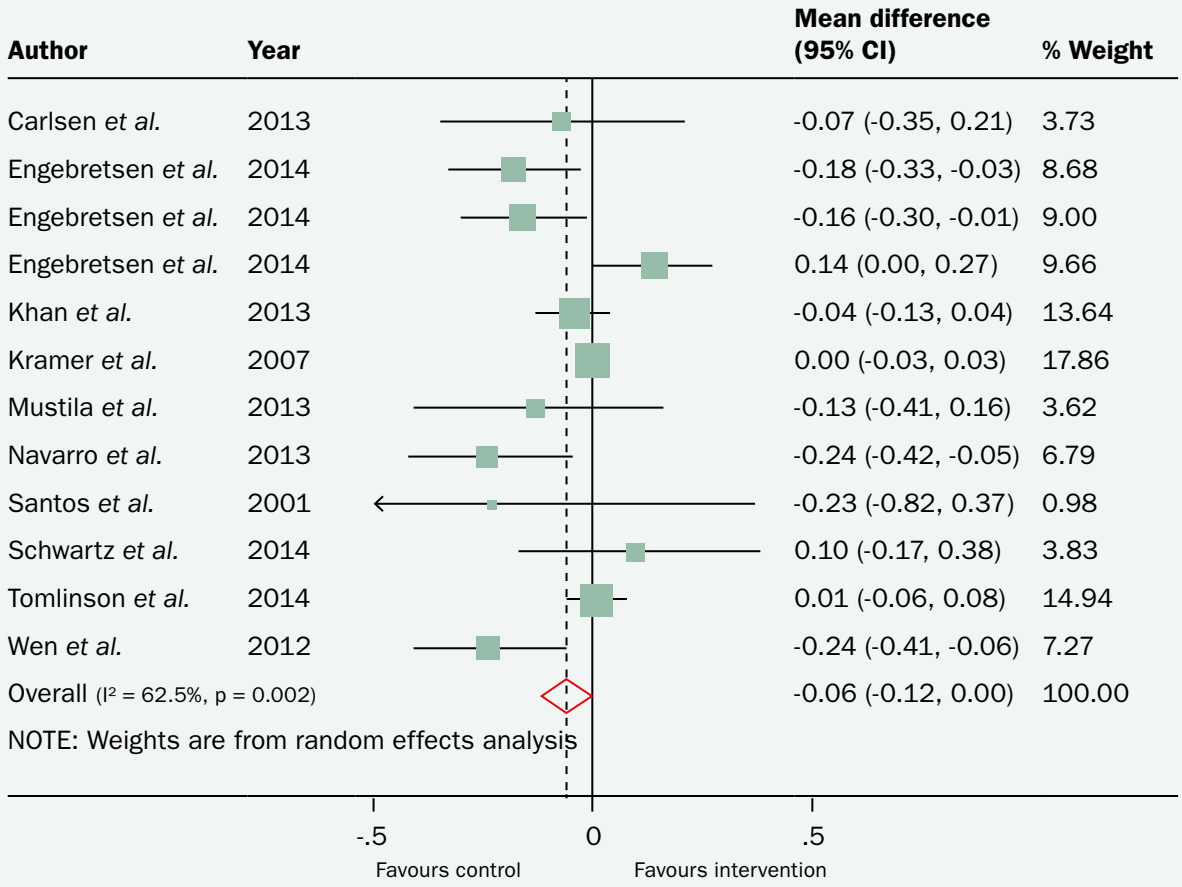
Increased breastfeeding duration was promoted through a variety of interventions, including lactation counselling, health education and group sessions. The level of *compliance* with interventions for each study was unclear; low compliance may attenuate the true effect. The two meta-analyses encompassed studies from 11 countries: Australia, Bangladesh, Belarus, Brazil, Burkina Faso, Denmark, Dominican Republic, Finland, India, South Africa and Uganda.

### Table 28: Summary of meta-analyses of randomised controlled trials from published reviews investigating having been breastfed and adiposity

| Published review | Outcome | Increment/contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Giugliani *et al.* (2015) [347]** | Weight z-score | Increased BF duration (varied interventions) vs usual care/no intervention | **SMD** 0.03 (-0.06, 0.12) | 78 | 16 | 14,736 |
| | BMI or weight-for-height z-score | Increased BF duration (varied interventions) vs usual care/no intervention | **SMD** -0.06 (-0.12, 0.00) | 61 | 12 | 29,063 |

**Abbreviations used:** BF = breastfeeding; SMD = standardised mean difference.

**Figure 15: Meta-analysis [347] of randomised controlled trials of BMI or weight-for-height z-score and breastfeeding in infants**




*Standardised mean differences in BMI or weight/length or height in different studies, comparing intervention versus control groups [347]. Please note the Engebretsen* et al. *(2014) trial was conducted in three countries (Burkina Faso, Uganda and South Africa) and so provided three estimates.*

*For references to studies included in the meta-analysis, please consult the published review [347].*

### Meta-analyses – prospective cohort studies

Seven published reviews [348–354] conducted eight meta-analyses of prospective *cohort studies* investigating duration of having been breastfed and adiposity, measured over various durations. All eight meta-analyses reported significant protective relationships, with having been breastfed being associated with lower BMI or odds of overweight or obesity at follow-up; see **Table 29**. There was considerable overlap of included studies; see Table 12 in the Energy balance and body fatness literature review 2017. The meta-analysis conducted by Horta *et al.* (2015) [349] had the largest number of unique studies at 42.

The definitions of infant feeding categories, for both breastfeeding and the comparator feeding group, varied between the studies. Associations were generally stronger among studies which reported on exclusively breastfed infants, rather than 'ever' versus 'never' breastfed infants. Follow-up length of the individual studies ranged from less than 1 year up to 70 years; see Table 14 in the Energy balance and body fatness literature review 2017. Typically, associations were stronger when follow-up occurred in infancy or childhood than in adulthood.

### Table 29: Summary of meta-analyses of prospective cohort studies from published reviews investigating having been breastfed and adiposity

| Published review | Outcome | Increment/ contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Owen *et al.* (2005a) [348]** | BMI | BF vs formula fed (varied definitions) | **MD** -0.04 (-0.05, -0.02) kg/m² | NR | 36 | 355,301 |
| **Horta *et al.* (2015) [349]** | Odds of overweight or obesity | BF vs not-BF (varied definitions) | **OR** 0.79 (0.73, 0.85) | 12 | 54 | NR |
| **Yan *et al.* (2014) [350]** | | BF vs not-BF (varied definitions) | **OR** 0.78 (0.73, 0.82) | NR | 15 | 141,247 |
| **Weng *et al.* (2012) [351]** | | Ever BF vs never BF (varied definitions) | **OR** 0.85 (0.74, 0.99) | 73 | 10 | NR |
| **Arenz *et al.* (2004) [352]** | | BF vs not-BF (varied definitions) | **OR** 0.73 (0.64, 0.85) | NR | 2 | 4,389 |
| **Owen *et al.* (2005b) [353]** | | BF vs formula fed | **OR** 0.87 (0.85, 0.89) | NR* | 29 | 298,900 |
| **Harder *et al.* (2005) [354]** | | Total duration of BF (up to 12 months) | **Regression coefficient** 0.94 (0.89, 0.98) | NR | 17 | 121,072 |
| | | Per month of BF | **OR** 0.96 (0.94, 0.98) | NR | 11 | 74,102 |

*$I^2$ value not reported; test for heterogeneity $\chi^2_{28} = 111$, $p < 0.001$.

**Abbreviations used:** BF = breastfed or breastfeeding; MD = mean difference; NR = not reported; OR = odds ratio.

Four published reviews [348, 350, 353, 354] did not stratify results by study design and their meta-analysis results included case control, cross-sectional and historical cohort studies. The majority of studies included in each meta-analysis were prospective cohort studies.

#### Studies not included in meta-analyses – randomised controlled trials

One randomised controlled trial [358] conducted in Guinea Bissau investigating the promotion of exclusive breastfeeding was identified through one published review [347]. Both results, for weight and weight-for-age z-score, reported protective effects, with interventions to promote exclusive breastfeeding being associated with lower adiposity after 151 to 180 days, relative to usual care. See Table 15 in the Energy balance and body fatness literature review 2017. For references and results of the nine trials with fewer than 1,000 participants, please see Section 1.3 in the Energy balance and body fatness literature review 2017.

#### Studies not included in meta-analyses – prospective cohort studies

Four prospective cohort studies [359–362] investigating having been breastfed were identified through two published reviews [353, 355] providing five results. All five results reported protective associations, where having been breastfed was associated with lower adiposity at follow-up, of which three were statistically significant. Adiposity was marked by weight-for-age z-score, percentage overweight, odds of 'elevated weight gain' and odds of overweight or obesity. Follow-up ranged from 2 to 21 years. See Table 16 in the Energy balance and body fatness literature review 2017. For references and results of the 13 studies with fewer than 1,000 participants, please see Section 1.3 in the Energy balance and body fatness literature review 2017.

## MECHANISMS

Having been breastfed may promote *energy balance*, and thus decreased risk of excess weight gain over time, by a number of mechanisms (for summaries, see Mameli *et al.* (2016) [363], Bartok and Ventura (2009) [364] and Victora *et al.* (2016) [345]).

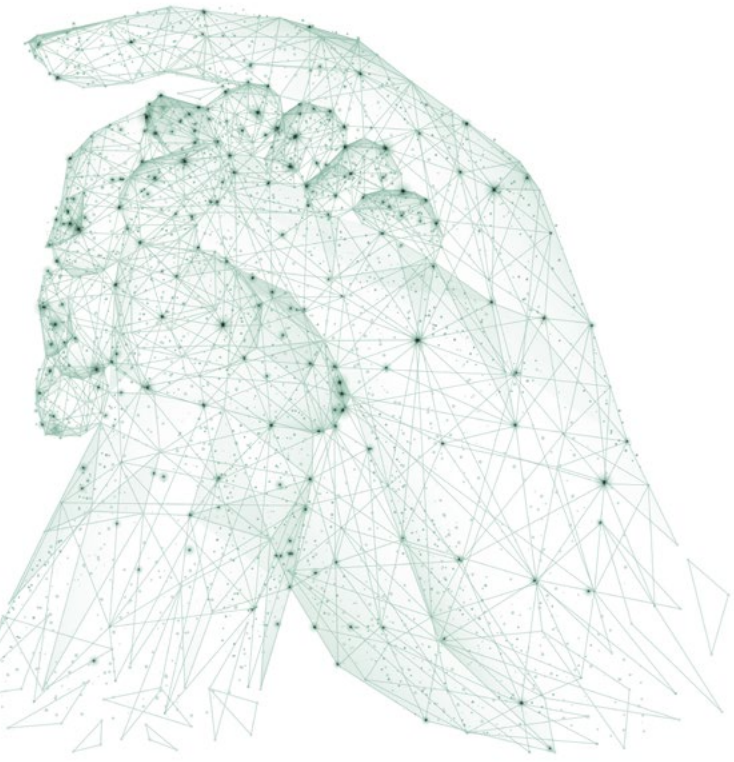
- **Breast milk composition**
  - **Energy [363]:** Formula feeding is typically associated with higher energy density and higher volumes of milk consumed, leading to 15 to 23 per cent higher total energy intake in 3- to 18-month-old infants. For formula-fed infants, a higher energy intake endures during the weaning period.
  - **Protein [363, 364]:** Compared with breast milk, formula milks typically have a higher protein content. According to the 'early protein hypothesis', higher protein intakes during infancy can influence the infant's growth pattern and increase the risk of later obesity development.
  - **Fats [363, 364]:** Relative to formula milks, breast milk has a higher fat content, particularly long chain polyunsaturated fatty acids. This composition is associated with lower levels of skeletal muscle glucose in breastfed infants. In addition, the ratio between omega 6 and omega 3 fatty acids found in formula milks may stimulate fat cell growth and differentiation and may promote *inflammation*.
  - **Other bioactive components [345, 364]:** Breast milk contains many *bioactive components*, such as immunoglobulins, enzymes, *hormones*, *cytokines*, growth factors and gut-brain peptides, which may modulate the infant's metabolism. Breast milk may also mitigate the usual adverse effect of peroxisome proliferator-activated receptor-gamma *polymorphisms* on adiposity and metabolism by containing peroxisome proliferator-activated receptor-modulating constituents such as long-chain polyunsaturated fatty acids and prostaglandin-J.
  - **Modulation of the infant gut microbiome [345]:** After delivery mode (vaginal versus caesarean), feeding mode (breast versus formula) is the major determinant of initial microbiome colonisers in the infant. The differences in gut *microbiome* composition between breast- and formula-fed infants are maintained by specific *oligosaccharides* in breast milk acting as prebiotics, supporting the growth of specific bacteria species.
  - **Epigenetic programming [345]:** Fat globules in breast milk contain secreted micro-RNAs which may target infant gene expression; the micro-RNAs secreted are modulated by maternal diet.
- **Behavioural factors [364]:** Caregiver feeding behaviours may override infant self-regulation when formula feeding, leading to excess caloric intake. It is postulated that the trust breastfeeding mothers learn from early infant feeding experiences may translate into less controlling feeding practices in the infant's later life, ultimately leading to better self-regulation and lower adiposity.
- **Confounding factors [364]:** The association between breastfeeding and reduced risk of adiposity could be explained by confounding factors, such as maternal weight, education, *socioeconomic status* and age, indirectly influencing offspring weight gain independently of infant feeding practice. Controlling for these factors in cohort studies weakens, but does not eliminate, the association.

### CUP PANEL'S CONCLUSION

The evidence was generally consistent. Meta-analyses of randomised controlled trials reported mixed results: one non-significant positive (adverse) effect and one borderline significant protective effect. Meta-analyses of prospective cohort studies all reported significant protective associations. These results were supported by findings from individual studies not included in meta-analyses. The categorisation of breastfeeding as an *exposure* varied between studies. There is evidence of biological plausibility.

**The CUP Panel concluded:**

- **Having been breastfed probably protects against excess weight gain, overweight and obesity in children.**



## 7.13 Lactation

*(Also see Energy balance and body fatness literature review 2017: Section 1.2)*

Three published reviews were identified: Neville *et al.* (2014) [365], Ip *et al.* (2007) [366], and He *et al.* (2015) [367].

All three published reviews [365–367] were assessed as high quality (for the quality assessment process, please see the protocol in the Energy balance and body fatness literature review 2017).

Weight gain is a normal part of pregnancy and adequate weight gain is required for optimal pregnancy outcomes. Recommendations exist from the Institute of Medicine for healthy weight gain ranges based on pre-pregnancy *BMI* categories [368]. Higher weight gain during pregnancy is correlated with increased postpartum weight retention [369]; however, following delivery, many women report not returning to their pre-pregnancy weights. The factors contributing to this are complex.

### Meta-analyses – randomised controlled trials

One published review [367] conducted a *meta-analysis* of *randomised controlled trials* investigating exclusive breastfeeding or mixed feeding compared with formula feeding and postpartum weight retention in mothers (**Table 30**). Women who breastfed their infants retained less postpartum weight (lost more weight) than those who fed their infants formula (SMD 0.57 [95% CI 0.19, 0.94] kilograms).

### Meta-analyses – prospective cohort studies

The same published review [367] conducted a meta-analysis of prospective *cohort studies* and reported that women who breastfed their infants lost more weight than those who fed their infants formula (SMD 1.18 [95% CI 0.74, 1.62] kilograms; **Table 30**). The assessment of *exposure* varied between studies.

### Meta-analyses – combined randomised controlled trials and prospective cohort studies

When combining results from both randomised controlled trials and prospective *cohort studies*, the published review [367] stratified results by duration of breastfeeding (**Table 30**). There was no clear relationship between duration of breastfeeding and degree of postpartum weight retention in women. The associations were often confounded by other factors such as gestational weight gain, *physical activity* level and pre-pregnancy weight, and it is not possible to rule out residual confounding.

### Studies not included in meta-analyses – prospective cohort studies

Nine prospective cohort studies [370–378] investigating lactation in women were identified through two published reviews [365, 366] providing 12 results. Seven out of 12 results reported significant protective associations, with lactation being associated with lower *adiposity* at follow-up. Adiposity was marked by weight change and skinfold thickness, and follow-up ranged from 6 weeks to 15 years. The level of *adjustment* for *confounding factors* varied between studies, with three studies not adjusting for any [371, 374, 377, 378]. One published review [365] noted evidence of selection *bias*, with many of the studies being in higher *socioeconomic status* subgroups. See Table 10 in the Energy balance and body fatness literature review 2017. For references and results of the 26 studies with fewer than 500 participants, please see Section 1.2 in the Energy balance and body fatness literature review 2017.

### Table 30: Summary of meta-analyses from published reviews investigating lactation and adiposity in the mother

| Published review | Outcome | Increment/contrast | Result (95% CI) | $I^2$ (%) | No. studies | Participants |
|---|---|---|---|---|---|---|
| **Meta-analyses of randomised controlled trials** | | | | | | |
| **He *et al.* (2015) [367]** | Postpartum weight retention | Exclusive breastfeeding or mixed feeding vs formula feeding | **SMD** 0.57 (0.19, 0.94) kg | NR | 3 | NR |
| **Meta-analyses of prospective cohort studies** | | | | | | |
| **He *et al.* (2015) [367]** | Postpartum weight retention | Exclusive breastfeeding or mixed feeding vs formula feeding | **SMD** 1.18 (0.74, 1.62) kg | NR | 8 | NR |
| **Meta-analyses of combined randomised controlled trials and prospective cohort studies** | | | | | | |
| **He *et al.* (2015) [367]** | Postpartum weight retention | Breastfeeding duration 1 to ≤3 months | **SMD** -0.09 (-0.76, 0.58) kg | NR | 4 | NR |
| | | Breastfeeding duration 3–6 months | **SMD** 0.87 (0.57, 1.17) kg | NR | 11 | NR |
| | | Breastfeeding duration 6 to ≤ 9 months | **SMD** 0.21 (-0.42, 0.83) kg | NR | 3 | NR |
| | | Breastfeeding duration 9 to ≤ 12 months | **SMD** 0.37 (0.14, 0.61) kg | NR | 3 | NR |

**Abbreviations used:** kg = kilograms; NR = not reported; SMD = standardised mean difference.

### MECHANISMS

Lactation may promote *energy balance* and thus decrease risk of weight gain over time for the mother through several mechanisms. However, this relationship is complex and not fully understood:

- **Increased total energy expenditure:** Lactation adds an additional component to total energy expenditure; without compensatory increases in energy intake, this may promote energy balance and weight maintenance or negative energy balance and weight loss. Furthermore, during pregnancy, multiple metabolic changes occur in the mother, including visceral fat accumulation and increased *insulin resistance*, which are thought to be reversed more rapidly with lactation [379].
- **Confounding factors:** The association of lower postpartum weight retention may be explained by other correlates with breastfeeding; for example, mothers who choose to breastfeed are more likely to engage in other healthy behaviours [380].
- **Reverse causation:** *Reverse causation* is possible, as women who have overweight or obesity are less likely to initiate breastfeeding and tend to lactate for shorter durations than women who are not overweight [381, 382].

### CUP PANEL'S CONCLUSION

The evidence was generally limited. Results from meta-analyses of randomised controlled trials reported less postpartum weight retention in breastfeeding mothers than in non-breastfeeding or mixed-feeding mothers. A similar association was reported from a meta-analysis of prospective cohort studies. Mixed results were reported when randomised controlled trials and prospective cohort studies were meta-analysed together and stratified by duration of breastfeeding. Individual prospective cohort studies tended to report protective associations for longer-term outcomes but many were confounded by other variables. There is some evidence of biological plausibility.

**The CUP Panel concluded:**

- **The evidence that lactation decreases the risk of weight gain, overweight and obesity in the mother is limited.**

## 7.14 Other

Other *exposures* were evaluated including, but not limited to, dairy, alcohol, total protein, total carbohydrate, *glycaemic load*, artificially sweetened drinks and fruit juices. The effect of sleep was also part of the evidence review. However, data were either of too low quality or too inconsistent, or the number of studies too few, to allow conclusions to be reached. The list of exposures judged as 'Limited – no conclusion' is summarised in the **Matrix**.

# 8. Integration of the evidence

The CUP Panel has drawn conclusions about *exposures* which decrease the risk of weight gain, overweight and obesity and exposures which increase the risk, as outlined in **Section 7**. However, the Panel emphasises that none of the exposures can be regarded as absolutely 'singular' and each must be understood in the context of all the others, for several reasons.

Many exposures are correlated with each other. In part this is because exposures with similar effects often cluster together; for example, people who are physically active tend to have healthier lifestyles in other respects [5]. The correlation may be due to inherent properties of the food or drinks; for example, wholegrains are a source of *dietary fibre* and so a diet high in wholegrains will concomitantly be higher in dietary fibre. Equally, the correlation may be due to patterns of consumption; for example, meals of 'fast foods' are commonly accompanied by sugar sweetened drinks. When several exposures are correlated this may be observed as a dietary pattern, such as the 'Western type' diet (characterised by high intakes of free sugars, meat and dietary fat) or the *'Mediterranean type' dietary pattern*.

Many exposures physiologically interact with each other. For example, a short-term study in free-living men [383] showed that as the level of energy density of an ad libitum diet increased (low, medium and high; achieved through manipulation of percentage energy from fat), total energy intake significantly increased, leading to positive *energy balance*. When a *physical activity* component was introduced, the effect on energy balance was mitigated [384]. Sedentary individuals who were not consciously controlling their intake would need to have a very low energy density diet in order to maintain energy balance, whereas more active individuals tolerated a comparatively higher energy density diet while still maintaining energy balance [72].

There are also common, or complementary, biological mechanisms by which a set of exposures may influence energy balance (for an explanation of the contextual framework and energy balance, see **Section 3**). **Table 31** outlines the key mechanisms through which diet and physical activity influence the equilibrium between energy intake and energy expenditure – either promoting energy balance (and over time leading to weight maintenance and decreased risk of weight gain, overweight and obesity) or promoting positive energy balance (and over time leading to weight gain, overweight and obesity); also see **Appendix 2**. Common mechanisms may operate through shared properties of the foods or drinks, such as wholegrains, fruit and vegetables all being sources of dietary fibre, which can enhance *satiation* by increasing chewing, slowing gastric emptying and elevating stomach distension, and stimulating cholecystokinin [155–158]. The mechanisms of different exposures may also complement each other, such as increased physical activity sensitising an individual to *satiety* signals and foods containing dietary fibre promoting such satiety signals, ultimately promoting energy balance. This is also observed for exposures which promote positive energy balance. For example, increased time spent sedentary disrupts effective appetite signalling [65], increasing vulnerability to the effects of consuming sugar sweetened drinks, where normal feedback mechanisms to compensate for increased energy intake are not promoted [71].

## Table 31: Summary of common and complementary mechanisms of how exposures promote energy balance (weight maintenance) or positive energy balance (weight gain)

| Promotes energy balance (weight maintenance) | | |
|---|---|---|
| ***Aerobic physical activity (including walking)*** | ***Wholegrains; Foods containing dietary fibre; Fruit and vegetables*** | ***'Mediterranean type' dietary pattern*** |
| • Increases total energy expenditure<br>• Improves appetite sensitivity<br>• Favourable effects on lipid metabolism and insulin sensitivity | • Low energy density<br>• Promotes satiety and satiation<br>• Modifies digestion, absorption and metabolism favouring energy balance<br>• Low glycaemic index<br>• Micronutrients influence energy homeostasis | • Source of dietary fibre<br>• Favourable dietary fat composition<br>• Low glycaemic index<br>• Lower bioavailability of energy<br>• Dietary polyphenol content influencing energy homeostasis<br>• Associated with higher levels of physical activity |
| **Promotes positive energy balance (weight gain)** | | |
| ***Sedentary behaviours; Screen time*** | ***Sugar sweetened drinks; Refined grains; 'Fast foods'*** | ***'Western type' diet*** |
| • Decreases total energy expenditure<br>• Dysregulates appetite sensitivity<br>• Increases exposure to marketing and promotions<br>• Part of overall pattern of behaviours related to positive energy balance<br>• Displace more active pursuits | • High energy density<br>• Lack of compensation for high energy intake<br>• May modify fat deposition and fat tissue synthesis<br>• Alters hedonics associated with food and drink<br>• High glycaemic index<br>• Higher intake may displace other foods associated with energy balance<br>• Higher degree of processing<br>• Embodies a cluster of characteristics promoting positive energy balance<br>• Lack of control of preparation and service | • High energy density<br>• Unfavourable influences on appetite, for example desensitisation to appetite signals |

This table is a summary only; please see **Appendix 2: Mechanisms** for further details.

Individually, there are varying degrees of certainty about the strength of the evidence for each 'singular' exposure. This is captured through the application of the grading criteria to the evidence (see **Appendix 1**) and the CUP Panel's separate conclusions for each exposure (see the **Matrix**). However, the CUP Panel has greater confidence that any effects on energy balance can be ascribed to clusters of the individual exposures (including both strong and limited evidence conclusions), for the reasons described above. Increased aerobic physical activity alongside consumption of wholegrains, foods containing dietary fibre, and fruit and vegetables, and greater adherence to a 'Mediterranean type' dietary pattern is more likely to decrease the risk of weight gain, overweight and obesity than any given single exposure. Conversely, increased sedentary behaviours, including screen time, in combination with a 'Western type' diet and consumption of sugar sweetened drinks, 'fast foods' and refined grains is more likely to increase the risk of weight gain, overweight and obesity than any exposure in isolation. This moves away from a 'reductionist' approach to diet, nutrition and physical activity and towards a more synthetic, integrated picture of the relationships. This concept, as applied to the evidence available in this report, is depicted in **Figure 16**.

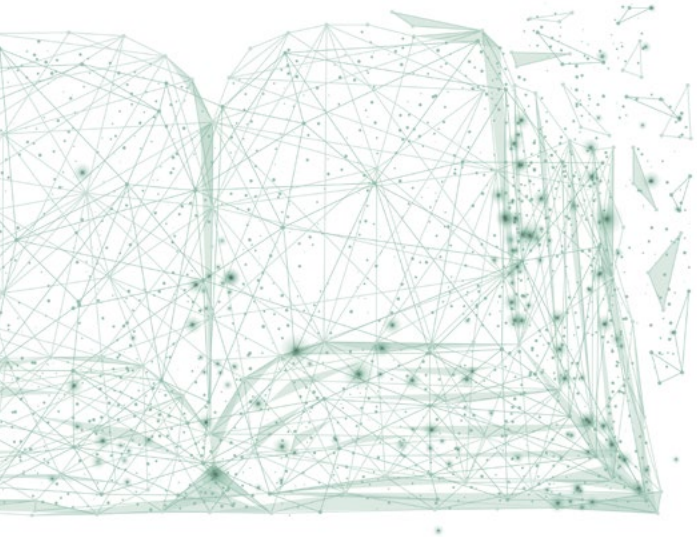
## Figure 16: Diet and physical activity factors and their influence on energy balance and body weight


The combination of food and drink consumed and activity (or inactivity) undertaken by an individual can promote energy balance and weight maintenance, or positive energy balance and weight gain. This influence on energy balance is mediated by a collection of physiological mechanisms acting directly or indirectly on appetite regulation. The mechanisms often act synergistically (see **Table 31** and **Appendix 2**). Furthermore, the outcome of body composition (weight maintenance or weight gain) operates a positive feedback loop within the energy balance system, further promoting weight maintenance or weight gain (see also **Section 3** and **Figure 3**). The impact of a given combination of foods, drinks and activity via the physiological mechanisms is influenced by host variability, in terms of genetics, epigenetics and the gut microbiome. The decision to consume particular (combinations of) foods and drinks, or to (not) partake in activity, is influenced by economic, social and environmental factors operating at global, national, regional and local levels. At a personal level these factors are experienced as the availability, affordability, awareness and acceptability of healthy diets and physical activity, relative to unhealthy diets and physical inactivity (see **Box 12**).

Breastfeeding – lactating as a mother or having been breastfed as an infant – is frequently correlated with other health-promoting behaviours, particularly in *high-income countries* [380]. For this reason, having been breastfed and lactation can be considered as part of the overall pattern of exposures which promote energy balance.

Exposures which decrease or increase the risk of weight gain, overweight and obesity are also singularly and collectively influenced by upstream factors beyond people's personal control (see **Box 12**).

The overall pattern of exposures described above, judged to collectively decrease the risk of weight gain, overweight and obesity, is not a complete 'diet'. In this report, the evidence and judgements are restricted to a predefined list of exposures showing specific links to body weight. The pattern of exposures resulting from the process of collating, judging and integrating the evidence is lacking important components of a balanced diet, such as sources of protein. The CUP Panel's Cancer Prevention Recommendations, which includes guidance on dietary intake and physical activity, are described fully in Recommendations and public health and policy implications.



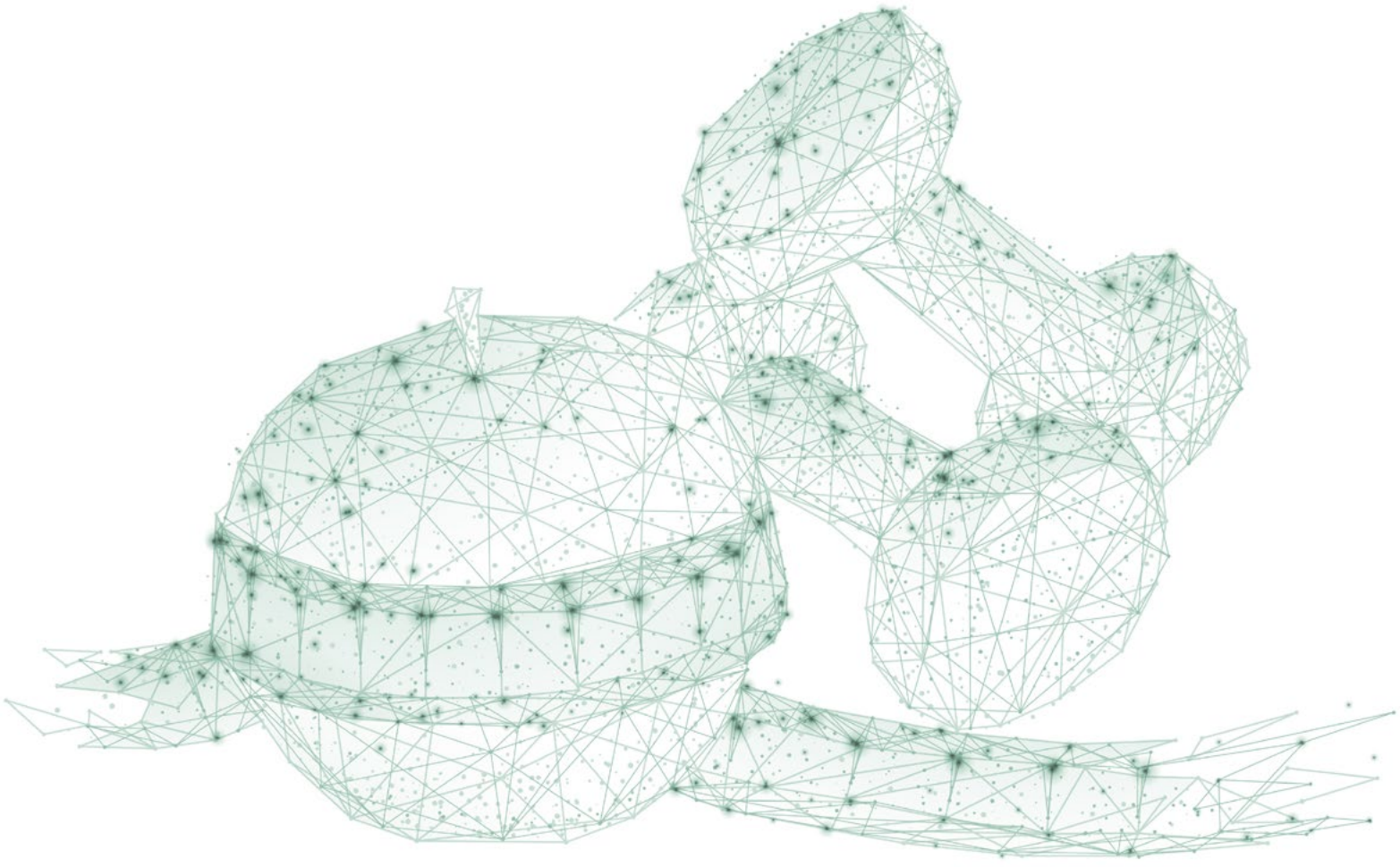
### Box 12: Integration of policy action

The maintenance of energy balance described in **Figure 16** exists within and interacts with a complex web of determinants [385]. Broadly these are economic, social and environmental factors that operate at global, national and local levels. At a personal level these are experienced as the availability, affordability, awareness and acceptability of healthy diets and physical activity, relative to unhealthy diets and physical inactivity (see also Figure 1.1 in WCRF/AICR 2009 Policy Report [386]).

In order to effect change, policy action is needed to tackle the many drivers of weight gain, overweight and obesity. Just as the exposures that increase or decrease the risk of weight gain should not be regarded as 'singular', no singular policy action is going to be effective in solving the obesity crisis. Instead, comprehensive action is needed that tackles the many drivers of long-term positive energy balance. By understanding the drivers of weight gain, it is possible to develop healthy public policy to create environments for individuals and communities that are conducive to following a healthy diet and being physically active, which promote maintaining energy balance. The role of government is therefore critical, working in conjunction with all sectors of society, to target the upstream factors and create health-enabling environments (see Section 4 in Recommendations and public health and policy implications). Multiple actions working together create synergy and lead to greater impact. For a full overview of public health and policy implications, see Recommendations and public health and policy implications.

# 9. Comparison to Second Expert Report

Overall the updated evidence presented here is consistent with the 2007 Second Expert Report; the conclusions drawn at both time points are comparable. Conclusions derived from both describe broadly similar dietary and lifestyle patterns conducive to weight maintenance (the exposures judged to decrease the risk of weight gain, overweight and obesity) or weight gain (the exposures judged to increase the risk of weight gain, overweight and obesity). Whereas in 2007 the Panel opted to group the *exposures* within the matrix to capture the energy density of the diet, in this update the Panel has chosen to include individual exposures with a discussion on the integration of the evidence in **Section 8** of this report.



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# Abbreviations

## General

Please note that full terms for specific abbreviations used in results tables are given at the bottom of each results table. General abbreviations used in the text are given below.

| | |
|---|---|
| **AICR** | American Institute for Cancer Research |
| **BMI** | Body mass index |
| **BMR** | Basal metabolic rate |
| **CI** | Confidence interval |
| **CUP** | Continuous Update Project |
| **GLP-1** | Glucagon-like peptide 1 |
| **MD** | Mean difference |
| **NCD(s)** | Non-communicable disease(s) |
| **PYY** | Peptide-tyrosine-tyrosine |
| **SLR** | Systematic literature review |
| **SMD** | Standardised mean difference |
| **WCRF** | World Cancer Research Fund |
| **WMD** | Weighted mean difference |

## Study and report name abbreviations

| | |
|---|---|
| **ALSPAC** | Avon Longitudinal Study of Parents and Children |
| **ARIC** | Atherosclerosis Risk in Communities |
| **AusDiab** | Australian Diabetes Obesity and Lifestyle |
| **CARDIA** | Coronary Artery Risk Development in Young Adults |
| **ECHO cohort** | Etiology of Childhood Obesity cohort |
| **EPIC** | European Prospective Investigation into Cancer and Nutrition |
| **EPIC-DiOGenes** | EPIC–Diet, Obesity and Genes |

| | |
|---|---|
| **EPIC-PANACEA** | EPIC–Physical Activity, Nutrition, Alcohol, Cessation of Smoking, and Eating out of Home in Relation to Anthropometry |
| **HEAPS** | Health, Eating and Play Study |
| **HPFS** | Health Professionals' Follow-up Study |
| **IDEA cohort** | Identifying Determinants of Eating and Activity cohort |
| **MONICA1** | Monitoring of Trends and Determinants in Cardiovascular Disease |
| **MRC NSHD** | Medical Research Council National Survey of Health and Development |
| **NHS** | Nurses' Health Study |
| **NICE** | National Institute for Health and Care Excellence |
| **NLSAH** | National Longitudinal Study of Adolescent Health |
| **PREDIMED** | Prevención con Dieta Mediterránea (Prevention with Mediterranean Diet) |
| **Project EAT** | Project Eating Among Teens |
| **SUN cohort** | Seguimiento University of Navarra cohort |
| **USDA [DGAC]** | United States Department of Agriculture [Dietary Guidelines Advisory Committee] |

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# Appendix 1: Criteria for grading evidence

See also Judging the evidence, Section 8.

Adapted from Chapter 3 of the 2007 Second Expert Report [103]. Listed here are the criteria agreed by the Panel that were necessary to support the judgements shown in the matrices. The grades shown here are 'convincing', 'probable', 'limited – suggestive', 'limited – no conclusion' and 'substantial effect on risk unlikely'. In effect, the criteria define these terms.

These criteria were used in a modified form for breast cancer survivors (see CUP Breast cancer survivors report 2014).

## CONVINCING (STRONG EVIDENCE)

Evidence strong enough to support a judgement of a convincing causal (or protective) relationship, which justifies making recommendations designed to reduce the risk of cancer. The evidence is robust enough to be unlikely to be modified in the foreseeable future as new evidence accumulates.

All of the following are generally required:

- Evidence from more than one study type.
- Evidence from at least two independent cohort studies.
- No substantial unexplained heterogeneity within or between study types or in different populations relating to the presence or absence of an association, or direction of effect.
- Good-quality studies to exclude with confidence the possibility that the observed association results from random or systematic error, including confounding, measurement error and selection bias.
- 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.
- Strong and plausible experimental evidence, either from human studies or relevant animal models, that typical human exposures can lead to relevant cancer outcomes.

## PROBABLE (STRONG EVIDENCE)

Evidence strong enough to support a judgement of a probable causal (or protective) relationship, which generally justifies recommendations designed to reduce the risk of cancer.

All of the following are generally required:

- Evidence from at least two independent cohort studies or at least five case-control studies.
- No substantial unexplained heterogeneity between or within study types in the presence or absence of an association, or direction of effect.
- Good-quality studies to exclude with confidence the possibility that the observed association results from random or systematic error, including confounding, measurement error and selection bias.
- Evidence for biological plausibility.

## LIMITED – SUGGESTIVE

Evidence that is too limited to permit a probable or convincing causal judgement but is suggestive of a direction of effect. The evidence may be limited in amount or by methodological flaws but shows a generally consistent direction of effect. This judgement is broad and includes associations where the evidence falls only slightly below that required to infer a probably causal association through to those where the evidence is only marginally strong enough to identify a direction of effect. This judgement is very rarely sufficient to justify recommendations designed to reduce the risk of cancer; any exceptions to this require special, explicit justification.

All of the following are generally required:

- Evidence from at least two independent cohort studies or at least five case-control studies.
- The direction of effect is generally consistent though some unexplained heterogeneity may be present.
- Evidence for biological plausibility.

## LIMITED – NO CONCLUSION

Evidence is so limited that no firm conclusion can be made. This judgement represents an entry level and is intended to allow any exposure for which there are sufficient data to warrant Panel consideration, but where insufficient evidence exists to permit a more definitive grading. This does not necessarily mean a limited quantity of evidence. A body of evidence for a particular exposure might be graded 'limited – no conclusion' for a number of reasons. The evidence may be limited by the amount of evidence in terms of the number of studies available, by inconsistency of direction of effect, by methodological flaws (for example, lack of adjustment for known confounders) or by any combination of these factors.

When an exposure is graded 'limited – no conclusion', this does not necessarily indicate that the Panel has judged that there is evidence of no relationship. With further good-quality research, any exposure graded in this way might in the future be shown to increase or decrease the risk of cancer. Where there is sufficient evidence to give confidence that an exposure is unlikely to have an effect on cancer risk, this exposure will be judged 'substantial effect on risk unlikely'.

There are also many exposures for which there is such limited evidence that no judgement is possible. In these cases, evidence is recorded in the full CUP SLRs on the World Cancer Research Fund International website (dietandcancerreport.org). However, such evidence is usually not included in the summaries.

## SUBSTANTIAL EFFECT ON RISK UNLIKELY (STRONG EVIDENCE)

Evidence is strong enough to support a judgement that a particular food, nutrition or physical activity exposure is unlikely to have a substantial causal relation to a cancer outcome. The evidence should be robust enough to be unlikely to be modified in the foreseeable future as new evidence accumulates.

All of the following are generally required:

- Evidence from more than one study type.
- Evidence from at least two independent cohort studies.
- Summary estimate of effect close to 1.0 for comparison of high- versus low-exposure categories.
- No substantial unexplained heterogeneity within or between study types or in different populations.
- Good-quality studies to exclude, with confidence, the possibility that the absence of an observed association results from random or systematic error, including inadequate power, imprecision or error in exposure measurement, inadequate range of exposure, confounding and selection bias.
- Absence of a demonstrable biological gradient ('dose–response').
- Absence of strong and plausible experimental evidence, from either human studies or relevant animal models, that typical human exposure levels lead to relevant cancer outcomes.

Factors that might misleadingly imply an absence of effect include imprecision of the exposure assessment, insufficient range of exposure in the study population and inadequate statistical power. Defects such as these and in other study design attributes might lead to a false conclusion of no effect.

The presence of a plausible, relevant biological mechanism does not necessarily rule out a judgement of 'substantial effect on risk unlikely'. But the presence of robust evidence from appropriate animal models or humans that a specific mechanism exists or that typical exposures can lead to cancer outcomes argues against such a judgement.

Because of the uncertainty inherent in concluding that an exposure has no effect on risk, the criteria used to judge an exposure 'substantial effect on risk unlikely' are roughly equivalent to the criteria used with at least a 'probable' level of confidence. Conclusions of 'substantial effect on risk unlikely' with a lower confidence than this would not be helpful and could overlap with judgements of 'limited – suggestive' or 'limited – no conclusion'.

## SPECIAL UPGRADING FACTORS

These are factors that form part of the assessment of the evidence that, when present, can upgrade the judgement reached. An exposure that might be deemed a 'limited – suggestive' causal factor in the absence, for example, of a biological gradient, might be upgraded to 'probable' if one were present. The application of these factors (listed below) requires judgement, and the way in which these judgements affect the final conclusion in the matrix are stated.

Factors may include the following:

- 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.
- A particularly large summary effect size (an odds ratio or relative risk of 2.0 or more, depending on the unit of exposure) after appropriate control for confounders.
- Evidence from randomised trials in humans.
- Evidence from appropriately controlled experiments demonstrating one or more plausible and specific mechanisms actually operating in humans.
- Robust and reproducible evidence from experimental studies in appropriate animal models showing that typical human exposures can lead to relevant cancer outcomes.

# Appendix 2: Mechanisms

## Common and complementary mechanisms of dietary and physical activity exposures promoting energy balance (weight maintenance) or positive energy balance (weight gain)

### Promotes energy balance (weight maintenance)

#### *Aerobic physical activity (including walking)*

**Increased total energy expenditure:**

- Physical activity is a major contributor to total energy expenditure; as total energy expenditure increases, this can lead to energy balance (assuming energy expenditure is equalled by energy intake through foods and drinks), or to negative energy balance (assuming insufficient compensation by energy intake).

**Appetite sensitivity:**

- Higher levels of physical activity sensitise individuals to appetite signals, directly potentiating satiety signals via the gastrointestinal tract (reviewed in Blundell *et al.* (2012) [65] and MacLean *et al.* (2017) [66]). This promotes energy balance at a higher level of total energy intake (and expenditure). In addition, habitually active people appear to be able to better compensate for higher energy density diets [296].
- Increased physical activity is also associated with shifts in body composition, favouring lean mass over fat mass [297]; increased lean mass relative to fat mass alters resting metabolic rate, energy demand and drive to eat [66]; also see **Section 3** on fundamental concepts.

**Lipid metabolism and insulin sensitivity:** Endurance aerobic activity, such as long-distance running, promotes fat oxidation, which may explain the favourable effects of such activities on changes to body fat (for a summary, see Hespanhol *et al.* (2015) [266]). In addition, increased physical activity has beneficial effects for *insulin* sensitivity [298].

#### *Wholegrains; Foods containing dietary fibre; Fruit and vegetables*

**Low energy density foods:** Eating foods with lower energy density reduces the likelihood of passive overconsumption. In general, people tend to consume roughly the same amount of food from day to day, measured by bulk and weight, indicating that appetite is more influenced by mass of food (weight and volume) than the intrinsic amount of energy, at least in the short to medium term [67, 145].

**Satiety and satiation:**

- Increased satiation – the termination of a current meal owing to a feeling of fullness – when eating wholegrains may be due to the additional chewing required, related to their fibre content, particle size and structural integrity. This may be modified by the degree of processing. (For a summary, see Karl and Saltzman (2012) [115].)
- Fibre may increase satiation by increasing chewing, slowing gastric emptying and elevating stomach distension, and stimulating cholecystokinin release [155–158].

**Modified digestion, absorption and metabolism:**

- Eating a meal of barley kernels (relative to white bread) led to increased release of GLP-1, as well as depressing energy intake and hunger over two subsequent meals [116]. However, these results may not be applicable to all wholegrains in general.
- Some limited evidence in human trials has shown that consumption of wholegrains can favourably modulate glycaemic response to both the current and the subsequent meal. For example, a favourable (depressed) glycaemic response was observed following a standardised breakfast when barley kernels were consumed the previous evening compared with an equivalent amount of refined-grain wheat bread [117, 118] (for a summary, see Karl and Saltzman (2012) [115]). However, these results may be specific to barley kernels and not wholegrains in general.
- It is hypothesised that fermentation of wholegrains in the bowel influences appetite. Gut microbiota can ferment certain wholegrain fibres to produce *short chain fatty acids*. These can influence glucose and lipid metabolism and stimulate the secretion of gut *hormones* implicated in appetite regulation, gastrointestinal transit and glucose metabolism, such as PYY and GLP-1 [119].
- The increased viscosity of soluble fibre can reduce the overall rate and extent of digestion, which may also result in a blunted post-prandial glycaemic and insulinaemic response to carbohydrates [158].
- Fibre-induced delayed absorption and the resultant presence of *macronutrients* in the distal small intestine, known as the ileal brake, mediate the release of several gut hormones such as PYY and GLP-1 [159].

**Low glycaemic index:** Most non-starchy vegetables tend to have a low glycaemic index; foods with lower glycaemic indices tend to promote favourable insulin responses and post-prandial blood glucose profiles, enhancing appropriate appetite regulation [146].

**Micronutrients:** Fruits and vegetables contain high concentrations of a range of micronutrients and other phytochemicals, including antioxidants and phytoestrogens, that may also have a beneficial influence on energy homeostatic pathways [147, 148].

- Several flavonoid subclasses have been shown to decrease energy intake, increase glucose uptake in muscle in vivo and decrease glucose uptake in adipose tissue in vivo (animal models and short-term human studies) (for a summary, see Bertoia *et al.* (2016) [123]).

### *'Mediterranean type' dietary pattern*

**Source of dietary fibre:** The 'Mediterranean diet' is a dietary pattern rich in plant foods, which provide a high amount and wide variety of both soluble and insoluble dietary fibres (see **Foods containing dietary fibre** above).

**Dietary fat composition:** Typically, the 'Mediterranean type' dietary pattern is high in unsaturated fatty acids relative to saturated fatty acids. Experimental studies in humans have demonstrated that dietary fatty acid composition can influence fat oxidation and daily energy expenditure; in particular oleic acid, a mono-unsaturated fatty acid, may increase oxidation and energy expenditure [169, 170]. This is consistent with results from the PREDIMED trial, which showed no adverse effect on body weight from long-term adherence to a 'Mediterranean type' dietary pattern, supplemented with either olive oil or nuts, compared with the control group [171].

**Low glycaemic index:** The 'Mediterranean type' dietary pattern has a low glycaemic load [172]; foods with lower glycaemic indices tend to promote favourable insulin responses and post-prandial blood glucose profiles, enhancing appropriate appetite regulation [146].

**Available energy:** Some foods common in the 'Mediterranean type' dietary pattern, for example nuts and seeds, resist digestion and absorption, leading to lower bioavailability of energy [173–175].

**Dietary polyphenol content:** A cross-sectional study within the PREDIMED trial reported a significant inverse association between urinary polyphenol concentrations and body weight [176]. It is suggested that the diversity in structure and function of polyphenols mean they could influence a variety of metabolic pathways, such as inhibition of lipogenesis, stimulation of catabolic pathways, reduction of chronic inflammation and upregulation of uncoupling proteins. However, further studies are required to confirm the roles and interactions of the polyphenol group; for a review of existing studies, see Guo *et al.* (2017) [176].

**Associated with higher levels of physical activity:** Traditional lifestyles in the Mediterranean region, similar to other traditional lifestyles around the world, are associated with higher levels of habitual physical activity. Increased physical activity leads to favourable shifts in body composition, appetite regulation and insulin sensitivity (see **Aerobic physical activity** above and Section 3 on fundamental concepts).

## Promotes positive energy balance (weight gain)

### *Sedentary behaviours; Screen time*

**Decreased total energy expenditure:** Physical activity is the main variable contributor to total energy expenditure. If physical activity level is low (through increased sedentary time) then total energy expenditure will decrease; this can lead to positive energy balance (assuming insufficient compensation by decreased energy intake).

**Appetite dysregulation:** Lack of physical activity (through increased time spent sedentary) impairs satiety sensitivity and appetite signals [65]. At low levels of energy expenditure (and when food and drink are freely available), adequate suppression of appetite to maintain energy balance may be compromised [66, 296] (also see Section 3 on fundamental concepts).

**Exposure to marketing and promotions:** Time spent watching television or using other screen devices may increase exposure to marketing of foods and drinks that promote weight gain, leading to increased preference for, purchasing of and intake of such foods, at least in children and adolescents [318, 319].

**Pattern of behaviours:** Time spent watching television or using other screen devices may be accompanied by relatively uninhibited consumption of energy-dense foods, for example through distraction, which may be eaten in large portion sizes [320–322], and can occur in the absence of advertising or marketing [343].

**Displacement:** Time spent watching television or using other screen devices may displace opportunities for more active pursuits [316, 317, 344].

***Sugar sweetened drinks; Refined grains; 'Fast foods'***

**High energy density foods:** Consuming foods and drinks with higher energy densities increases the likelihood of passive overconsumption. In general, people tend to consume roughly the same amount of food from day to day, measured by bulk and weight, indicating that appetite is more influenced by mass of food (weight and volume) than the intrinsic amount of energy, at least in the short to medium term [67, 145].

**Lack of compensation:** Energy from sugars may not be compensated for in the same way when consumed in a soft drink as when consumed as part of a solid meal: energy in liquid form appears to be less effective in inducing satiation or satiety [71], and so may promote excess energy intake.

**Modified fat deposition:** It is hypothesised that consumption of high fructose corn syrup or sucrose, the key sweetening agents of many soft drinks, may promote the deposition of liver, muscle and visceral fat and an increase in serum lipids independently of an effect on body weight (reviewed in Malik and Hu (2015) [206]).

**Altered hedonics:** Increased intake of high-sugar foods and drinks has been associated with greater reward response and decreased inhibitory response to such foods and drinks [207, 208].

**High glycaemic index:** Refined grain products frequently have a high glycaemic index, provoking high insulin responses and a fast glucose decline [151]. It is hypothesised that these properties could increase hunger and enhance lipogenesis (see next point), thereby promoting obesity (for a summary, see Fogelholm *et al.* (2012) [160]).

**Fat tissue synthesis:** Animal feeding studies suggest that consumption of refined grain products can promote fat synthesis even when total energy intake is unchanged [180].

**Displacement:** It is possible that higher intakes of refined grains reflect lower consumption of other dietary factors that might promote energy balance and protect against weight gain (see also **Section 5.2**).

**Degree of processing:** Highly processed foods, such as those typically served at 'fast foods' outlets (for example, French fries (chips) and nuggets), have generally undergone industrial processing and may be unrecognisable from their original plant or animal source. They are frequently high in energy (see point above). Data reported from the EPIC cohort show that high levels of trans fatty acids in the blood were associated with a lower likelihood of weight loss and increased risk of weight gain [229]; plasma trans fatty acids were interpreted as a *biomarker* of dietary exposure to industrially processed foods.

**Cluster of characteristics:** Excess energy intake is also promoted through a cluster of characteristics embodied by 'fast foods', such as being highly palatable, served in large portions, high in energy density (see above point), affordable and easy to access. 'Fast foods' are also frequently consumed alongside sugar sweetened drinks, which have their own positive energy balance promoting effects.

**Preparation and service:** Increased intake of energy is observed when eating in 'fast food' outlets and restaurants [230-232]. This may be mediated by environmental cues which prompt increased energy intake [233] such as offers to increase portion size or add more food items, or lack of control over initial portion size [234] or ingredients (see **Sections 7.5**, **7.6** and **7.8**).

***'Western type' diet***

**High energy density foods:**

- Eating foods with higher energy density increases the likelihood of passive overconsumption. In general, people tend to consume roughly the same amount of food from day to day, measured by bulk and weight, indicating that appetite is more influenced by mass of food (weight and volume) than the intrinsic amount of energy, at least in the short to medium term [67, 145].
- Meat, and some meat products in particular, may be energy dense, especially if high in fat, and thereby may increase total energy intake [256].

**Unfavourable influences on appetite:**

- Prolonged consumption of a high-fat diet may desensitise individuals to a number of appetite signals, such as release of gastrointestinal hormones [257].
- Increased intake of high-sugar and high-fat foods has been associated with greater reward response and decreased inhibitory response to such foods [207, 208].
- The orosensory properties of fat, and foods high in fat, improve palatability [207, 258, 259] and may lead to voluntary overconsumption [260]. Similar preferences have been observed for palatable foods high in sugars [207, 261]. However, replication of these results in human studies is limited.
- Dietary protein has a stronger satiating effect than other macronutrients (fats and carbohydrates) [262]; as meat is high in protein it is possible that diets containing meat low in fat may have a beneficial impact on appetite cues. However, some small human trials suggest that meat- or vegetarian-based sources of protein do not differ in their satiating effects [263–265].

# Notes

# 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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