Fibre, the gut microbiome & breast cancer



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Peer reviewed by two members of Breast Cancer UK independent Science Panel

1. Summary

All studies reviewed in this briefing have found a diet high in fibre is linked to a decreased breast cancer risk. The British Nutrition Foundation recommends the average adult consumes at least 30g of fibre per day. Dietary fibre has many effects on the body, especially on digestion and the composition of microorganisms in your gut. A varied diet rich in fibre, such as the Mediterranean diet - which includes high consumption of whole grains - supports a diverse and stable gut microbiome (the total population of gut microorganisms) and contributes significantly to gut health. Fibre may help prevent breast cancer through several proposed mechanisms which include preventing the reabsorption of oestrogens from the gut into the blood; binding oestrogen and thus increasing faecal excretion; and helping to reduce the risk of becoming overweight or obese.

2. Introduction

Breast cancer is the most common cancer in women globally (1). In the UK, there are around 55,500 new cases of breast cancer in women and 370 in men, every year (2). A person's risk of developing breast cancer depends on many factors, including age, circulating oestrogen), hormones (in particular genetics, diet, lifestyle and the environment (3).

More than four decades ago, dietary fibre was hypothesised to lower the risk of breast cancer based on findings suggesting that women who were vegetarian had increased faecal excretion of oestrogens and decreased

plasma concentration of these hormones compared with omnivorous women (4, 5). Oestrogen is a well-established risk factor for breast cancer (6). Since then, studies numerous have whether a diet high in fibre can decrease the risk of breast cancer. In this brief, evaluate studies on this topic published between 2009 and 2022. We discuss potential mechanisms also high-fibre associated with а diet lowering breast cancer risk.

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3. What is fibre?

The term "dietary fibre" covers various food components that cannot be broken down by the body's enzymes in the human small intestine and enter the large intestine undigested (7).

Dietary fibre occurs in its natural form, almost exclusively in plants. An exception is chitin, which, depending on the definition, may also be considered dietary fibre (8). Chitin is the main component of the body shell of insects, spiders, crustaceans and the cell walls of fungi (9).

Most dietary fibre consists of carbohydrates. Another type of fibre is lignin, a group of highly complex phenolic compounds responsible for the hardening of plant cell walls. Due to advances in food technology, dietary fibre can be extracted from natural sources or produced synthetically (8).

3.1 Classification of fibre

Fibre can be classified into two categories: soluble and insoluble fibre. Soluble fibre dissolves in water and may help lower glucose levels as well as blood cholesterol. Foods with soluble fibre include oats, chia seeds, nuts, beans, lentils, apples, and blueberries. Insoluble fibre does not dissolve in water and can help food move through digestive system. It the promotes regularity and helps prevent constipation. Foods with insoluble fibre include whole wheat products (especially wheat bran), quinoa, brown rice, legumes, leafy greens like kale and fruits with edible skins like pears and

apples (see table 1) (10). Most plant foods contain a mixture of both - soluble and insoluble (11).

Fibre can also be classified by its viscosity (viscous vs non-viscous) and fermentability (fermentable vs non-fermentable). Viscous fibre forms a gellike substance that "sits" in the gut (7). This can influence how quickly the body absorbs certain nutrients like sugar. Fermentable fibre can affect the number and type of bacteria in the gut because it acts as food for gut bacteria that break down and ferment it.

Nonfermentable fibre that is not broken down by bacteria, travels intact to the colon and can add bulk and weight to stools, so it is easier to pass (10). Fibrecontaining foods usually have a mix of different fibre types and so one key to good health is to include a variety of plant foods to get all the benefits of fibre (7).

The National Academy of Medicine distinguishes fibre that occurs naturally in plant foods (dietary fibre) and isolated or synthetic fibre that may be added to foods or used as dietary <u>supplements</u> (functional fibre) (see table 1) (8).



Table 1. Types of fibre and sources (following Harvard T.H. Chan School of Public Health (10) and Linus Pauling Institute (8))

Dietary Fibre	Characteristics	Found in
Lignin	Insoluble; triggers mucus secretion in the colon; adds bulk to stools; has a laxative effect.	Wheat and maize bran, nuts, flaxseeds/linseeds, vegetables, unripe bananas
β-Glucans	Soluble, highly fermentable fibre; metabolised and fermented in the small intestine; acts as a prebiotic (promoting the growth of beneficial intestinal microorganisms); can add bulk to stools, no laxative effect; may help normalise blood glucose and cholesterol levels (see figure 1).	oats and barley
Cellulose & hemicellulose	Insoluble; absorbs water; adds bulk to stool, can have a laxative effect.	Cereal grains and the cell walls of many fruits and vegetables
Pectins	Linear polysaccharides made of 300 - 1,000 monosaccharides, primarily galacturonic acid residues linked by α-1,4 glycosidic bonds, soluble and viscous.	Berries and other fruit
Guar gum	Soluble, fermentable fibre; viscous gel texture; is often added to foods as a thickener; metabolised and fermented in the small intestine; no laxative effect; may help normalise blood sugar and cholesterol levels.	Isolated from ground seeds of the guar plant
Inulin, oligofructose, oligosaccharides, fructooligosaccharides	Soluble, fermentable fibre; may help to bulk stool; laxative effect; normalises blood glucose; act as a prebiotic; can cause bloating or stomach upset to people with irritable bowel syndrome	Onions, chicory root, asparagus, and Jerusalem artichokes
Resistant starch	Soluble, fermentable fibre that acts as a prebiotic; adds bulk to stools; has minimal laxative effect; may help to normalise blood sugar and cholesterol levels.	Bananas and legumes; also formed by food processing or cooling and reheating (starch loses its original structure due to heating or cooking. If starch is later cooled, a new structure is formed)



Table 1. Types of fibre and sources (following Harvard T.H. Chan School of Public Health (10) and Linus Pauling Institute (8))

Manufactured functional fibres	Characteristics	Found in
Psyllium	Soluble, viscous, nonfermentable fibre that holds onto water and softens and bulks stools; has a laxative effect; ingredient in overthe-counter laxatives and high-fibre cereals; may help to normalise blood sugar and cholesterol levels.	Extracted from psyllium seeds
Polydextrose and polyols	Soluble fibre; can increase stool bulk and has a mild laxative effect; minimal effect on blood sugar or cholesterol levels; used in food as a sweetener, to improve texture, maintain moisture, or increase fibre content.	Made of glucose and sorbitol, a sugar alcohol
Inulin, oligosaccharides, pectins, resistant starch, gums	Soluble fibres derived from plant foods; can be modified into a concentrated form that is added to foods or fibre supplements.	Onions, chicory root, asparagus, and Jerusalem artichokes

In plants, dietary fibre is found both as cell wall components (such as cellulose, hemicellulose, pectin or lignin) and intracellularly (such as plant mucilage or gums and storage polysaccharides) (table 1). Dietary fibre predominantly consists of the monosaccharides (simple sugars) glucose, fructose, arabinose and ribose various derivatives of as well as monosaccharides. Although most fibre consists of carbohydrates, they are resistant to digestive enzymes due to special bonds (e.g., β -1,3-, β -1-4glycosidic) and arrive intact in the large intestine.

Cellulose, the most abundant compound in the biosphere, consists exclusively of β -1,4-glycosidically bound glucose units. Mammals lack specific enzymes to break apart cellulose – in contrast to the α -glycosidically bound amylose in starch and glucose units in glycogen (see Figures 1, 2, 3) (8).



Amylose: α-1,4 glucosidic bonds

Cellulose: J3-1,4 glucosidic bonds

β-Glucan: mixed β-1,3 and β-1,4 glucosidic bonds

Figure 1: Chemical structures of amylose, cellulose and beta-glucan (8).

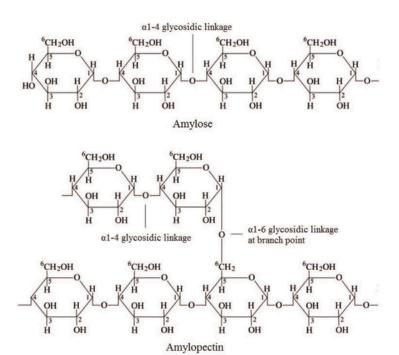


Figure 2: Chemical structure of starch with amylose and amylopectin units. In the starch grains of plants, starch is present in two different variants: Amylose (20-30%) and amylopectin (70-80%) – each with different properties (12).

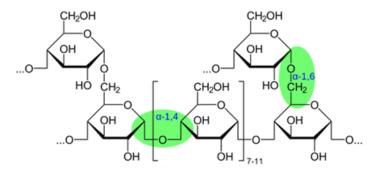


Figure 3: Glycogen is composed of two major bonds, which are α -1,4 and α -1,6 glycosidic bonds – these bonds give rise to linear chains and branching points, respectively (13).



3.2 Sources of fibre

Various vegetables and legumes, e.g., artichokes, broad beans, soybeans, and chickpeas, as well as nuts and seeds - especially ground flaxseed with 24 g dietary fibre per 100 g - have a high fibre content. Whole grains and

products made from them, such as bread and pasta, and bran are also rich in fibre. Cooked whole-grain pasta provides about 5 g of dietary fibre per 100 g, while cooked white pasta made from durum wheat semolina provides only about 2 g per 100 g (see table 2) (14).

Table 2. Dietary fibre content of various food sources (following Dhingra, D. et al. (2012) (14)).

Source	Dietary fibre (g/100 g edible portion)		
	Total	Insoluble	Soluble
Grains			
Barley	17.3	-	-
Corn	13.4	-	-
Oats	10.3	6.5	3.8
Rice (dry)	1.3	6.5	3.8
Rice (cooked)	0.7	0.7	0
Wheat (whole grain)	12.6	10.2	2.3
Wheat germ	14	12.9	1.1
Vegetables			
Green Beans	1.9	1.4	0.5
Soy	15	-	-
Peas, green frozen	3.5	3.2	0.3
Kidney beans, canned	6.3	4.7	1.6
Lentils, raw	11.4	10.3	1.1
Lima beans, canned	4.2	3.8	0.4
White beans, raw	17.7	13.4	4.3
Potato, no skin	1.3	1	0.3
Bitter gourd	16.6	13.5	3.1
Beetroot	7.8	5.4	2.4



Vegetables			
Fenugreek leaves	4.9	4.2	0.7
Ladyfinger	4.3	3	1.3
Spinach, raw	2.6	2.1	0.5
Turnips	2	1.5	0.5
Tomato, raw	1.2	0.8	0.4
Green onions, raw	2.2	2.2	0
Eggplant	6.6	5.3	1.3
Cucumbers, peeled	0.6	0.5	0.1
Cauliflower, raw	1.8	1.1	0.7
Celery, raw	1.5	1	0.5
Carrot, raw	2.5	2.3	0.2
Broccoli, raw	3.29	3	0.29
Fruits			
Apple, unpeeled			
Apple, unpecieu	2	1.8	0.2
Kiwi	3.39	2.61	0.2
Kiwi	3.39	2.61	0.8
Kiwi Mango	3.39 1.8	2.61 1.06	0.8 0.74
Kiwi Mango Pineapple	3.39 1.8 1.2	2.61 1.06 1.1	0.8 0.74 0.1
Kiwi Mango Pineapple Pomegranate	3.39 1.8 1.2 0.6	2.61 1.06 1.1 0.49	0.8 0.74 0.1 0.11
Kiwi Mango Pineapple Pomegranate Watermelon	3.39 1.8 1.2 0.6 0.5	2.61 1.06 1.1 0.49 0.3	0.8 0.74 0.1 0.11 0.2
Kiwi Mango Pineapple Pomegranate Watermelon Grapes	3.39 1.8 1.2 0.6 0.5 1.2	2.61 1.06 1.1 0.49 0.3 0.7	0.8 0.74 0.1 0.11 0.2 0.5
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Kiwi Mango Pineapple Pomegranate Watermelon Grapes Oranges Plums Strawberry	3.39 1.8 1.2 0.6 0.5 1.2 1.8 1.6 2.2	2.61 1.06 1.1 0.49 0.3 0.7 0.7 1.3	0.8 0.74 0.1 0.11 0.2 0.5 1.1 0.9 0.9



Nuts and seeds			
Almonds	11.2	10.1	1.1
Coconut, raw	9	8.5	0.5
Peanut, dry roasted	8	7.5	0.5
Cashew, oil roasted	6	-	-
Sesame seed	7.79	5.89	1.9
Flaxseed	22.33	10.15	12.18

^{*-} means: the info is not available.

4. What is the function of fibre in the body?

Dietary fibre affects the body in a number of ways, most notably digestion. It is also associated with preventive health effects.

4.1 Role in digestion

Dietary fibre affects digestion in several ways. It influences transit time of food in the stomach and intestines, mass and consistency of stools and frequency of bowel emptying (15), satiety (16) and nutrient absorption (14). It also serves "prebiotics" which as are food ingredients for protective bacterial species, thereby encouraging growth of favourable microorganisms in the gut (17). The effects of fibre will depend on its composition and location within the digestive tract. The fermentation of dietary fibre also produces various short-chain fatty acids, some of which are available to the body as an energy source (18).

4.2 Effects on general health

Higher dietary fibre intake is associated with a reduction in the risk of all-cause mortality (19-21) and reduces the risk of dying from cardiovascular diseases (22, 23) or cancer (22, 24).

Increased dietary fibre intake shows protective effects on coronary heart disease (25) and stroke (26) as well as diabetes mellitus type 2 (27), obesity LDL (low (28).total and density lipoprotein) cholesterol concentrations (29), hypertension (30) and colorectal cancer (31). Many studies also find an association between fibre intake and a decreased risk of breast cancer (32), which will be discussed in detail in section 6.











Protective effects are partly associated with total dietary fibre intake and partly with fibre from individual sources, such as fruit or cereals. Therefore, for maximum health benefits, dietary fibre from different sources should be eaten.

5. The gut microbiota and its effect on health

The human gastrointestinal tract is not only a digestive organ, but also a habitat for very large number а microorganisms. It harbours bacteria, fungi, and viruses, archaea, together in a complex environment. It has been estimated that approximately 3.3 million microbial genes are present in the entire so called "metagenome" (total genome of the gut microbiota), which may contain up to 3.8×10^{13} bacterial cells (33, 34), weighing up to two kilograms (35).

The bacteria in the intestine have many different roles: For example, they help with digestion, stimulate the immune system, are involved in the formation of vitamins and amino acids, hormones (including oestrogen) and chemical messengers and strengthen the intestinal barrier so that pathogens or substances that cause disease cannot enter the body (36, 37).

5.1 Food and its effect on intestinal bacteria

The composition of the microbiome is significantly influenced by what and how much a person eats. Your diet provides intestinal bacteria with food that they can use for their metabolism. Some

microorganisms metabolise food substances that humans alone would not be able to digest. While degrading food, they produce important substances that influence human metabolism (34).

Fibre

Dietary fibre food serves as for intestinal microorganisms. Some soluble dietary fibres - called MAC (Microbiota Accessible Carbohydrates) - are largely degraded beneficial by intestinal microorganisms. In the process, microorganisms form, among other things, short-chain fatty acids (SCFAs) such as acetate, propionate especially butyrate. These serve as a source of energy for the mucous membrane cells in the intestine and thus promote the formation of mucus (38). At the same time, they strengthen the intestinal barrier, contribute to an acidic environment and have a positive effect on blood sugar and fat metabolism (39) and the regulation of appetite (40).

Choosing whole grain products and thus consuming plenty of dietary fibre promotes the activity of beneficial bacterial species that form these helpful SCFAs. A subgroup of dietary fibre include prebiotics such as inulin, resistant starches, gums, pectin or oligofructose (see table 1) (37). They can also serve as food for the beneficial bacterial species and thus support a composition favourable of microbiota. Prebiotics are mainly found in vegetables such as chicory, garlic, Jerusalem artichokes, asparagus, leeks and onions (41).



6. Evidence that fibre reduces breast cancer risk

All studies included in this briefing (from 2009 to 2022) found a high fibre consumption to be associated with a decreased breast cancer risk (23, 32, 42-56).

Observational studies are those which investigate the rate of an outcome in groups that were differently exposed to a risk factor. They are used to assess associations, but the potential for biases means that these associations might not be causal (57). However, the studies discussed here included adjustment for many important potential risk factors for breast cancer, so called confounders (something, other than the factor being studied, that could be causing the results seen in a study). Some examples of these include age, physical activity, smoking, alcohol intake, energy intake, BMI, height, oral contraceptive use and hormone replacement therapy use.

Of the 11 single observational studies which were conducted between 2009 and 2022, all of them found that a high fibre consumption (including total fibre consumption, soluble and insoluble fibre consumption, fibre from fruit, vegetables, cereals) was associated with a decreased risk of breast cancer,

including both pre- and postmenopausal (42-52).

Six reviews and meta-analyses, results combining the of several observational studies, giving the results more statistical power, also concluded that a diet high in fibre was linked to a decreased breast cancer risk (23, 32, 53-55, 58, 59). A 2011 meta-analysis an 11% breast cancer reduction in the groups with the highest fibre intake and a 7% decrease in the risk of breast cancer for every 10g/d increment of dietary fibre intake (which is about one apple and two slices of whole wheat bread) (54, 60). An inverse association between dietary fibre intake and breast cancer risk was also found in a 2012 meta-analysis when fibre intake exceeded levels of 25g/day. Intake of soluble fibre, fruit fibre, vegetable fibre or cereal fibre was also inversely associated with breast cancer risk (55). A 12% decrease in breast cancer risk with dietary fibre intake was found in a 2016 meta-analysis. The study found that for every 10g/d increment in dietary fibre intake there was a 4% reduction in breast cancer risk (53). A dose-response meta-analysis concluded that dietary fibre may reduce the risk of breast cancer, especially in high doses (59).

Finally, a 2020 review suggests that a high intake of total, soluble fibre and











fibre from fruit was associated with a reduced overall breast cancer incidence (32).

One umbrella review, among the highest levels of evidence currently available in science, combining the results of many meta-analyses, concluded that those consuming the highest amounts of dietary fibre may benefit from a small reduction in the incidence of breast cancer (56).

A high fibre consumption may also play a role in survival after a breast cancer diagnosis. A 2021 systematic review and meta-analysis of cohort studies concluded that a higher intake of dietary fibre decreases the risk of mortality after a breast cancer diagnosis (61).

7. Breast cancer and the microbiome

Intestinal microbiota dysbiosis, an abnormal composition of the microbiome, has been linked to a higher risk of breast cancer (43). The reason for this may be that certain gut bacteria production alter the of beneficial anticancer metabolites and/or disrupt oestrogenic metabolism in the gut (62).

8. Mechanisms that may explain how fibre could reduce breast cancer risk

There are numerous proposed mechanisms that may explain how dietary fibre might reduce the risk of breast cancer; some of these include:

"A HIGH FIBRE CONSUMPTION MAY ALSO PLAY A ROLE IN SURVIVAL AFTER A BREAST CANCER DIAGNOSIS."

1. A high-fibre diet inhibits the reabsorption of oestrogens (55, 63). Oestrogen is a well-established risk factor for breast cancer. This is mainly because oestrogen encourages cells to divide more rapidly, and an increased rate of cell division of healthy cells increases the possibility of mutations occurring, including those that lead to breast cancer (6).

The gut microbiome plays a crucial role regulating circulating oestrogen levels. Specific microorganisms in the microbiome, called the oestrobolome, specifically do this. The oestrobolome is defined as "the aggregate of enteric bacterial genes whose products are capable of metabolizing oestrogens" (64). One key metabolic pathway for glucuronidation oestrogens is **Figure** 4). Oestrogens (such as oestradiol) can be conjugated (attached) to glucuronic acid (see nr.1 in the graphic). This makes them water soluble so they can be excreted from the body, sometimes via the small intestine. Once in the small intestine (see nr. 2) they can ultimately be eliminated from the body via faeces. Some gut bacteria produce an enzyme called β-glucuronidase (see nr. 3) - this enzyme does the opposite of glucuronidation and uncouples the oestrogen from the glucuronic acid molecule (see nr. 4).

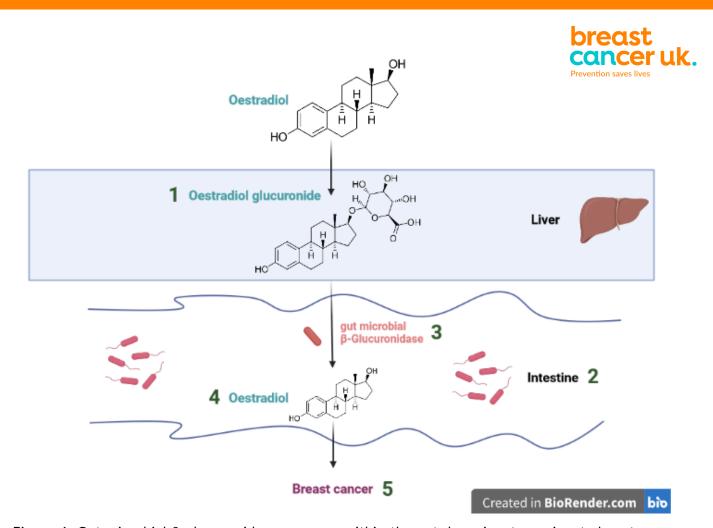


Figure 4: Gut microbial β -glucuronidase enzymes within the gut deconjugate conjugated oestrogens (e.g., oestradiol) to free oestrogen (see nr. 3 in the graphic). This allows unbound oestrogens to be recirculated through the bloodstream, possibly contributing to an increased risk of oestrogen-responsive breast cancers (67).

oestrogen is now no longer packaged and ready to be excreted, but instead may be reabsorbed, potentially leading to elevated oestrogens in your blood. Excess β-glucuronidase activity may be associated with an increased risk of oestrogen-responsive breast cancers (see nr. 5). Dietary fibre affects the composition of intestinal microbiota and may reduce intestinal β-glucuronidase activity, thus, resulting in a reduced reabsorption of oestrogens and reduce circulating levels of oestrogen (65, 66).

2. Dietary fibre can also promote the formation of short-chain fatty acids, especially butyrate, propionate, and acetate, which are produced by bacterial fermentation in the colon (68). Studies have shown that an increase in short-

chain fatty acids can have a protective against breast development (69, 70), and they can influence numerous cancer characteristics, such as cell proliferation (increase in the number of cells), apoptosis (programmed cell death), cell expression, invasion, gene and metabolism in breast cancer (69), in order to reduce risk.

3. Dietary fibre may play a role in the control of insulin resistance (when cells in the body don't respond well to insulin and cannot easily take up glucose from the blood) a known risk factor for breast cancer. It also helps control levels of circulating insulin-like growth factor, high levels of this is also a breast cancer risk factor (71, 72).



- 4. It has been proposed that dietary fibre can bind to oestrogens in the colon and increase their faecal excretion (56).
- 5. High intake of dietary fibre may also prevent overweight and obesity, which is an established risk factor for postmenopausal breast cancer (73).

9. Intake of fibre in the UK and recommended fibre intake

The British Nutrition Foundation recommends 30g/day of fibre for adults in the UK. The average intake of UK adults is 20g fibre per day (7).

Table 3 shows an example of how an intake of 39.6 g dietary fibre per day can be achieved (74).

An example of a diet rich in fibre is the typical traditional Mediterranean diet which is rich in whole grains, legumes and dried fruits. It provides at least 14 g of vegetable fibre for every 1,000 kcal per day (75).

"HIGH INTAKE OF DIETARY FIBRE MAY ALSO PREVENT OVERWEIGHT AND OBESITY, WHICH IS AN ESTABLISHED RISK FACTOR FOR POSTMENOPAUSAL BREAST CANCER."

Table 3. An example of a meal plan to achieve a daily fibre intake of 39.6g (based on an NHS recommendation; not calorie-controlled) (74).

Breakfast	Fibre
Two thick slices of wholemeal toasted bread (6.6g of fibre) topped with one sliced banana (1.4g), 100g of orange (2.4g)	10.4g
Lunch	Fibre
A baked jacket potato with the skin on (4.7g), half a can (about a 200g portion) of reduced-sugar and reduced-salt baked beans in tomato sauce (9.8g) One apple (1.2g)	15.7g
Dinner	Fibre
Mixed vegetable tomato-based curry cooked with onion and spices (6.6g) with boiled wholegrain rice (2.7g) Lower fat fruit yoghurt (0.4g)	9.7g
Snack	Fibre
A small handful of unsalted nuts without added sugars (30g), such as almonds	3.8g
	Total: 39.6g

The above example is only an illustration, as the amount of fibre in any food can depend on how it is made or prepared and on how much of it you eat. Most pre-packaged foods have a nutrition label on the side or back of the packaging, which can include a guide about how much dietary fibre the food contains.



10. Conclusions

The findings of this briefing support the hypothesis that the consumption of foods high in fibre could help reduce breast cancer risk. Our findings have important public health implications. In the UK, breast cancer remains the most common cancer in women. On the other hand, dietary fibre intake in the UK is ~20 g/day, which is only two thirds of

the 30g/day recommended by The British Nutrition Foundation. Given the high incidence and large burden of breast cancer, increasing dietary fibre intake in the general population is of great public health significance with respect to breast cancer prevention. In addition to adequate fibre intake in the diet, it is also important to maintain a calorie and nutrient balanced diet, in addition to an active lifestyle.

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About Breast Cancer UK

Who we are?

Breast Cancer UK aims to prevent breast cancer through scientific research, collaboration, education and policy change. We educate and raise awareness of the risk factors for breast cancer and provide practical information to help people reduce these risks. We campaign to ensure government policies support the prevention of breast cancer. And we fund scientific research that helps to better understand what risk factors contribute to breast cancer, and how to address them For further information on breast cancer risk factors please visit our website www.breastcanceruk.org.uk

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