

# Dietary Fiber Intake and Risk of Pancreatic Cancer

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Contributor: Pietro Ferrara

Dietary fiber intake reduces the risk of pancreatic cancer.

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## 1. Introduction

Pancreatic cancer has one of the worst prognoses among cancers, with a high case fatality rate and an overall 5-year survival rate of around 5% <sup>[1][2]</sup>. Although the epidemiological burden of pancreatic cancer varies greatly across countries, the most recent Global Burden of Diseases, Injuries, and Risk Factors Study found that the number of deaths, incident cases, and disability-adjusted life years attributable to the disease has more than doubled globally from 1990 to 2017, with the highest incidence and mortality rates recorded in high-income countries <sup>[3]</sup>.

Cigarette smoking, alcohol consumption, chronic pancreatitis, obesity, and diabetes mellitus have all been identified as risk factors for this illness <sup>[4]</sup>. In terms of diet, some associations between individual foods or nutrients (e.g., red or processed meat, foods high in saturated fatty acids or fructose, etc.) and the risk of pancreatic cancer have been examined in the literature, but results are still scarce <sup>[5][6]</sup>. A recent systematic review on the role of dietary patterns suggested that those characterized by high consumption of fruit and vegetables, whole grains, low-fat foods, and antioxidant nutrients (for instance, vitamin C and beta carotene) may reduce the risk of pancreatic cancer <sup>[5]</sup>. These findings were also consistent with previous research linking the Mediterranean diet to a lower risk of pancreatic and other cancers <sup>[7]</sup>, owing to a combination of nutrients and food components which seem to play a protective role.

Fiber intake has been ascertained as an essential component of a healthy diet <sup>[8]</sup>. The beneficial role of fiber may be attributable to physical, anti-inflammatory, and prebiotic mechanisms, while the health benefits of dietary fiber encompass both metabolic and overall health <sup>[9]</sup>. In particular, reliable associations have been observed between a higher dietary fiber intake and a lower risk of developing neoplasms, including certain gastrointestinal tumors, namely colon and rectal cancers, and colorectal adenoma <sup>[10][11][12]</sup>. The protective role of fiber has been attributed to a number of potential physical and biological effects, although the mechanisms involved remain unclear. Evidence so far available has suggested that fiber may have a favorable role in reducing insulin resistance and insensitivity, aside from conferring effective protection due to anti-inflammatory pathways, with a resulting positive effect on pancreatic carcinogenesis <sup>[10][13]</sup>.

## 2. Dietary Fiber Intake and Risk of Pancreatic Cancer

Dietary fiber intake has a preventive effect against pancreatic cancer risk. Worth noting is that the strength of the association increased when the analysis was differentiated based on the type of fiber considered (soluble or insoluble), and subgrouped by gender (highlighting a reduction of around 60% of pancreatic risk among women, compared to 30% lower risk among men), and study design (higher in case-control studies). However, results showed a weak inverse borderline association when the diagnosis relied on cancer registries, or when only cohort studies were considered. The strongest link between dietary fiber intake and pancreatic cancer was seen when only case-control studies were included rather than cohort studies, which is likely due to the small number of cohort studies found. Moreover, the period of the three cohort studies varied significantly (ranging from 10 to 30 years of follow-up). Cohort studies are also more prone to selection bias due to the lost-to-follow-up phenomenon, especially for extremely long studies. Even case-control studies, however, are prone to some limitations, such as recall bias, mainly because the difference between cohort and case-control studies is that in case-control studies, the exposure (in this case, dietary fiber intake) has already occurred in the past. Similarly, while the use of population-based cancer registries is of utmost importance for cancer surveillance, certain considerations (such as reporting delays and gaps) may limit their use. In particular, as suggested by Izquierdo et al., some disadvantages have been acknowledged in regard to the assessment of risk factors that are less detectable over longer time periods due to recall problems and difficulties in obtaining medical records from the distant past <sup>[14]</sup>. In terms of potential measurement bias, it should be taken into account that, generally speaking, dietary intake is usually

influenced by some important methodological issue. Two of the main difficulties faced are measurement and, by extension, quantification of dietary intake. One of the most frequently criticized elements is the accuracy in quantifying dietary intakes, primarily due to the measurement methods' inherent limitations (food diary, 24 h dietary recall, and food frequency questionnaire). These limitations are intrinsically linked to certain specific biases, including recall bias, misreporting, misclassification, and a variety of different forms of measurement error. The impact of these potential biases could be attributed to the slightly reduced beneficial effect of dietary fiber intake and risk of pancreatic cancer that we found when only studies with validated dietary assessment tools were included; or, when studies also including proxies (as husband/wife or caregivers) were excluded. Given that, in many cases, patients were no longer alive when the studies were performed, dietary assessments were conducted by interviewing patients or proxies in several studies. In this sensitivity analysis, we found that the reduction in pancreatic risk was marginally lower after accounting for a possible overestimation of dietary fiber intake reported by the proxies.

Dietary fiber is defined in the literature as non-digestible carbohydrates plus lignin [54], which can be classified as "soluble" or "insoluble", depending on its components (soluble fiber is mainly characterized by pectins, whereas, insoluble fiber is mainly based on cellulose). Despite the fact that this differentiation was mainly suggested to explore potential differences in biological mechanisms, data have shown that the two types of fibers function synergistically to improve health.

Finally, public health recommendations and healthy dietary guidelines all recommend a higher consumption of dietary fiber, even if no specific recommendations are available with regard to dietary fiber intake and pancreatic cancer. In fact, the most recent updated version of the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) report, which is used as a reference for cancer prevention through diet and nutrition, found limited evidence on dietary fiber intake and pancreatic cancer risk [6].

There are several potential biological mechanisms that can explain the beneficial effects of dietary fiber intake. Firstly, dietary fiber is associated with the stool bulk effect, which reduces carcinogen exposure in the intestinal lumen as well as secondary bile acid production by increasing transit speed [6]. Secondly, fiber disrupts the microbiota metabolism by stimulating the production of short-chain fatty acids (SCFA) through fiber fermentation. The production of these SCFA, in turn, lowers colonic pH and inhibits the growth of pathogenic microorganisms [13]. SCFA can also modulate inflammation [15], which has an effect on the risk of pancreatic cancer [16]. Dietary fiber intake also seems to improve glycemic control and other key risk factors such as abdominal obesity, metabolic syndrome, and insulin sensitivity [17], all of which are associated with an increased risk of cancer [18][19][20]. Moreover, low insulin sensitivity, insulin resistance, and type 2 diabetes are risk factors for pancreatic cancer [21]. Considering the above, it should be also mentioned that dietary fiber intake potentially correlates with other lifestyle and behavioral factors which might influence the risk for pancreatic cancer—namely obesity, alcohol intake, smoking—and a possible total synergic effect has to be also considered in further research [22].

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