

### Science & Society The Fiber Gap and the Disappearing Gut Microbiome: Implications for Human Nutrition

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Increasing evidence indicates that modern lifestyle, and specifically a Western diet, has led to a substantial depletion of the human gut microbiome. This loss is implicated in the rampant increase of chronic diseases, providing an incentive to fundamentally transform human nutrition towards being more holistic and microbiome-focused.

#### Lifestyle-Induced Microbiome Depletion and its Implications for Health

Humans have evolved with dense microbial populations that colonize their gastrointestinal tract and are integral to our biology, for example, through the provision of signals that aid the development of the immune system. There is convincing evidence from research in animal models that a disruption of this host-microbiome symbiosis leads to an increase in immune-mediated pathologies related to chronic non-communicable diseases (NCDs), such as obesity, cardiovascular disease, colon cancer, allergies, other atopic diseases (including asthma), autism, and autoimmune diseases [1]. The role of the gut microbiome in NCDs is difficult to test in humans, but disease risk is epidemiologically linked to practices that disrupt the establishment of the gut microbiota early in life (such as cesarean sections, antibiotics, formula feeding), and pathologies are often associated with an aberrant microbiome. Importantly, most NCDs have increased substantially within the past decades, suggesting that modern

lifestyle might have led to a loss of bacterial symbionts that are protective [2]. In fact, comparisons of the gut microbiota in unindustrialized rural human communities from South America, Africa, and Papua New Guinea (which generally have a low prevalence of NCDs) with that of communities in the USA and Europe provide compelling evidence for a substantial decline of gut microbiome diversity through industrialization [3].

## A Low-Fiber Diet is a Key Driver of Microbiome Depletion

It is likely that a combination of factors (antibiotics, modern clinical practices, sanitation, dietary habits) have caused the decline in gut microbiome diversity. However, the only factor that has been empirically shown to be important is a diet low in microbiota-accessible carbohydrates (MACs), which are indigestible dietary carbohydrates that become available to the microbes that colonize the intestine. Research in mice showed that feeding a diet low in MACs substantially depleted gut microbiota diversity over the duration of only a few generations [4]. Intake of dietary fiber, which is the main source of MACs in the diet of adult humans, is negligibly low in the Western world when compared with both the diet consumed in nonindustrialized societies and that of our ancestors [5]. Such a low-fiber diet provides insufficient nutrients for the gut microbes, leading not only to the loss of species reliant on these substrates but also to a reduction in the production of fermentation end products with important physiological and immunological functions [6]. In other words, by shifting to a diet that is fundamentally different to the diet under which the human-microbiome interrelationship evolved, we might have disrupted this symbiosis, reducing or removing the evolutionary routed benefits provided by the microbes. The notion that this process might have contributed to the rise of NCDs and a substantial degree of morbidity and mortality provides a strong incentive to consider attempts to conserve and potentially restore the gut microbiome.

#### Dietary Fiber Can Increase Microbiome Diversity and Prevent NCDs, but Consumption Is Not Sufficient

Dietary fiber and whole grains have been shown to increase diversity of the human fecal microbiota [7,8]. Epidemiological studies further consistently show significant inverse associations between dietary fiber intake and microbiome-associated NCDs, and all-cause mortality, and research in animal disease models supports a beneficial role. Human intervention studies are often inconclusive, but inconsistencies may stem from a variety of reasons that have not yet been sufficiently considered. First, interindividual differences in composition of the gut microbiome, which is especially pronounced in industrialized societies [9], results in an individualized response to dietary fiber that may increase variation in the findings from human trials [10]. Second, most human intervention studies are performed with daily amounts of daily fiber that are much lower than those consumed by our ancestors, and therefore might not lead to detectable physiological changes. Accordingly, moving African Americans to a traditional South African diet with a daily dose of 55 g of dietary fiber was efficient to improve markers of colon cancer within 2 weeks [11].

The available data indicate a considerable potential for dietary fiber to elevate microbiome diversity and prevent NCDs, but consumption is on average only half of what is recommended in dietary guidelines, which is referred to as the 'fiber gap' [12]. Given that host-microbiome symbiosis evolved with a diet that contained substantially more fiber than what is currently recommended, the real 'fiber gap' for optimal health and conservation of microbial diversity might be even larger than currently appreciated [5]. These evolutionary considerations, the appreciation of the gut microbiome's role in human health, and especially the recent findings on the 'disappearing microbiome', now provide a clear incentive for societywide efforts to fundamentally change the



Dietary Fibers	Fiber Products	Potential Food Products
Resistant starch	ActiStar <sup>®</sup> RM Fibersym <sup>®</sup> RW <sup>a</sup> Hi-MAIZE <sup>®</sup> 260 <sup>a</sup> PENFIBE <sup>®</sup> RS4	Flour-based foods, breads, pastries, pasta, snacks
Arabinoxylan	Biofiber Gum NAXUS <sup>®</sup>	Flour-based foods, beverages, soups/sauces
β-Glucan	B-CAN <sup>™</sup> PromOat <sup>®a</sup> Wellmune <sup>®</sup> Yestimun <sup>®</sup>	Flour-based foods, beverages, soups/sauces
Cellulose	GRINDSTED <sup>®</sup> MCC MICROCEL Solka-Floc <sup>®</sup> Vitacel <sup>®</sup>	Flour-based foods, dairy products
Inulin/oligofructose	Actilight <sup>® a</sup> Frutalose <sup>®</sup> L90 <sup>a</sup> NUTRAFLORA <sup>® a</sup> Oliggo-Fiber <sup>®</sup> DS2 <sup>a</sup> Orafti <sup>®</sup> Synergy1 <sup>a</sup>	Beverages, confectionery, preserves, dairy products, flour-based foods, soups/sauces
Galactooligosaccharide, xylooligosaccharide	Bimuno <sup>® a</sup> BIOLIGO <sup>®</sup> GL Vivinal <sup>®</sup> GOS <sup>a</sup> Longlive XOS <sup>a</sup> NovaGreen XOS	Beverages, confectionery, preserves, dairy products, flour-based foods, soups/sauces
Human milk oligosaccharides	Mum's Sweet Secret Glycom	Infant formula
Polydextrose	STA-LITE <sup>® a</sup> Litesse <sup>®</sup> II <sup>a</sup> NUTRIOSE <sup>®</sup> FB <sup>a</sup>	Beverages, confectionery, preserves, dairy products, flour-based foods, soups/sauces
Soluble corn fiber	PROMITOR <sup>® a</sup>	Beverages, confectionery, preserves, dairy products, flour-based foods, soups/sauces
Alginate	Algogel <sup>™ a</sup> KIMICA ALGIN Manugel DMB <sup>a</sup>	Beverages, confectionery, preserves, dairy products
Pectin	Citrus Pectin USP GENU <sup>®</sup> Pectin C74 <sup>a</sup> Unipectine <sup>®</sup>	Confectionery, preserves, dairy products
Gum arabic/acacia gum	Agri-Spray Acacia <sup>®</sup> EmulGold <sup>® a</sup> Fibregum <sup>™ a</sup> Gum Arabic SD	Beverages, confectionery, preserves, dairy products, soups/sauces
Guar gum	GuarNT <sup>®</sup> Ricol Rg-250 Viscogum <sup>™</sup> Guar Gumª	Confectionery, preserves, dairy products, soups/sauces
Fiber-rich raw materials	'Best' Pea Fiber <sup>a</sup> Corn Z-Trim <sup>®</sup> Cranberry Fiber Fibrex <sup>®</sup> Sugar Beet <sup>a</sup> FIBRIM <sup>®</sup> Soy Unicel <sup>®</sup> WF	Beverages, confectionery, preserves, dairy products, flour-based foods, soups/sauces

#### Table 1. A Nonexhaustive List of Dietary Fibers Available on the Market, Product Names, and Food Products In Which These Fibers Could Be Used

<sup>a</sup>Dietary fibers with established microbiota-accessible carbohydrates.

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