

Colorectal Cancer in Africa: Causes, Dietary Intervention, and Lifestyle Change

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Abstract

Colorectal cancer (CRC) is a menace in the global public health system. According to GLOBOCAN

reports, colorectal cancer is the second most diagnosed cancer in the world with more than 1.9 million cases and 935,000 deaths in 2020 alone. Diet plays a key role in exposing humans to environmental carcinogens and anti-carcinogens, consequently mitigating or aiding in the development of various cancers. CRC is most prevalent in western countries with a high intake of saturated fats, refined carbohydrates, and processed meat. CRC was an extremely rare disease in Africa some decades ago, but the situation is fast changing. The traditional African diet consists of leafy, roots and cruciferous vegetables, fruits, roots, tubers and plantains, legumes, whole grains, and spices, all of which have been shown to possess protective effects against CRC. However, the effect of urbanization has contributed to the shift of dietary choices among the African population to consuming more ultra-processed foods with high levels of unhealthy components that have originated from colorectal cancer prevalent regions. This review evaluates the current nutritional challenges of the African diet to

colorectal cancer and the potential roles of the traditional African diets and lifestyle modification in the prevention and management of colorectal cancer.

Introduction

Cancer is a world-leading cause of death and decrease in the life expectancy [1]. According to GLOBOCAN reports, colorectal cancer is the second most diagnosed cancer, accounting for over 1.9 million cases and 935,000 deaths in 2020 alone [1]. The early stages of CRC are asymptomatic and its progression from benign, non-cancerous growths called polyps into cancer is often slow with a multistep process of cellular, structural, and genetic alterations [2]. Individuals with family or personal history of CRC, lynch syndrome, inflammatory bowel diseases (IBDs), presence of diabetes mellitus type 2, obesity and people of age ≥ 50 years are at higher risks of developing CRC [2]. Like most chronic diseases, certain controllable lifestyle behaviors such as sedentary activities, heavy intake of western diet, tobacco and alcohol elevates the risk of CRC as well [2].

The typical African diet consists of staple starch, fibre-rich foods, fruits, and plant-sourced proteins, all of which are linked with a decreased risk of CRC [3]. In the past, CRC was almost nonexistent in Africa [4]. However, urbanization has led to the increase in sedentary lifestyle and adoption of unhealthy diets in the form of refined carbohydrates, high fat foods and processed red meat among the African populace. These types of diet has been linked to colorectal cancer and other chronic diseases in several studies. Although, Africa still has a low incidence of CRC worldwide [3] but the shift in lifestyle choices may have contributed to the current incidence of CRC in the continent. According to the GLOBOCAN cancer fact sheets, the world burden of colon and rectum cancer in Africa are estimated to be 2.9% (with 33,299 cases) and 3.7% (with 26,779 cases) respectively compared to Asia at 49.6% (with 569,186 cases) and 57.8% (with 423,569 cases) respectively [5].

This review discussed African traditional dietary intervention and lifestyle modification for the prevention

and management of colorectal cancer.

2.0. Colon Cancer: Pathophysiology, Causes, Implications

Cancer could be described as an uninhibited, uncontrolled growth of abnormal cells spreading within the tissues, organs, or systems of the body. Risk factors associated with cancers could be peripheral if regularly exposed to hazardous chemicals, radiation, and infectious diseases; or viscerally when cell growth abnormalities are associated with hormonal alterations, gene mutations and immune state [6]. Physiological state of individuals, age and hereditary factors could also influence whether one is likely to have cancer.

Cancers are of various types which affect organs and tissues such as colon, breast, prostate, bone, blood etc. [7]. For CRC, the growth and dispersal of neoplastic alterations are evident and characterized by tumoural growth in the bowel regions of the body [8]. Obviously, significant alterations of the sequence of DNA (mutations) represent this initial event [8]. Though the prevalence of colon cancer varies from country to country, amongst numerous factors with reference to socio- class, individuals with low standards of living especially in the areas of nutrition and hygiene are more likely associated with increased risk of colon cancer. Among the important risk factors of this cancer include family or personal history of adenomatous polyps, presence of diseases such as diabetes mellitus, obesity, inflammatory bowel diseases (IBD), and history of Lynch syndrome [9]. Racial or ethnic background also plays a role as a high record of mortality and morbidity due to this disease have been documented in black Americans and Jews of Ashkenazi descent [9]. In spite of facts showing that genetic and environmental factors perform significant roles in the oncogenesis of the colon, extended studies had suggested that dietary interventions might be utilized for fundamental and defensive roles in the body to deter the development of colon carcinoma [10].

2.1. Colon Cancer in Africa (epidemiology, economic implications, Statistics of occurrence and survival rate)

Globally, colorectal cancer is ranked third most

common among cancers after breast and lung cancers [11]. The screening process has shown that it remains the most avoidable major cancer. There appears to be a complex genetic relationship in the component of the initiation, promotion, and progression of colorectal cancer, which poses a risk of its development [6]. Presently, over 1.2 million people are diagnosed annually, though rarely seen in individuals under the age of 40, it usually occurs in people at 60 and over.

Despite the economics linked with the screening and the availability of certified screening tools, the prevalence rate of the disease is expected to rise to 33.5% in 2020. Globally, the economic affliction posed by colon cancer is overwhelming and stated to be in surplus of \$33,000,000,000 per annum [12, 13]. While this disease tends to ravage the African race, it is imperative that recommended screenings centres and equipment should be provided most especially in the rural areas. Global Statistics has shown that cancer of the colon is higher in Western countries than in Africa. In Black Americans, an estimated 6.5% of people in the U.S, while 0.4% occur with people in Sub-Saharan Africa.

3.0 Traditional Dietary prevention and management of Colon cancer in Africa

Diet plays a key role in exposing humans to environmental carcinogens and anti-carcinogens, consequently mitigating or aiding in the development of various cancers [14]. African diet has demonstrated a protective role against colon cancer due to the high fibre content of the diet [15]. Dietary fibre is the major component in African dishes that offers protection against colon cancer as it clearly differentiates the African diet from the Western diet that is characterized by consumption of more fatty foods and refined products. A study reported that switching the diet of African American patients to the traditional African diet influenced gut bacteria in such manner that could prevent cancer development [16].

3.1. Recent Nutritional and Pharmacological Interventions among African Population

Makki *et al.* [17] reported that the traditional African diet plays a protective role against gut tumor promoters such as Carcinoma embryonic antigen (CEA), Cyclooxygenase-2 (Cox-2), A33-transmembrane glycoprotein member of the immunoglobulin superfamily, Telomere/telomerase-TERT, Urokinase-type plasminogen activator receptor (uPAR) gene, Fibroblast growth factor 18 (FGF18), endothelial cell type-specific tyrosine kinase domain-containing receptor (KDR) [18] modifies colonic bacterial fermentation and alters gut motility. Dietary fiber also binds bile acids in the gut and prevents the conversion of primary to secondary bile acids. The fermentation of fiber by colon bacteria generates volatile short chain fatty acid (SCFA) that induces apoptosis and inhibits neoplastic tumor development. Dietary fiber also lessens the risk of colon cancer by reducing nitric oxide, inflammatory markers, insulin resistance and increasing fecal bulk, lessening the potential interactions between fecal mutagens and colon mucosa [19]. Several animal experiments, clinical trials and epidemiological studies have shown reduced risk of colorectal cancer with increased consumption of dietary fiber [20]. However, it has been observed that the type of fiber consumed determines the protective effect as many studies have found little to no protective effect with cereal fiber and a significant protective effect with vegetable and fruit fiber.

Vegetables

In Africa, vegetables being an important part of the traditional diet are consumed daily by the rural populations due to their accessibility, affordability, and availability. They consist of dark green leafy vegetables (amaranth, spinach, jute leaves, baobab leaves, water leaves, cassava leaves, cowpea leaves, pumpkin leaves), root vegetables (onions, garlics, carrot, ginger, beet roots) and cruciferous vegetables (turnips, cabbage, lettuce, broccoli). Vegetables are rich sources of retinol, ascorbic acid, folate, and minerals such as iron and magnesium [41]. Retinol and ascorbic acid are strong antioxidants and anti-tumorigenic. Folates stabilize tumor suppressor genes and prevent increase in cell proliferation [42]. The phytochemical content of vegeta-

bles also confers its protective role against colorectal cancer (see Table 1). Major phytochemicals found in vegetables such as flavonoids, terpenoid, alkaloids and phenolic compounds are potent inhibitors of reactive oxygen species, are cytotoxic and prevent the alteration of DNA. Cruciferous vegetables have been reported to induce phase I and II metabolism 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP), decreasing the occurrence of colon cancer [43]. Allium vegetables (onions, garlic) serve as an essential flavoring base in most African soups and stews. A 29 months hospital-based case-control study that consecutively recruited 833 cases of CRC and matched them to 833 controls by age not more than 2.5 years of difference, reported that consuming high total allium vegetables decreased the chances of colorectal cancer in adults by 79% [44]. This was attributed to their disulphide content that suppresses cell division in human colon cancer cell lines. Vegetables are also rich sources of dietary fiber. Sufficient intake of both green and yellow vegetables provides insoluble dietary fibre that serves as a protective factor for these cancer types [45].

Fruits

Fruits are an important part of the African traditional diet. Commonly consumed fruits in Africa include vegetable fruits such as tomatoes, pepper, cucumbers, and eggplant. The regular fruits include avocado, baobab fruit, citrus fruits, guava, mango, pawpaw, pineapple, watermelon, passion fruit, banana, and jackfruit. Most of which are genetically unmodified. Although, studies have not confirmed any association between genetically modified foods and cancer, despite the risks and concerns associated with GMO foods [46]. Fruits are good sources of dietary fiber, vitamins (A, B, C and E), minerals (potassium, magnesium, phosphorus, selenium) and phytochemicals (flavonoids, phenols). Ascorbic acid, a major component in citrus fruits, is associated with tumor regression in advanced diseases and chemo sensitizing colorectal cancer cells [47]. Other antioxidative vitamins in fruits such as retinol and tocopherol reduce the toxic effect of reactive oxygen

species (ROS) in cancer causation and they decrease epithelial cell proliferation [48]. Fruits are also rich in minerals such as phosphorus, selenium, potassium, zinc, and magnesium that offer a protective role for colorectal cancer by increasing the expression of antioxidant enzymes and boosting the immune response. The stew base in most African countries are spicy fruits such as sweet pepper and habanero pepper which are rich in antioxidants (See table 1). Capsaicin, a major phytochemical in peppers was reported to possess cytotoxic, anti-proliferative and pro-apoptotic effects against colo 205 colorectal cancer cells in an in vitro study [49]. Lu *et al.* [49] also reported that capsaicin inhibited tumor growth in mice with colo 205 tumor xenografts.

African Starchy Staples

The main staples in Africa include roots and tubers (cassava, yam, potato, cocoyam, sweet potato), cereals (Sorghum, corn, millet, rice), and bananas (Plantain, green banana). Staple crops generally are rich in polyphenols, vitamins, and minerals with cancer-preventive properties. These food crops serve as the main energy source in African diet. Root and tubers are rich sources of non-digestible carbohydrates (NDCs) such as fiber and resistant starch. NDC undergoes anaerobic fermentation to produce short chain fatty acids: acetic acid, propionic acid and butyric acid which lower the pH of the intestinal lumen. The lowered PH levels favors the establishment of healthy gut microbiota to produce short chain fatty acid that alters preneoplastic lesions, suppress mutations and bind potential carcinogens in the colon [50]. Short chain fatty acids also directly interact with cells in the gut to elicit immunologic effects such as the regulation of T helper cells, lymphoid cells, cytotoxic T cells and B cells to improve host immunity, suppress inflammation and allergic responses [51]. The risk of colon cancer is reduced by about 40% with high intake of NDC from staples [52]. Grains form the bulk of staples and whole grains are majorly consumed in the rural parts compared to the urban centers. Tocopherol and selenium which are richly present in whole grains are strong antioxidants with

Table 1. Anti-colorectal cancer properties of some phytochemical constituents in some common African vegetables

| Phytochemical constituents | Vegetables | Anti-colorectal cancer properties | References |
|----------------------------|---|--|------------|
| Myricetin. | <i>Amaranthus spp.</i> | Cytotoxic, mutagenic, pro-apoptotic, autophagic effects | [21, 22] |
| Catechins | <i>Amaranthus spp</i> | Anti-tumorigenic, anti-metastatic effects | [23] |
| Apigenins | <i>Amaranthus spp</i> | Anti-proliferative, Anti-metastatic, chemosensitive effects | [24, 25] |
| Naringenin | <i>Amaranthus spp</i> | Pro-apoptotic, anti-proliferative effects | [26, 27] |
| Rutin | <i>Amaranthus spp</i> | Anti-metastatic and anti-proliferative effects, induced cell cycle arrest | [28] |
| Flavonoids | <i>Talinum triangulare, Basella alba; Telferia occidentalis; Adansonia digitata; Corchorus oleritorius; Chlophytum comosum, Solanum macrocarpon, Cymbopogon spp, Gongronema latifolium, Ocimum gratissimum, Capsicum spp, Vernonia amygdalia, Luffa cylindrica, Brassica Oleracea, Momordica charantia, Urtica massaica</i> | Pro-apoptotic, anti-inflammatory, anti-proliferative effects and modulation of gut microbiome | [29,30] |
| Alkaloids | <i>Talinum triangulare, Basella alba, Telferia occidentalis, Corchorus oleritorius, Solanum macrocarpon, Ocimum gratissimum, Vernonia amygdalia, Brassica Oleracea, Luffa cylindrica, Urtica massaica</i> | Anti-oxidative and anti-inflammatory effects against IBD and Crohn's disease, modulation of gut microbiome | [31] |
| Saponins | <i>Telferia occidentalis, Adansonia digitata, Corchorus oleritorius, Chlophytum comosum, Solanum macrocarpon, Cymbopogon spp, Ocimum gratissimum, Vernonia amygdalia, Brassica Oleracea, Luffa cylindrica, Urtica massaica</i> | Pro-apoptotic, anti-metastatic, cytotoxic effects, modulation of gut microbiome | [32, 33] |
| Tannins | <i>Talinum triangulare, Telferia occidentalis, Chlophytum comosum, Solanum macrocarpon, Abelmoschus esculentus, Brassica Oleracea, Vernonia amygdalia</i> | Anti-proliferative, anti-carcinogenic effects | [34] |
| Phytosterols | <i>Talinum triangulare</i> | Pro-apoptotic effects | [35] |
| Allicin | <i>Gongronema latifolium, Talinum triangulare</i> | Cytostatic, pro-apoptotic effects | [36] |
| Cardiac glycosides | <i>Basella alba, Adansonia digitata, Chlophytum comosum, Corchorus oleritorius, Abelmoschus esculentus, Luffa cylindrica</i> | Anti-proliferative, cytotoxic, anti-oxidative, pro-apoptotic effects | [37, 38] |
| Lignin | <i>Talinum triangulare</i> | Modulation of gut microbiome, reduction of serum cholesterol | [39] |
| Ascorbic acid | <i>Solanum macrocarpon, Vernonia amygdalia, Momordica charantia</i> | Anti-proliferative and pro-apoptotic effects | [40] |

colon cancer preventive properties. The consumption of whole grains was reported to significantly reduce the risk of colorectal cancer by 11% [53]. Table 2

Legumes

Legumes (soybean, pigeon pea, bambara nut, groundnut, beans) are important protein source in the African diet. Besides being rich sources of proteins, they also contain phytoestrogens. Genistein, a phytoestrogen in soy was reported to inhibit proliferation of HT-29 colon cancer cells by mediating a cancer promoter protein, EGF [54]. Flavonoids in leguminous foods are involved in the regulation of cellular proliferation and apoptosis in the colon. The high folate content of legumes is also responsible for the decrease in the risk of colon cancer. Higher consumption of legumes especially from soy has been reported to reduce the incidence of colorectal cancer in Asians [55]. High intake of meat has been associated with an elevated risk of colorectal cancer and substituting legumes as a source of protein may inversely reduce the risk of colorectal cancer.

Meat and Fat

Due to the high cost of meat and fats in many parts of Africa, the consumption is typically low. Africa obtains an average of 18% of total food energy from

dietary fat [62]. Much of the fat content in the traditional diets comes from plant oils that are rich in monounsaturated fats such groundnut, palm kernel, sesame, olive, sunflower, soybean, and coconut oils. The lower consumption of animal protein and fat in the traditional African diet may have contributed to the low incidence and risk of colon cancer among the African populace. The lesser consumption of saturated fats in the western diet is linked with a decrease in risk of developing colon cancer as saturated fat contributes to enhanced tumor formation [63]. An in-vivo examination carried out by Garcia-Villatoro *et al.* [64] showed that western diets are directly associated with colorectal cancer. The study administered mice with high-fat diet to simulate the mixed lipid composition in the average western diet and it was indicated that cryptic cell proliferation and colon mass multiplicity was promoted at the premalignant colon cancer lesion. The study also showed β -catenin expression and nuclear localization in actively proliferating cells in colon masses.

In addition, meat processing methods that applies high temperature that are peculiar in the west have also been linked with colon cancer risks. Among the first pyrolysis mutagens to be isolated and identified are the pyridoimidazole, pyridoindole and the quino

Table 2. Dietary Fiber content of common African seed legumes

| Scientific name | Common name | Total Dietary Fiber (%) | References |
|-------------------|-------------------------|-------------------------|------------|
| Glycine max | Soybean | 9.19-16.5 | [56] |
| Cicer arietinum | Chickpea | 18-22 | [57] |
| Arachis hypogaea | Groundnut | 8.5 | [58] |
| Cajanus cajan | Pigeon pea | 9.8-13.0 | [59] |
| Vigna unguiculata | Cow pea, Black eyed pea | 12.0-15,0 | [60] |
| Vigna subterranea | Bambara beans | 1.4-10.3% | [61] |

xalines, which are major mutagens found in high heat over processed beef [65]. A study has reported that South Africans who consumed a typical Westernized diet rich in saturated animal fat, cholesterol and animal protein had high blood lipid levels and were at increased susceptibility to colon cancer [19]. A diet with high fiber and low animal products is advantageous to colonic metabolism. The low sulfur amino acid content permits the overgrowth of methanogenic bacteria, which convert maldigested carbohydrate into SCFA [66]. The reason ulcerative colitis and other noninfective colonic diseases are so rare in Africans is related to low animal protein diet and consequent low colonic sulfite production.

Spices

Some spices such as turmeric, clove and red pepper are rich in antioxidant properties, hence can regulate cellular oxidative stress. Likewise, they have the capability of stopping the reactive oxygen species from being produced and disrupting the signal transduction pathways. These spices possess potential therapeutic effects in the management and treatment of cancers due to their anti-inflammatory, antioxidant, and immunomodulatory effects [67].

Curcumin, an important constituent of turmeric, possesses anti-tumor, anti-inflammatory and antioxidant properties [68]. Curcumin has been reported in several studies to inhibit cancer promoting signal pathways inducing apoptosis, inhibiting proliferation and hindering cell growth of cancer cells including colorectal cancer cells [69]. According to Yoon *et al.* [70] curcumin exhibits its anti-cancer effect at a dosage of 3,600mg/day.

4.0 Nutritional Challenges and Drawbacks Associated with Diet in Africa

Colon cancer has increased in Africa with the integration of the western diet into the traditional African diet characterized by the consumption of more processed foods [71]. These ultra- processed foods include baked products, sugary beverages, sweets, sugary cereals, and fizzy drinks. These foods have been easily introduced into

the African traditional diet because of their convenience and 'ready-to-eat' nature, hence the classic term 'fast foods' [72].

The influx of small-scale food enterprises comprising fast-food, drinks, desserts, cakes, and biscuit enterprises in modern times has significantly increased the consumption of ultra-processed food. Most of these processed foods have low nutritional value and are packed in unhealthy saturated fats, sugar, preservatives, and flavor enhancers. These components added to processed foods makes their consumption addictive. Moreso, these unhealthy components of processed foods are associated with an increase in risk of developing colon cancer as heavy consumption of sugary processed products in adolescents and adulthood, on a daily basis, doubles the risk of developing colon cancer before the age of 50 [73]. Sugar promotes cancerous tumors as the growth of polyps depends on the availability of glucose and fructose. Saturated fats cause an imbalance in intestinal bile acids and trigger inflammatory factors that promote tumor development [74]. Sodium nitrites, a common food additive found in processed meat products are metabolized into cancer causing N-nitroso compounds. Monosodium glutamates have been reported to increase the susceptibility of experimental animals to colon cancer [75].

Processed foods are also indirectly linked with an increase in risk of cancer by elevating factors responsible for colon cancer such as obesity and diabetes [76]. Chen *et al.* [77] reported that an exponential increase in consumption of processed foods increased the risk of cancer by 12%. The shift in the consumption of less whole grains to the consumption of refined grains has increased in the African traditional diet. Refined grains are often preferred for their appearance, texture, and taste but they have low nutritional value. Rice and wheat are the major examples of staple whole grains in Africa that are majorly refined. Refined grains have low fiber, mineral, vitamins, and phytochemicals (polyphenols and flavonoids) with antioxidant properties

that reduce cancer. Refined grains are now fortified with the lost nutrients but the health promoting phytochemicals that are anti-cancerous cannot be replaced. High intake of refined grains has also been associated with the increase in incidence of gastric and colon cancer [78].

There is an increase in availability of processed meat products such as sausage, ham, bacon, and cheese in Africa. The integration of these processed meat products in the traditional African diet also increases the risk of colon cancer. Moreover, the increased production of locally available processed meat products such as spiced beef strips, smoked and fried meat chunks have increased the consumption of red meat in African countries as most of these products are increasingly sold and purchased. The processing methods of meat in Africa is also of serious concern. In most households, meat is often deep fried in used oils. Moreover, the grilling and smoking method of meat products to produce barbecued products is common in various food-bar outlets in Africa. The fried and barbecued meats are preferable for their flavor and aroma, however the high temperature processing method used accompanied with the presence of smoke (in barbecued meat products) generates heterocyclic amines (HCAs) that increases susceptibility to colon cancer [79]. Processing methods used in meat preparation such as high temperature (120-230°C), smoking and inclusion of preservatives produce harmful carcinogenic substances such as heterocyclic amines, polycyclic hydrocarbons, N-nitroso compounds, and acrylamide. Increased meat consumption also causes heme iron overload that encourages cell growth and proliferation by generating reactive oxygen species, inducing oxidative stress, and catalyzing processes involving the formation of nitroso compounds [80].

5.0 What next? Lifestyle Changes among African Population

Colorectal cancer (CRC) has been reported as the third most common cancer. From the record of World Health Organization GLOBOCAN, nearly 1.2 million people were diagnosed with CRC and 608,000 deaths were recorded in 2008 [81]. Over the years, the occurrence of

CRC is considered rare among native Africans compared to the modern countries but with the increase in urbanization and industrialization, there has been a recorded rise in the incidence of colorectal cancer [82, 83] among the African populace.

The incidence of CRC in some West African countries was less than 0.003% about 40-50 years ago [4]. However, between 1954 and 2007, the incidence of colorectal cancer has increased by 7% and 87.42% in Nigeria and Ghana, respectively.

As reported in sub-Saharan Africa, CRC represents the fifth most common malignancy [84]. Studies have shown changes in diet and lifestyle play a vital role in the early prevention of CRC [85].

This increase in trends of CRC could be linked to etiological factors such as increase in consumption of alcohols, obesity, lack of physical activity, tobacco usage, highly refined diets low in fiber, carbonated drinks, fast foods. Alimentary factors are also linked to high CRC as observed in countries that consume high amounts of red meat and processed meat products.

Diet to Good Nutrition

The diets of average African are mostly carbohydrate based and the starches and polysaccharide (non-starch) in the diets are fermented by the bacteria in the colon into colon friendly acids such as acetic acid, propionic acid and butyric acid which are associated with low colon cancer risk.

The plant-based diets have been reported to be protective and this may be partly due to absence of meats which when cooked or processed may produce carcinogens and saturated acids which are injurious to health. Additionally, plant-based diets are a rich source of vitamins, phytochemicals and fibre which offer several health benefits like weight loss or weight maintenance which invariably reduce the risk of obesity which has been linked to CRC.

Likewise, there should be a drastic reduction in consumption of red and processed meats as they contain

high cholesterol, saturated fats leading to high levels of cholesterol in the serum and triglycerides associated with high CRC risk. Hence, a healthier diet of fruits, vegetables and whole grains combined with increased physical activities which result in healthy body weight should be adopted as a lifestyle as it is associated with being CRC free [86].

Physical Activity

Physical activity has been linked to reduce not only CRC but other forms of cancer while inactive lifestyle may cause a rise in the incidence of CRC. Physical activity has been said to not only reduce colon cancer risk but help in maintaining energy balance, enhance the immune system, regulate insulin levels, alter prostaglandin levels and enhance movement of the contents in the colon through the gut [87].

Alcohol

It has been stated that alcohol increases the chance of CRC by 60%, this is because its metabolism produces acetaldehyde and metabolites which promote carcinogenesis via its various mechanisms [88, 89]. Alcohol consumption can lead to malnutrition deficiencies of vitamins (such as B6 and B12), DNA synthesis and methylation [90].

Conclusion and Recommendation

Studies have shown that good nutrition and lifestyle modification have a significant impact on the occurrence of CRC. There is a great need for modification of lifestyle among the African populace to reduce the risk of CRC incidence. Processed foods low in fiber should be replaced with fruits and vegetables, high consumption of red meat can be replaced with fish or white meat from chicken, and a reduction in sugar intake or replacement with honey and date fruit (syrup/powder). Physical activity/exercise should be increased as it can help reduce the risk of obesity. Alcohol consumption should be avoided, and the use of spices should be inculcated in the preparation of meals as most of them (turmeric, chili pepper, ginger, garlic, etc.) have anti-cancer properties. Food supplements that possess anti-colorectal cancer

properties could be developed and specific dosage should be taken daily which could be widely promoted in various health facilities in all African countries and other countries in the world for best impact.

List of Abbreviations

GLOBOCAN- Global Cancer Incidence, Mortality and Prevalence No.

CRC- Colorectal cancer

IBDs - inflammatory bowel diseases

CEA- Carcinoma embryonic antigen

Cox-2- Cyclooxygenase-2

TERT- Telomere/telomerase

uPAR- Urokinase-type plasminogen activator receptor

FGF18- Fibroblast growth factor 18

KDR- kinase domain-containing receptor

SCFA- short chain fatty acid

HCAs- Heterocyclic amines

HT-29- Human colorectal adenocarcinoma

EGF- Epidermal Growth Factor

Colo205- Human, Caucasian, colon, adenocarcinoma

PhIP- 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine

ROS- reactive oxygen species

NDCs- Non digestible carbohydrates

References

1. Sung, H., Ferlay, J., Siegel, R.L., Laversanne, M., Soerjomataram, I., Jemal, A. and Bray, F. (2021) Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*, 71(3):209-249.
2. Simon, K., (2016) Colorectal cancer development and advances in screening. *Clinical interventions in aging*, 11:967.
3. Katsidzira, L., Gangaidzo, I., Thomson, S., Rusakaniko, S., Matenga, J. and Ramesar, R. (2017) The shifting epidemiology of colorectal cancer in sub-Saharan Africa. *The Lancet Gastroenterology & Hepatology*, 2

- (5):377-383.
4. Irabor, D.O. (2017). Emergence of colorectal cancer in West Africa: Accepting the inevitable. *Nigerian medical journal: journal of the Nigeria Medical Association*, 58(3):87.
 5. World Health Organization International Agency for Research on Cancer (IARC) (2020). GLOBOCAN 2020: Estimated cancer worldwide prevalence. <https://gco.iarc.fr/today/fact-sheets-cancers> Accessed on 23rd June, 2021.
 6. Hark L. and Darwin D. (2007). Nutrition for Life: The Definitive Guide to Eating well for good health. 258-259.
 7. Franke, A.J., Skelton IV, W.P., George, T.J. and Iqbal, A., (2020). A comprehensive review of randomized clinical trials shaping the landscape of rectal cancer therapy. *Clinical Colorectal Cancer*. 20(1):1-19
 8. Virostko, J., Capasso, A., Yankeelov, T.E. and Goodgame, B., 2019. Recent trends in the age at diagnosis of colorectal cancer in the US National Cancer Data Base, 2004-2015. *Cancer*, 125(21):3828-3835.
 9. American Cancer Society, 2020. Colorectal Cancer. <https://www.cancer.org/cancer/colon-rectal-cancer.html> Accessed on 30th, June 2021.
 10. Thanikachalam, K. and Khan, G., 2019. Colorectal cancer and nutrition. *Nutrients*, 11(1):164.
 11. WHO (2021). Cancer. <https://www.who.int/news-room/fact-sheets/detail/cancer> Accessed 16th, September 2021
 12. Arnold, M., Sierra, M.S., Laversanne, M., Soerjomataram, I., Jemal, A. and Bray, F. (2017). Global patterns and trends in colorectal cancer incidence and mortality. *Gut*, 66(4):683-691.
 13. Araghi, M., Soerjomataram, I., Jenkins, M., Brierley, J., Morris, E., Bray, F. and Arnold, M., (2019). Global trends in colorectal cancer mortality: projections to the year 2035. *International journal of cancer*, 144(12):2992-3000.
 14. National Research Council (1996) Carcinogens and Anticarcinogens in the Human Diet, *National Academy Press*, Washington, DC,
 15. Yang J and Yu J (2018). The association of diet, gut microbiota and colorectal cancer: what we eat may imply what we get. *Protein and Cell*. 9(5):474-487.
 16. O'Keefe, S.J., Li, J.V., Lahti, L., Ou, J., Carbonero, F., Mohammed, K., Posma, J.M., Kinross, J., Wahl, E., Ruder, E. and Vippera, K., (2015). Fat, fibre and cancer risk in African Americans and rural Africans. *Nature communications*, 6(1):1-14.
 17. Makki K., Deehan E., Walter J., and Backhed F. (2018) The impact of dietary fibre on gut microbiota in host health and disease. *Cell Host and Microbe*. 23 (6): 705-715.
 18. Rama, A. R., Aguilera, A., Melguizo, C., Caba, O. and Prados, J. (2015). Tissue Specific Promoters in Colorectal Cancer Hindawi Publishing Corporation Disease Markers 2015:1-9. <https://doi.org/10.1155/2015/390161>
 19. O'Keefe S, Kidd M, Noel G and Owira P (1999). Rarity of colon cancer in Africans is associated with low animal consumption and not fibre. *American Journal of Gastroenterol*. 94 (5):1373-80.
 20. Song, H. M., Park, G. H., Eo, H. J., Lee, J. W., Kim, M. K., Lee, J. R., Lee, M. H., Koo, J. S., and Jeong, J. B. (2015). Anti-proliferative effect of naringenin through p38-dependent downregulation of cyclin D1 in human colorectal cancer cells. *Biomolecules & therapeutics*, 23(4):339.
 21. Kim, M. E., Ha, T. K., Yoon, J. H., & Lee, J. S. (2014). Myricetin induces cell death of human colon cancer cells via BAX/BCL2-dependent pathway. *Anticancer research*, 34(2):701-706.
 22. Zhu, M. L., Zhang, P. M., Jiang, M., Yu, S. W., & Wang, L. (2020). Myricetin induces apoptosis and autophagy by inhibiting PI3K/Akt/mTOR signalling in human colon cancer cells. *BMC Complementary Medicine and Therapies*, 20(1):1-9.
 23. Sukhthankar, M., Yamaguchi, K., Lee, S. H., McEntee, M. F., Eling, T. E., Hara, Y., & Baek, S. J. (2008). A green tea component suppresses posttranslational expression of basic fibroblast growth factor in colorectal cancer. *Gastroenterology*, 134(7): 1972-1980.
 24. Xu, M., Wang, S., Song, Y. U., Yao, J., Huang, K., and Zhu,

- X. (2016). Apigenin suppresses colorectal cancer cell proliferation, migration and invasion via inhibition of the Wnt/ β -catenin signaling pathway. *Oncology letters*, 11(5):3075-3080.
25. Cheng, Y., Han, X., Mo, F., Zeng, H., Zhao, Y., Wang, H., Zheng, Y. & Ma, X. (2021). Apigenin inhibits the growth of colorectal cancer through down-regulation of E2F1/3 by miRNA-215-5p. *Phytomedicine*, 153603.
 26. Cheng, H., Jiang, X., Zhang, Q., Ma, J., Cheng, R., Yong, H., Shi, H., Zhou, X., Ge, L., and Gao, G. (2020). Naringin inhibits colorectal cancer cell growth by repressing the PI3K/AKT/mTOR signaling pathway. *Experimental and therapeutic medicine*, 19(6): 3798-3804.
 27. Song Y., Liu M., Yang F., Cui L., Lu X., and Chen C. (2015). Dietary fibre and risk of colorectal cancer. A case control study. *Asian Pacific Journal of Cancer prevention*. 16 (9):3747-3752.
 28. Jayameena, P., Sivakumari, K., Ashok, K., & Rajesh, S. (2018). Rutin: A potential anticancer drug against human colon cancer (HCT116) cells. *Int. J. Biol. Pharm. Allied Sci*, 7(9):1731-1745.
 29. Cho, Y. A., Lee, J., Oh, J. H., Chang, H. J., Sohn, D. K., Shin, A., and Kim, J. (2017). Dietary flavonoids, CYP1A1 genetic variants, and the risk of colorectal cancer in a Korean population. *Scientific reports*, 7 (1): 1-8.
 30. Li, Y., Zhang, T., and Chen, G. Y. (2018). Flavonoids and colorectal cancer prevention. *Antioxidants*, 7 (12):187.
 31. Peng, J., Zheng, T. T., Li, X., Liang, Y., Wang, L. J., Huang, Y. C., and Xiao, H. T. (2019). Plant-derived alkaloids: the promising disease-modifying agents for inflammatory bowel disease. *Frontiers in pharmacology*, 10: 351.
 32. Li, Y., Sun, Y., Fan, L., Zhang, F., Meng, J., Han, J., Guo, X., Zhang, R., Yue, Z., and Mei, Q. (2014). Paris saponin VII inhibits growth of colorectal cancer cells through Ras signaling pathway. *Biochemical pharmacology*, 88(2): 150-157.
 33. Xia, L., Zhang, B., Yan, Q., and Ruan, S. (2018). Effects of saponins of *patrinia villosa* against invasion and metastasis in colorectal cancer cell through NF- κ B signaling pathway and EMT. *Biochemical and biophysical research communications*, 503(3): 2152-2159.
 34. Yang, P., Ding, G. B., Liu, W., Fu, R., Sajid, A., and Li, Z. (2018). Tannic acid directly targets pyruvate kinase isoenzyme M2 to attenuate colon cancer cell proliferation. *Food & function*, 9(11):5547-5559.
 35. Choi, Y. H., Kong, K. R., Kim, Y., Jung, K. O., Kil, J. H., Rhee, S. H., and Park, K. Y. (2003). Induction of Bax and activation of caspases during β -sitosterol-mediated apoptosis in human colon cancer cells. *International journal of oncology*, 23(6): 1657-1662
 36. Bat-Chen, W., Golan, T., Peri, I., Ludmer, Z., and Schwartz, B. (2010). Allicin purified from fresh garlic cloves induces apoptosis in colon cancer cells via Nrf2. *Nutrition and cancer*, 62(7):947-957
 37. Felth, J., Rickardson, L., Rosén, J., Wickstrom, M., Fryknäs, M., Lindskog, M., Burlon, L., and Gullbo, J. (2009). Cytotoxic effects of cardiac glycosides in colon cancer cells, alone and in combination with standard chemotherapeutic drugs. *Journal of natural products*, 72(11):1969-1974
 38. Anderson, S. E., and Barton, C. E. (2017). The cardiac glycoside convallatoxin inhibits the growth of colorectal cancer cells in a p53-independent manner. *Molecular genetics and metabolism reports*, 13:42-45
 39. Sloan, D. A., Fleiszer, D. M., Richards, G. K., Murray, D., and Brown, R. A. (1993). The effect of the fiber components cellulose and lignin on experimental colon neoplasia. *Journal of surgical oncology*, 52(2):77-82
 40. Chen, X., Zhang, Z., Yang, H., Qiu, P., Wang, H., Wang, F., Zhao, Q., Fang, J. and Nie, J., (2020). Consumption of ultra-processed foods and health outcomes: a systematic review of epidemiological studies. *Nutrition journal*, 19(1):1-10.
 41. Marles R., 2017. Mineral nutrient composition of vegetables, fruits and grains: The content of report of apparent historical declines. *Journal of Food Composition and Analysis*. 56:93-103.
 42. Lima, M. and Silva, G. (2005). Colorectal cancer:

- Lifestyle and dietary factors. *Nutr Hosp.* 4:235-241.
43. Walters, D.G., Young, P.J., Agus, C., Knize, M.G., Boobis, A.R., Gooderham, N.J. and Lake, B.G., (2004). Cruciferous vegetable consumption alters the metabolism of the dietary carcinogen 2-amino-1-methyl-6-phenylimidazo [4, 5-b] pyridine (PhIP) in humans. *Carcinogenesis*, 25(9):1659-1669.
 44. Wu, X., Shi, J., Fang, W.X., Guo, X.Y., Zhang, L.Y., Liu, Y.P. and Li, Z. (2019). Allium vegetables are associated with reduced risk of colorectal cancer: A hospital-based matched case-control study in China. *Asia-Pacific Journal of Clinical Oncology*, 15 (5):e132-e141.
 45. Boeing, H., Dietrich, T., Hoffmann, K., Pischon, T., Ferrari, P., Lahmann, P.H., Boutron-Ruault, M.C., Clavel-Chapelon, F., Allen, N., Key, T. and Skeie, G., (2006). Intake of fruits and vegetables and risk of cancer of the upper aero-digestive tract: the prospective EPIC-study. *Cancer causes & control*, 17(7): 957-969.
 46. Prakash, D., Verma, S., Bhatia, R. and Tiwary, B.N., 2011. Risks and precautions of genetically modified organisms. *International Scholarly Research Notices*, 2011.
 47. Pawlowska, E., Szczepanska, J. and Blasiak, J., (2019). Pro-and antioxidant effects of vitamin C in cancer in correspondence to its dietary and pharmacological concentrations. *Oxidative Medicine and Cellular Longevity*, 2019.
 48. Larouche D, Hanna M, Chang S, Jacob S, Tetu B, Diorio C (2016). Evaluation of antioxidant intake in relation to inflammatory markers expression within the normal tissue of breast cancer patients. *Integrative Cancer Therapies*. 16 (4):492-195.
 49. Lu, H. F., Chen, Y. L., Yang, J. S., Yang, Y. Y., Liu, J. Y., Hsu, S. C., Lai, K. C., and Chung, J. G. (2010). Antitumor activity of capsaicin on human colon cancer cells in vitro and colo 205 tumor xenografts in vivo. *Journal of agricultural and food chemistry*, 58(24): 12999-13005
 50. Parada Venegas, D., De la Fuente, M.K., Landskron, G., González, M.J., Quera, R., Dijkstra, G., Harmsen, H.J., Faber, K.N. and Hermoso, M.A., (2019). Short chain fatty acids (SCFAs)-mediated gut epithelial and immune regulation and its relevance for inflammatory bowel diseases. *Frontiers in immunology*, 10:277.
 51. Kim, C. H. (2021). Control of lymphocyte functions by gut microbiota-derived short-chain fatty acids. *Cellular & molecular immunology*, 18(5): 1161-1171.
 52. Prado S, Castro V, Ferreira G and Fabi J (2019). Ingestion of non-digestible carbohydrates from plant source foods and decrease risk of colorectal cancer: A review on the biological effects and the mechanism of action. *Frontiers in Nutrition*. 6:72.
 53. Zhang, X.F., Wang, X.K., Tang, Y.J., Guan, X.X., Guo, Y., Fan, J.M. and Cui, L.L., (2020) Association of whole grains intake and the risk of digestive tract cancer: a systematic review and meta-analysis. *Nutrition journal*, 19:1-14.
 54. Qi, W., Weber, C. R., Wasland, K., and Savkovic, S. D. (2011). Genistein inhibits proliferation of colon cancer cells by attenuating a negative effect of epidermal growth factor on tumor suppressor FOXO3 activity. *BMC cancer*, 11(1): 1-9.
 55. Shin, A., Lee, J., Lee, J., Park, M.S., Park, J.W., Park, S.C., Oh, J.H. and Kim, J., (2015). Isoflavone and soyfood intake and colorectal cancer risk: a case-control study in Korea. *PloS one*, 10(11):.e0143228.
 56. Redondo-Cuenca, A., Villanueva-Suárez, M.J., Rodríguez-Sevilla, M.D. and Mateos-Aparicio, I., (2007). Chemical composition and dietary fibre of yellow and green commercial soybeans (*Glycine max*). *Food Chemistry*, 101(3):1216-1222.
 57. Jukanti, A.K., Gaur, P.M., Gowda, C.L.L. and Chibbar, R.N., (2012). Nutritional quality and health benefits of chickpea (*Cicer arietinum* L.): a review. *British Journal of Nutrition*, 108(S1):.S11-S26.
 58. Arya, S.S., Salve, A.R. and Chauhan, S., (2016). Peanuts as functional food: a review. *Journal of food science and technology*, 53(1):31-41.
 59. Amarteifio, J.O., Munthali, D.C., Karikari, S.K. and Morake, T.K., (2002). The composition of pigeon peas (*Cajanus cajan* (L. Millsp.) grown in Botswana. *Plant*

- Foods for Human Nutrition*, 57(2):173-177.
60. Kirse, A. and Karklina, D., (2015). Integrated evaluation of cowpea (*Vigna unguiculata* (L.) Walp.) and maple pea (*Pisum sativum* var. *arvense* L.) spreads. *Agronomy Research*, 13(4):956-968.
 61. Lin Tan, X., Azam-Ali, S., Goh, E.V., Mustafa, M.A., Chai, H.H., Kuan Ho, W., Mayes, S., Mabhaudhi, T., Azam-Ali, S. and Massawe, F., (2020). Bambara groundnut: An underutilized leguminous crop for global food security and nutrition. *Frontiers in Nutrition*, 7:276.
 62. Gebremedhin, S. and Bekele, T., (2021). Evaluating the African food supply against the nutrient intake goals set for preventing diet-related non-communicable diseases: 1990 to 2017 trend analysis. *Plos one*, 16(1):e0245241.
 63. Kim, M. and Park, K., (2018). Dietary fat intake and risk of colorectal cancer: a systematic review and meta-analysis of prospective studies. *Nutrients*, 10(12):1963
 64. Garcia-Villatoro, E.L., DeLuca, J.A., Callaway, E.S., Allred, K.F., Davidson, L.A., Hensel, M.E., Menon, R., Ivanov, I., Safe, S.H., Jayaraman, A. and Chapkin, R.S., (2020). Effects of high-fat diet and intestinal aryl hydrocarbon receptor deletion on colon carcinogenesis. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, 318(3):G451-G463.
 65. Bernstein, A.M., Song, M., Zhang, X., Pan, A., Wang, M., Fuchs, C.S., Le, N., Chan, A.T., Willett, W.C., Ogino, S. and Giovannucci, E.L., (2015). Processed and unprocessed red meat and risk of colorectal cancer: analysis by tumor location and modification by time. *PloS one*, 10(8):e0135959.
 66. Vippera K and Keefe S (2012). The microbiota and its metabolites in colonic mucosal health and cancer risk. *Nutrition in Clinical Practice*. 27 (5): 624-635.
 67. Li, S., Li, S.K., Gan, R.Y., Song, F.L., Kuang, L. and Li, H.B., (2013). Antioxidant capacities and total phenolic contents of infusions from 223 medicinal plants. *Industrial Crops and Products*, 51:289-298
 68. Lantz, R.C., Chen, G.J., Solyom, A.M., Jolad, S.D. and Timmermann, B.N., (2005). The effect of turmeric extracts on inflammatory mediator production. *Phytomedicine*, 12(6-7):445-452.
 69. Guo, L. D., Chen, X. J., Hu, Y. H., Yu, Z. J., Wang, D., & Liu, J. Z. (2013). Curcumin inhibits proliferation and induces apoptosis of human colorectal cancer cells by activating the mitochondria apoptotic pathway. *Phytotherapy Research*, 27(3), 422-430.
 70. Yoon, M. J., Kim, E. H., Lim, J. H., Kwon, T. K. and Choi, K. S., (2010). Superoxide anion and proteasomal dysfunction contribute to curcumin-induced paraptosis of malignant breast cancer cells. *Free Radical Biology and Medicine*, 48(5):13-726.
 71. Reardon, T., Tschirley, D., Liverpool-Tasie, L.S.O., Awokuse, T., Fanzo, J., Minten, B., Vos, R., Dolislager, M., Sauer, C., Dhar, R. and Vargas, C., (2021). The processed food revolution in African food systems and the double burden of malnutrition. *Global food security*, 28:100466.
 72. Hamrick, K.S. and Okrent, A., (2014). The role of time in fast-food purchasing behavior in the United States. *USDA-ERS Economic Research Report*, (178).
 73. Murphy, N., Campbell, P.T. and Gunter, M.J., 2021. Are sugar-sweetened beverages contributing to the rising occurrence of colorectal cancer in young adults?. *Gut*.
 74. Bojková, B., Winklewski, P.J. and Wszedybyl-Winkiewska, M., (2020). Dietary fat and cancer— which is good, which is bad, and the body of evidence. *International journal of molecular sciences*, 21(11):4114.
 75. Hata, K., Kubota, M., Shimizu, M., Moriwaki, H., Kuno, T., Tanaka, T., Hara, A., Hirose, Y. (2012). Monosodium glutamate induced diabetic mice are susceptible to azoxymethane induced colon tumorigenesis. *Carcinogenesis*. 33 (3):702-7.
 76. Soltani, G., Poursheikhani, A., Yassi, M., Hayatbakhsh, A., Kerachian, M. and Kerachian, M.A., (2019). Obesity, diabetes and the risk of colorectal adenoma and cancer. *BMC endocrine disorders*, 19(1):1-10.
 77. Chen, J., Qin, F., Li, Y., Mo, S., Deng, K., Huang, Y., and Liang, W. (2020). High-dose vitamin C tends to kill colorectal cancer with high MALAT1 expression. *Journal of oncology*, 2020.

78. Gaesser, G. (2020). Whole grains, refined grains and cancer risk: A systematic review of meta- analyses of observational studies. *Nutrients*, 12 (12):3756.
79. Akyan, N. (2015). Red meat and colorectal cancer. *Oncol Rev*. 9 (1):288.
80. Ward, M., Cross, A., Weisenburger, D. (2012). Heme iron from meat and risk of adenocarcinoma of the oesophageus and stomach. *European Journal of Cancer Prevention*. 21 (2):134-138.
81. Ferlay, J., Shin, H.R., Bray, F., Forman, D., Mathers, C. and Parkin, D.M., (2010). Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *International journal of cancer*, 127(12): 2893-2917.
82. Graham, A., Davies Adeloye, L.G., Theodoratou, E. and Campbell, H., (2012). Estimating the incidence of colorectal cancer in Sub-Saharan Africa: A systematic analysis. *Journal of global health*, 2(2).
83. Irabor, D. and Adedeji, O.A., (2009) Colorectal cancer in Nigeria: 40 years on. A review. *European journal of cancer care*, 18(2):110-115
84. Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R.L., Torre, L.A. and Jemal, A., (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*, 68 (6):394-424.
85. Vieira, A. R., L. Abar, D. S. M. Chan, S. Vingeliene, E. Polemiti, C. Stevens, D. Greenwood, and T. Norat. "Foods and beverages and colorectal cancer risk: a systematic review and meta-analysis of cohort studies, an update of the evidence of the WCRF-AICR Continuous Update Project."(2017) *Annals of Oncology* 28(8):1788-1802.
86. Yao, X. and Tian, Z., (2015). Dyslipidemia and colorectal cancer risk: a meta-analysis of prospective studies. *Cancer causes & control*, 26(2):257-268.
87. Slattery, M.L., Edwards, S., Curtin, K., Ma, K., Edwards, R., Holubkov, R. and Schaffer, D., (2003). Physical activity and colorectal cancer. *American journal of epidemiology*, 158(3):214-224.
88. Slattery, M.L., Potter, J., Caan, B., Edwards, S., Coates, A., Ma, K.N. and Berry, T.D., (1997). Energy balance and colon cancer—beyond physical activity. *Cancer research*, 57(1):75-80.
89. Varela-Rey, M., Woodhoo, A., Martinez-Chantar, M.L., Mato, J.M. and Lu, S.C., (2013). Alcohol, DNA methylation, and cancer. *Alcohol research: current reviews*, 35 (1):25.
90. Hiraoka, M. and Kagawa, Y., (2017). Genetic polymorphisms and folate status. *Congenital anomalies*, 57 (5):142-149.