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The Macrobiotic Diet in Cancer[1,2]

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ABSTRACT Macrobiotics is one of the most popular alternative or complementary comprehensive lifestyle approaches to cancer. The centerpiece of macrobiotics is a predominantly vegetarian, whole-foods diet that has gained popularity because of remarkable case reports of individuals who attributed recoveries from cancers with poor prognoses to macrobiotics and the substantial evidence that the many dietary factors recommended by macrobiotics are associated with decreased cancer risk. Women consuming macrobiotic diets have modestly lower circulating estrogen levels, suggesting a lower risk of breast cancer. This may be due in part to the high phytoestrogen content of the macrobiotic diet. As with most aspects of diet in cancer therapy, there has been limited research evaluating the effectiveness of the macrobiotic diet in alleviating suffering or prolonging survival of cancer patients. The few studies have compared the experience of cancer patients who tried macrobiotics with expected survival rates or assembled series of cases that may justify more rigorous research. On the basis of available evidence and its similarity to dietary recommendations for chronic disease prevention, the macrobiotic diet probably carries a reduced cancer risk. However, at present, the empirical scientific basis for or against recommendations for use of macrobiotics for cancer therapy is limited. Any such recommendations are likely to reflect biases of the recommender. Because of its popularity and the compelling evidence that dietary factors are important in cancer etiology and survival, further research to clarify whether the macrobiotic diet or similar dietary patterns are effective in cancer prevention and treatment is warranted. J. Nutr. 131: 3056S–3064S, 2001.

KEY WORDS: • *macrobiotic diet* • *neoplasms* • *vegetarianism* • *life change events* • *yin-yang* • *epidemiology*

Published in 1982, *Recalled by Life: The Story of My Recovery from Cancer* (1) recounted the autobiographical story of a physician, Dr. Anthony Sattilaro, who was diagnosed at age 49 y with prostate cancer with multiple bone metastases. Given a poor prognosis and feeling that he had nothing to lose, Dr. Sattilaro adopted a macrobiotic, predominantly vegetarian, whole-foods diet soon after diagnosis. Follow-up examinations at 1 and 4 y after diagnosis revealed complete resolution of metastatic bone lesions. Articles recounting his story appeared in publications such as the *Saturday Evening Post* (August, 1980) and *Life* magazine (August, 1982). Publication of Dr. Sattilaro's story was preceded in 1979 by another autobiographical book, *Healing Miracles from Macrobiotics* (2), which described the recovery of a music professor, Dr. Jean Kohler, from pancreatic cancer, and was followed in 1983 with the publication of Michio Kushi's *The Cancer Prevention Diet* [reissued in 1993 (3)], which detailed the macrobiotic approach to cancer. Based on these and other stories of recovery from cancer [see, for example (4–7)], macrobiotics has become known popularly as a comprehensive dietary and lifestyle approach to cancer.

The general notion that diet may influence carcinogenesis is not new nor particularly out of the mainstream of biomed-

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ical thought. The roles that various dietary factors may play in the process of carcinogenesis and the voluminous epidemiologic literature that demonstrates associations of foods or nutrients with the prevention of cancer were reviewed by the American Institute for Cancer Research and the World Cancer Research Fund in their 1997 report (8). Based on this extensive review, a series of dietary recommendations for the prevention of cancer was developed for the report. These recommendations suggested that a plant-based diet that minimized consumption of red meat and processed meat and emphasized consumption of a variety of vegetables, fruits and whole-grain cereals, would decrease the risk of a variety of cancers.

The dietary pattern promoted by macrobiotics, although derived largely from philosophical principles (9), is predominantly vegetarian, emphasizing natural, minimally processed foods. Thus, it is broadly compatible with many dietary recommendations, not just for the prevention of cancer (8,10) but also for the prevention of other chronic diseases (11,12) and the promotion of health (13). Although it may thus be reasonable to suggest that a macrobiotic diet may form the foundation of a dietary approach for the prevention of these diseases, it is unknown whether diet may prolong survival, reduce unpleasant side-effects of chemotherapy or radiation or prevent recurrence of cancer. The overall lack of empirical evidence on this topic was noted recently by the American Cancer Society (14). This paper is focused on the evidence relating macrobiotic diets to cancer.

What is macrobiotics?

Broadly, macrobiotics is not just a therapeutic approach to cancer. Rather, the word macrobiotics has been used to describe a philosophy, a cultural movement and an eating pattern. The word macrobiotic was used by the 18th century German physician Christoph Hufeland to describe a program for good health and prolonging life (15) and was used more recently by British sinologist Joseph Needham (16) to describe the philosophy underlying much of the Chinese view of science and medicine. The specific context in which macrobiotics has come to be thought of as an approach to cancer was popularized initially by Japanese philosopher George Ohsawa and his students, in particular, Michio Kushi (17).

Most people who would describe themselves as following a macrobiotic lifestyle probably have not been diagnosed with cancer or other serious illnesses; hence it is a misperception for macrobiotics to be perceived strictly as a diet for treatment of disease. Michio Kushi, the most well-known proponent of macrobiotics in the world, has authored books describing the philosophical bases of macrobiotics (9,18) as well as his own motivations for devoting his life to macrobiotics (18). His dedication to macrobiotics came out of his experiences as an eyewitness to the devastation of World War II, his subsequent studies in political science and a search for solutions for world peace. He wrote, "I realized that it was essential to recover genuine food, largely of natural, organic quality, and make it available to every family at reasonable cost. Only then could consciousness be transformed and world peace achieved" (18, p. 30). Kushi described his use of the word macrobiotics:

"I adopted 'macrobiotics' in its original meaning, as the universal way of health and longevity which encompasses the largest possible view not only of diet but also of all dimensions of human life, natural order, and cosmic evolution. Macrobiotics embraces behavior, thought, breathing, exercise, relationships, customs, cultures, ideas, and consciousness, as well as individual and collective lifestyles found throughout the world.

"In this sense, macrobiotics is not simply or mainly a diet. Macrobiotics is the universal way of life with which humanity has developed biologically, psychologically, and spiritually and with which we will maintain our health, freedom, and happiness. Macrobiotics includes a dietary approach but its purpose is to ensure the survival of the human race and its further evolution on this planet. In macrobiotics—the natural intuitive wisdom of East and West, North and South—I found the Medicine for Humanity that I had been seeking."

Despite the broad view of macrobiotics presented by these excerpts, in recent years, macrobiotics has come to be known largely as a dietary approach to cancer. This is no doubt due in part to the case histories noted above (1–7). This is also evidenced in part by the Office of Technology Assessment's publication, *Unconventional Cancer Treatments*, in which macrobiotic diets are listed along with the Gerson Treatment and Kelley Regimens as a common dietary approach to the treatment of cancer (19). The well-regarded book on complementary cancer therapies by Lerner, *Choices in Healing: Integrating the Best of Conventional and Complementary Approaches to Cancer* (20), devotes one chapter to macrobiotics. Indeed, the macrobiotic diet is one of the most popular alternative approaches used by people with cancer (19,21–23).

Aside from diet, other aspects of the application of macrobiotic principles may also be beneficial for cancer prevention, including an emphasis on physical activity, avoidance of exposures to pesticides and other chemicals as well as to electromagnetic radiation, and stress reduction (3,9). Macrobiotic philosophy promotes the concept that phenomena are universal and interrelated, and thus the practice of macrobiotics engenders a respect for the spiritual nature of life (9). In addition, a lifestyle intervention such as macrobiotics presupposes active participation of the individual. Eating macrobiotically can restore a sense of power and agency as the patient takes active steps to alter the course of treatment. Conventional cancer treatments, on the other hand, are inherently disempowering because the patient is the recipient of therapy that can be overwhelmingly painful and debilitating and completely out of the patient's control. These factors may also be important in cancer prevention and survival and in improving the quality of life of people with cancer (24,25).

Macrobiotic dietary guidelines

The standard macrobiotic diet provides a framework that is modified depending on one's age, sex, level of activity, personal needs and environment. It incorporates a respect for traditional food and for climatic and seasonal influences on food availability and personal and societal activity. It is also based in large part on the application of Eastern philosophical principles of yin and yang and related expressions of energetics such as the theory of five transformations (9). Thus, the macrobiotic diet is tailored to meet the needs of an individual rather than reflect a rigid set of structures.

The standard macrobiotic diet can be described from a macronutrient perspective as one that emphasizes a high complex carbohydrate, low fat diet. One survey of 50 people consuming a macrobiotic diet noted that total fat intake averaged 23% of energy and total carbohydrate intake averaged 65% of energy (26). Saturated fat intake averaged an extremely low 4.5% of energy, less than polyunsaturated fat intake, which averaged 7.1% of energy. Dietary cholesterol intake averaged 76 mg/d, demonstrating that although the

macrobiotic diet is not a strict vegetarian diet, it is very low in animal intake.

To the extent possible, foods are recommended to be organically grown and minimally processed. The diet consists of the following types of foods (3,9): *1*) 40–60% by weight whole cereal grains. This includes brown rice, barley, millet, oats, wheat, corn, rye, buckwheat and other less common grains and products made from them such as noodles, pasta and bread. *2*) 20–30% vegetables, preferably locally grown, prepared in a variety of ways. This may include smaller amounts of raw or pickled vegetables. *3*) 5–10% beans of various types, such as azuki, chickpeas or lentils; bean products such as tofu, tempeh or natto. *4*) Regular consumption of sea vegetables, cooked with the beans or as separate dishes. *5*) Occasional foods to be consumed a few times per week or less often, including fruits, white meat fish, and seeds and nuts.

Foods that are generally avoided on a standard macrobiotic diet include meat and poultry, animal fats including lard or butter, eggs, dairy products, refined sugars and foods containing artificial sweeteners or other chemical additives. Consumption of genetically modified foods is also discouraged. In the context of cancer, these restrictions may be absolute for a period of time until some recovery has occurred. The stories of both Sattilaro (1) and Kohler (2) detail an initial period in which all animal foods and fruit were to be avoided, followed subsequently by periods in which these foods were reintroduced into their diets.

More recently, Michio Kushi, the primary proponent of macrobiotics, introduced the macrobiotic Great Life Pyramid. This is presented in **Figure 1**. As can be seen, it differs from other alternative food guide pyramids (such as the Mediterranean food guide pyramid (27) or vegetarian food guide pyramid (28) in its explicit inclusion of sea vegetables and a deemphasis, but not exclusion, of fruit (but not vegetable) intake. Like other alternative food guide pyramids and unlike the USDA Food Guide Pyramid (29), red meat and dairy food intakes are minimized.

Potential anticarcinogenic properties of the macrobiotic diet. Many aspects of the dietary pattern promoted under standard macrobiotic dietary recommendations have been suggested to have anticancer effects. For example, whole grains have been emphasized as a centerpiece of macrobiotic dietary recommendations for many years. There is growing evidence that whole grain consumption decreases the risk of cancers at various sites (30,31). The effects of whole grains on cancer prevention are probably not limited to dietary fiber effects but may also involve effects on estrogen metabolism, glucose and insulin metabolism, and oxidative processes (32). A wide variety of vegetables are also recommended for regular consumption. The evidence that vegetable intake is associated with decreased risk of cancer is large and consistent and was reviewed in the American Institute for Cancer Research and World Cancer Research Fund report (8). This report noted that increasing consumption of vegetables and fruits from ~250 to 400 g/d may be associated with a 23% decreased risk of cancer worldwide. It has been suggested that sea vegetables, promoted in macrobiotics and an important part of traditional East Asian cuisine, may decrease risk of breast cancer (33,34)

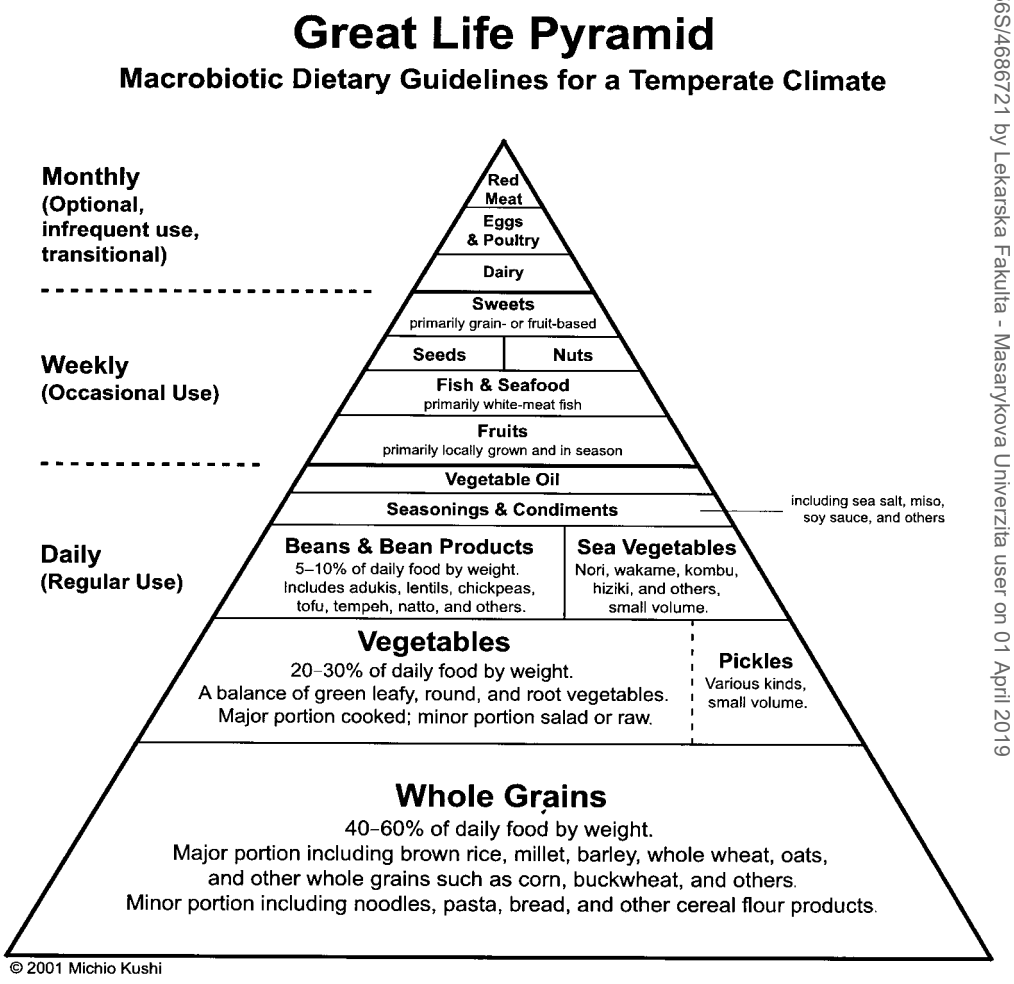

FIGURE 1 The Great Life Pyramid, showing macrobiotic dietary guidelines for a temperate climate. Note that these are guidelines that may be adjusted for climate and environment, cultural or ethnic heritage, gender, age, activity level, individual health concerns and personal needs and other considerations. Food consumed should be of natural quality, organically grown as much as possible and traditionally or naturally processed.

and endometrial cancer (35). These associations may be accounted for in part by the antitumor activities of fucoidan, a sulfated polysaccharide found almost exclusively in brown seaweed (36), and fucoxanthin, the carotenoid responsible for the brown color of brown seaweed (37,38).

The role of beans and bean products, particularly soyfoods, in cancer prevention continues to garner substantial interest. The interest in soy is based in part on the lower overall cancer rates in the Far East, where soyfoods are a traditional part of the diet, compared with the U.S. and other Western countries, where soyfoods are consumed in much smaller quantities. Some evidence shows that soy intake is associated with decreased risk of hormone-dependent cancers such as those of the breast (39–41), endometrium (35) and prostate (42) and may also decrease risk of other cancers such as those of the stomach, although this may be limited to nonfermented soyfoods (43). Soyfoods and other legumes may decrease risk of cancer because of the presence of various compounds that may have anticancer effects, including protease inhibitors and saponins (44). There has been a particular interest in the role of phytoestrogens such as genistein and daidzein, which are found in high concentration in soybeans. These isoflavonoid compounds may not only influence estrogen metabolism but may also have antioxidant and antiangiogenesis effects and may influence signal transduction and inhibit the action of DNA topoisomerases (45). Phytoestrogen exposure through the macrobiotic diet is discussed below.

Some foods that are linked to increased cancer risk are minimized in standard macrobiotic dietary recommendations. In contrast to the cancer-prevention effects of whole grains, refined grains, which are not recommended in macrobiotics, may actually increase risk of cancer (46). With the exception of fish, animal food intake is generally minimized in macrobiotics. There is growing evidence that red meat intake increases the risk of cancers of the colon and rectum (47) as well as cancers of the prostate (48), pancreas (49) and perhaps other sites (8). Eggs may be associated with increased risk of colorectal (8) and ovarian cancer (50), and dairy food intake is associated with increased risk of cancers of the prostate (8,48,51), kidney (8) and ovary (50). A preference for natural, organically grown foods would minimize exposure to pesticides, herbicides and other such chemicals. Although the association of dietary exposure to such chemicals and cancer risk is controversial, some reports have suggested that exposure to such compounds should be minimized (52).

Potential detrimental effects of a macrobiotic diet. Because early macrobiotic books emphasized the use of a 10-d grain-only "fast" as a cleansing regimen (53), a mistaken perception arose that the goal of macrobiotics was to achieve such a 100% grain-only diet. This led to early condemnation of "Zen" macrobiotic diets by the American Medical Association (54). Although this view of macrobiotics was clearly mistaken, a vegetarian diet devoid of animal products can be consistent with macrobiotic principles. Case reports of infants with symptoms of malnutrition, including deficiencies of vitamin B-12 and vitamin D, have been reported in the literature (55–57). With systematic surveys of groups of infants and families following a macrobiotic lifestyle, the possibility of the occurrence of such nutritional deficiencies has been documented (58–64). Although the direct relevance to cancer prevention and therapy of such observations of nutrient deficiencies, observed primarily in infants and growing children, is questionable, such reports largely form the basis for warnings against use of macrobiotic diets for cancer treatment (65). The link that is made in such warnings is based on the problems of cachexia and weight loss among cancer patients, thus the supposition that risk of nutritional deficiencies should be minimized. On the other hand, it has been suggested that these same qualities may be responsible in part for the cancerostatic and therapeutic potential of macrobiotics diets (66).

Biomedical literature related to macrobiotics and cancer

Macrobiotics and cancer prevention. Few studies have looked specifically at the macrobiotic diet in the context of cancer prevention. Studies by Goldin et al. (67,68) comparing women eating a macrobiotic diet with women eating a typical U.S. diet suggest differences in estrogen metabolism (**Table 1**). Women eating a macrobiotic diet had substantially higher fecal excretion and lower urinary excretion of estrogens, with somewhat lower serum levels of estradiol. Goldin et al. (68) suggested that these differences indicated a lower risk for breast cancer for the women eating macrobiotically. Although these conclusions were somewhat speculative, several prospective cohort studies published since these observations have reported a direct association between elevated blood estradiol levels and subsequent risk of breast cancer (69). Differences in urinary estrogen excretion along the lines of those observed with macrobiotics have also been associated with decreased breast cancer risk (70). If the cross-sectional observations of Goldin et al. (67,68) are confirmed in intervention studies in which following a macrobiotic diet results in lower blood estradiol levels, this would strengthen the inference that macrobiotic diets may decrease risk of hormone-dependent cancers. Such a study, funded by the National Institutes of Health's National Center for Complementary and Alternative Medicine, is currently underway at Columbia University.

In subsequent studies by Adlercreutz et al. (71,72), it was demonstrated that women consuming a macrobiotic diet had dramatically higher urinary excretion levels of lignans such as enterolactone or enterodiol and of isoflavonoids such as daidzein and equol than did women consuming a lacto-ovo-vegetarian diet or an omnivorous diet; women with breast cancer had the lowest urinary excretion levels of these phytoestrogens. This is shown in **Table 2**, which is taken from a paper by

TABLE 1

Fecal, urinary and plasma hormone levels among women consuming macrobiotic or usual American diets[1,2]

Hormone	Omnivores (n = 10)	Macrobiotics (n = 10)
Fecal excretion, *nmol/24 h*		
Estrone	0.83 (0.70–0.99)	1.96 (1.68–2.29)
Estradiol	0.61 (0.52–0.72)	1.52 (1.30–1.78)†
Estriol	0.72 (0.63–0.83)	1.72 (1.50–1.98)‡
Total estrogens	2.33 (2.01–2.70)	5.40 (4.70–6.21)†
Urinary excretion, *nmol/24 h*		
Estrone	15.3 (13.8–17.0)	16.8 (15.0–18.8)
Estradiol	9.3 (8.6–10.0)	9.3 (8.5–10.2)
Estriol	21.0 (19.1–23.1)	13.2 (11.6–15.0)†
Estriol-3-glucuronide	38.5 (36.0–41.2)	28.0 (24.8–31.6)
Plasma levels, *nmol/L*		
Estrone	0.40 (0.36–0.44)	0.34 (0.32–0.36)
Estradiol	0.32 (0.29–0.36)	0.26 (0.23–0.39)
Testosterone	1.13 (1.05–1.22)	1.15 (1.08–1.22)
Androstenedione	4.38 (4.17–4.60)	4.91 (4.68–5.16)

[1] Adapted from Goldin et al. (68).
[2] Values are geometric means and standard error ranges.
† Significantly different from omnivores, $P < 0.05$.
‡ Significantly different from omnivores, $P < 0.01$.

TABLE 2

Urinary excretion of lignans and isoflavonic phytoestrogens in young women on various habitual diets[1,2]

	Omnivores	Lactovegetarians	Macrobiotics
		nmol/24 h	
Boston women			
Enterolactone	2050	4170	17680
Enterodiol	280	740	6260
Daidzein	320	1260	3460
Equol	69	100	868
O-Desmethylangolensin	33	106	378
Helsinki women			
Enterolactone	2460	3650	
Enterodiol	203	368	
Daidzein	219	275	
Equol	102	64	
O-Desmethylangolensin	25	43	

[1] Adlercreutz et al. (71), with permission from Elsevier Science.
[2] Values are geometric means.

Adlercreutz et al. (71). For example, omnivores in Boston were observed to excrete ~2050 nmol enterolactone/24 h, whereas lactovegetarians excreted ~4170 nmol/24 h and women eating macrobiotically excreted 17,680 nmol/24 h (71). For other urinary phytoestrogens, lactovegetarians excreted between 1.4 and 3.9 times the amount excreted by omnivores, whereas women eating macrobiotically excreted from 11 to 22 times the levels seen in omnivores. Although the evidence that phytoestrogens are important in breast or other cancers is still controversial, at least one study reported an inverse association of urinary excretion of phytoestrogens with risk of breast cancer (73).

The markedly higher phytoestrogen excretion levels among women consuming a macrobiotic diet are likely a result of the foods eaten by these women. Concentrated sources of lignans in the macrobiotic diet include whole grains, seeds and other foods. Soyfoods and other legumes that are sources of phytoestrogenic isoflavonoids are also consumed regularly. Indeed, there was a strong correlation ($r = 0.99$) between grain intake and urinary enterolactone excretion on a group basis, comparing women consuming various diets (71). Overall, the above combined results suggest that a macrobiotic dietary pattern may carry a lower risk of breast and other hormone-dependent cancers such as those of the prostate or endometrium than other vegetarian diets or typical omnivorous diets.

Note that although studies of direct relevance to the role of the macrobiotic diet in cancer prevention are few, several studies investigated the macrobiotic diet in the context of cardiovascular disease risk. As may be expected from the dietary patterns and food recommendations of macrobiotics, these studies demonstrate consistently that people consuming a macrobiotic diet are at lower risk of cardiovascular disease than is the general population because of substantially lower blood cholesterol levels (26,74–78), lower blood pressure (74,75) and higher plasma levels of antioxidants relative to cholesterol (79). These studies also indicate that people consuming a macrobiotic diet have low body weight (75,76), which is also associated with decreased risk of several cancers (8).

Macrobiotics and cancer therapy. In addition to the accounts of individual recovery from cancer by Kohler and Sattilaro cited earlier, a number of other reports of recovery from cancer have been published in recent years. These include complete books, such as accounts of recovery from malignant melanoma by a nurse (4), from pancreatic cancer by a physician (5) and from carcinosarcoma of the uterus with multiple metastases (6), and compilations of case histories (7). As noted by the Office of Technology Assessment, however, "although these various accounts reflect the authors' beliefs that they were helped by following a macrobiotic diet, they are nevertheless inadequate to make an objective assessment of the efficacy of the diet in treating cancer" (19, p. 64).

At least four attempts have been made to obtain more systematic information regarding the efficacy of the macrobiotic approach to cancer. All were hampered by a retrospective design. The first effort was conducted under the direction of one of the coauthors (R.H.L.), then Director of the Clinical Nutrition Unit at University Hospital in Boston. He and his colleagues attempted to follow up individuals who had visited the Office of Michio Kushi for cancer during 1981–1984. An unfunded proposal for this project was submitted to the American Institute for Cancer Research in 1984 but was rejected because the peer reviewers felt that macrobiotics was unworthy of investigation. After securing a modest amount of independent funding, in 1986, questionnaires were sent to 548 subjects who sought counseling from Michio Kushi because of cancer between 1981 and 1984. Subjects were limited to those with a U.S. address in Kushi's files. Ninety-eight responses were received, for a response rate of 17.9%. Profiles of respondents indicated that 68% were alive. Ninety-one percent of subjects received at least one form of standard therapy such as chemotherapy, and 56% used unconventional therapies other than macrobiotics, such as vitamin and mineral supplementation (20%), visualization (20%) and laetrile (7%). Sixty-one percent reported close adherence to macrobiotic recommendations, 10% partial adherence and 1% none at all.

As noted in **Table 3**, subjective reports of beneficial effects of macrobiotics on cancer were reported by substantial proportions of respondents. Subjective improvements were noted in tolerance to chemotherapy or radiation, overall health, emotional well-being and family-social relationships. A substantial majority of respondents reported that spouses (90%) and family members (82%) were generally supportive of the use of macrobiotics, whereas only a minority of respondents (25%) reported that their physicians were supportive. Indeed, a similar proportion of respondents (19%) reported that their physicians were opposed to their use of macrobiotics and 6% did not inform their physician. The other 50% reported that their physicians were indifferent to the use of macrobiotics.

Because diagnoses were not confirmed by medical records or other objective documentation and because of the low overall

TABLE 3

Proportion of respondents reporting subjective effects of macrobiotics on topics related to living with cancer, among 98 cancer patients who sought macrobiotic counseling, 1986

	Effect of macrobiotics		
Topic	Beneficial	Detrimental	No effect
		%	
Tolerance to chemotherapy or radiation	59	2	39
Overall health	82	3	10
Emotional well-being	85	6	7
Family-social relationships	43	19	32
Overall effect of macrobiotics	68	4	24

response rate of 17.9%, it is difficult to make much of the results of this attempt to obtain more systematic information about the effects of macrobiotics on cancer patients. Unfortunately, because of a lack of financial and other resources, it was impossible at the time either to obtain medical records or to attempt to increase response rates to provide better precision of survey responses. However, the results of this survey do suggest that most people with cancer who seek personal advice about macrobiotics do so in addition to or after conventional therapy. It also indicated that a substantial proportion of such patients encountered opposition from their physicians or did not inform their physician at all regarding their use of macrobiotics for cancer.

A second attempt was conducted by Gordon Saxe while a graduate student at Tulane University, and under the direction of James Carter (19,80). This is the only effort to evaluate macrobiotics for cancer that has been published in the peer-reviewed literature (80). This study involved two components, one focused on primary pancreatic cancer, the other focused on advanced prostate cancer. In both cases, study subjects were individuals who had sought advice about macrobiotics from a certified counselor. Through the use of records kept by macrobiotic counselors, 109 people were identified who had seen a counselor for pancreatic cancer in 1980–1984. Attempts were made to recontact these individuals, and 36 of them (or their next-of-kin) could be reached. Of these, 23 reported that they had followed a macrobiotic diet for at least 3 mo. The median survival of the 23 individuals who had followed macrobiotics was 13 mo after diagnosis compared with a median survival for pancreatic cancer patients from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program of 3 mo (81).

Unfortunately, this report was flawed in that comparison of survival times were biased in favor of macrobiotics. Most importantly, the 23 individuals in the macrobiotic series had to have survived at least 3 mo in order to be included. As noted by the SEER data, 50% of all people diagnosed with pancreatic cancer are dead at 3 mo after diagnosis. Lack of information on other factors that may influence survival in both the macrobiotic series of people with pancreatic cancer and the people in the SEER program also limits the interpretability of this study. The prostate cancer component of the Tulane study was similarly flawed. In this study, the 11 individuals with prostate cancer had a median survival of 81 mo compared with a median survival of 45 mo in matched control subjects. It was unclear on what criteria control subjects were matched or from where they were selected.

A third attempt at obtaining objective information about the efficacy of macrobiotics in cancer therapy was a compilation of cases by Vivien Newbold, a physician in Pennsylvania. Newbold collected information on six case histories of patients who used macrobiotics for their cancer; all but one of these were biopsy-proven (19). The Office of Technology Assessment requested an independent review of these cases by several mainstream and unconventional physicians who were consultants to their report on unconventional cancer therapies (19). Although the cases appeared to be well-described, the three mainstream physicians who were asked to review the cases did not find that they provided compelling evidence of benefit from macrobiotics. In most of the cases, the effects of conventional therapy could not be ruled out adequately; one case had no verification of the continued presence of cancer at the time macrobiotics was started. The unconventional physicians found the cases to be more supportive of a role for macrobiotics but disagreed on the extent of support in these cases. The Office of Technology Assessment did suggest, however, that "If cases such as Newbold's were presented in the medical literature, it might help stimulate interest among clinical investigators in conducting controlled, prospective trials of macrobiotic regimens" (19, p. 66).

The fourth attempt to examine macrobiotics in the context of cancer therapy was initiated in 1994. As a first step in determining whether an alternative therapy is worthy of investigation, the Division of Cancer Treatment, National Cancer Institute, established criteria for identifying best cases that may indicate a promising alternative therapy. This project was an effort to assemble such a best-case series of individuals with cancer who had followed a macrobiotic diet. The objective of this study was to determine whether a basis sufficient to justify further rigorous studies of the macrobiotic approach to cancer exists. Preliminary findings from this study were presented at the 1996 Annual Meeting of the American Public Health Association.

Potential best cases were identified by counselors affiliated with the Kushi Institute (Becket, MA) and other macrobiotic centers and through press releases in six macrobiotic or alternative health magazines. From late 1994 through September 1995, 233 such people were identified. A questionnaire was sent to these individuals to determine eligibility for consideration as a best case. A total of 126 (54%) responded; of these, 37 were ineligible because of their use of chemotherapy or radiation concurrent with macrobiotics, surgical removal of tumor, nonmacrobiotic diets, inadequate diagnosis or noncancerous condition or no clinical follow-up after initial medical therapy. Detailed questionnaires and permission to obtain medical records were sent to the remaining 89 individuals. A total of 72 cases of individuals who had tried macrobiotics for cancer, and for whom at least some medical records were obtained, were thereby assembled. These 72 cases include cancers of the prostate (26%), breast (16%), malignant melanoma (10%), astrocytoma (7%) and other cancers. Although review of these cases is incomplete, preliminary indications suggested that several of these cases warrant inclusion in a best-case series.

This study was supported initially by a grant from the National Institutes of Health's Office of Alternative Medicine (a predecessor to the National Center for Complementary and Alternative Medicine). Hampered by various bureaucratic hurdles and limited funds, the study was not completed at the time of initial funding. However, funding from the Centers for Disease Control and Prevention under the direction of one of us (J.T.) has allowed this study to proceed.

In summary, none of the four attempts to establish a basis for documenting a rationale for further investigation of macrobiotics in the context of cancer therapy has been particularly successful. Although they have documented a real interest in the use of macrobiotics and indeed have also identified individuals who attribute some benefit to macrobiotics, none provides a strong basis for determining whether macrobiotics is effective for cancer.

Summary and future directions

Macrobiotic diets are among the most popular alternative approaches to management of cancer in use in the United States today (19,21–23). This interest in macrobiotics is fueled by the lack of effective conventional therapies for many of the major cancers and by case reports of dramatic recovery from cancer in which macrobiotics was used (1–7). The recognition that dietary factors play a prominent role in cancer prevention (8) and that standard macrobiotic dietary recommendations are one expression of public health recommendations to de-

crease cancer risk (8,10) has also increased interest in the macrobiotic approach to cancer. There is also increasing recognition that dietary factors may play a role in the progression of cancer after diagnosis despite the relatively few studies to examine these relationships (14).

Although no studies have examined directly the effect of macrobiotics on cancer prevention, studies have indicated that women following a macrobiotic diet have somewhat lower plasma estradiol levels (67,68) and higher urinary excretion levels of phytoestrogen metabolites (71,72) and therefore may be at lower risk of hormone-dependent cancers. In addition, various foods or food groups recommended for consumption in standard macrobiotic dietary recommendations are associated with decreased risk of cancer, and other foods that are generally minimized in macrobiotic diets are thought to increase the risk of cancer. Thus, it is reasonable to suggest that the macrobiotic diet may carry a substantially reduced risk of cancer in comparison with standard U.S. dietary patterns.

The primary attempts to investigate macrobiotics in the context of cancer treatment have been to assemble series of cases of individuals who may have benefited from their use of macrobiotics for cancer. Such case series may provide a stronger justification for investigation of the role of the macrobiotic diet in cancer, but they are only an incremental step above the individual case histories recounted in popular books (1–7). To determine whether the macrobiotic diet—or any diet—is effective in preventing recurrence of cancer, enhancing quality of life or prolonging survival from cancer, more systematic studies using recognized study designs such as those of analytic epidemiology will be required. For example, using the tools of observational epidemiology, it may be possible to determine whether people following a macrobiotic lifestyle are at reduced risk of cancer or whether people with cancer who elect to follow macrobiotics enhance their quality of life and improve survival. Epidemiologic studies such as these prospective investigations are, in general, underutilized in either the study of alternative or complementary health practices or in the study of cancer recurrence and survival.

In designing intervention studies of the efficacy for cancer prevention or treatment of an intervention such as macrobiotics, it is clear that the fact that macrobiotics is not a single agent must be taken into account. The macrobiotic diet is individualized and multidimensional. In addition to the diet, psychosocial aspects of the adoption of macrobiotics may also play key roles in its effectiveness, as suggested by other studies indicating the potential importance of such factors (24,25,82–87). Although observational studies may attempt to measure the joint effects of both biological and psychosocial effects of macrobiotics, retrospective studies may be compromised by methodological issues such as biases in recall of relevant exposures. On the other hand, randomized, controlled trials of a behaviorally oriented and complex intervention such as macrobiotics may result in an underestimate of the magnitude of potential benefit. This is because the effects of the intervention may be modified by the extent of the subject's interest and active participation. Although randomization is idealized as the optimal method by which efficacy of an intervention is judged, it has several potential shortcomings, especially in instances in which interventions are wholly behavioral or have an important behavioral component (88–91). This clearly would be the case with macrobiotics. Hybrid designs that compare randomization with self-selection may allow the study of the effect of crucially important motivational and expectancy variables on participation and outcome (89,91–93). Such designs also offer a model that permits exploration of the effect of transition from pure efficacy research toward real-world clinical effectiveness. The explicit study of self-selection also can be seen as promoting subjects' roles as active partners in the choice and management of their health care (20,94). The study of macrobiotics represents an excellent opportunity to put these principles of study design into play.

In the absence of such studies, the role of macrobiotics or other dietary or lifestyle interventions in cancer therapy, remains in the realm of speculation. Although such speculation may be informed by direct experience or an understanding of possible biological mechanisms, comments regarding the effectiveness of diet in cancer therapy are likely to expose the biases of the commentator as much as provide insight into the possible role that diet may play in this area. Studies for secondary prevention of breast cancer such as the ongoing Women's Intervention Nutrition Study (95) examining a low fat diet and the Women's Healthy Eating and Living Study (96) examining a vegetarian diet, are necessary to determine whether dietary factors, including the macrobiotic diet, may be helpful in the context of cancer therapy.

In summary, the role of the macrobiotic diet in cancer prevention and survival has not been investigated adequately to justify scientifically the recommendation that macrobiotics be used in the context of cancer. However, the lack of studies that examine directly the effects of macrobiotics on cancer prevention, survival or quality of life cannot be taken as evidence against a beneficial effect of macrobiotics. In particular, there is extensive indirect evidence that macrobiotic dietary patterns are associated with reduced cancer risk as well as the potentially reassuring results of the few studies that evaluated directly the effects of the macrobiotic diet on estrogen metabolism and cardiovascular risk. Finally, the popularity of macrobiotics among cancer patients underscores the importance of evaluating the value of macrobiotics for cancer prevention and survival.

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This paper is dedicated to Ms. Aveline Tomoko Kushi (February 27, 1923–July 3, 2001).

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