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CANCER – RELATIONSHIP TO LIFESTYLES

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INTRODUCTION

Cancer incidence varies substantially across different regions of the world. It is well recognized that genetic and environmental factors, particularly lifestyle, play separate and combined roles as risk factors of cancer. Nevertheless, the debate about the contribution of nature versus nurture in cancer epidemiology has been on-going for ages (Fisher 1958) and is still in vogue (Hoover 2000).

Attempts to determine the relative contribution of environment *versus* genetic factors to cancer incidence can be gleaned from observations in migrant populations. Within a few decades the Japanese immigrants in Hawaii and California had breast cancer rates approaching those of the Hawaiian white population and significantly higher than those of native Japanese. Conversely stomach cancer rates become significantly lower among Japanese in Hawaii than among native Japanese. Clearly, environmental factors, mainly lifestyle, seem to be more at play than genetic factors in these comparisons. But to be definitive, more comprehensive analyses are required.

This paper examines the importance of lifestyle factors in the 6 most common cancers in the Caribbean - prostate, breast, cervix, stomach, lung and colorectal.

CANCER MORTALITY IN THE CARIBBEAN

Although cancer is a major public health problem worldwide attention has traditionally focused more on cancer in the developed world. Caribbean countries have experienced an unprecedented epidemiological transition over the last few decades where total food availability has greatly improved, but much of the increase in caloric intake is due to fat. (Sinha 1995) This increased caloric and fat intake has been accompanied by a dramatic rise in obesity, cardiovascular diseases and cancer. This disease transition has brought into sharp focus the need for developing countries such as those in the Caribbean to target these chronic diseases for more direct attention. Figure 1 shows that mortality rates from all cancers in some Caribbean countries are as high as in North America. For specific cancer sites such as prostate and cervix the mortality rates in the Caribbean are much higher than in the USA where the reverse is true for lung cancer. (Table 1)

Table 2 shows the six cancers causing the highest mortality in the Caribbean relative to the USA as the base rate. The global mortality rate is also included for comparison. Clearly cancers of the prostate and cervix in the Caribbean are among the highest in the world.

- The gravity of the problem has deepened over the years. Between the 1960s and 1990s the increase in mortality from nutrition-related cancer ranged from a low of 1.3% in Belize to 12.9% in St. Vincent (Table 3). Not only are the rates of some cancers in the Caribbean higher than in North America but the trends in the former are increasing while the latter are decreasing. This trend emphasizes the critical point regarding priority setting for such chronic diseases. The point goes deeper. The cost of treating cancer is enormous and is more than six times higher in developing countries than in developed countries (Cromwell, 1979). This imbalance in cost arises because the hospital procedures have a high foreign-exchange content, involving specialized training of staff and purchase of drugs and equipment. While the program of cancer treatment must continue in the Caribbean, it cannot be the long term approach to combat cancer. This paper contends that lifestyle factor, particularly dietary habits, must be central to efforts to control cancer in the region. The following observations add weight to this contention.

Figure 2A shows the strong correlation (r = .86) between Energy fat and all cancers. Although the correlation with breast cancer (Figure 2B) is not as strong (r= .57) the positive pattern is evident. Conversely, the negative correlation with plant foods for all cancers (r = .82) and for breast cancer (r = .52) also demonstrate a clear

trend (Figures 3A& 3B). Even though ecological analyses of risk are not definitive, the strong correlations shown here are compelling.

PREVENTION

Many cancers, if detected and treated early, may never cause problems again. Early cancer treatment can almost be regarded as another form of prevention. But cancer prevention strictly refers to the process of reducing the age-specific incidence rate of cancer. Efforts to prevent cancer should therefore be directed at the main causal groups. There are four such target groups (1) the background "spontaneous" group where random mutations occur in normal people. The prospect of totally eliminating it is bleak because all types of cancer occur at a background rate in nature due to these random events; (2) The environmental group where mutations may be caused by smoking, alcohol, diet, chemicals, radiation, viruses, or a combination of these factors. These may cause damage to the DNA, interfere with its repair or promote the growth of damaged cells; (3) The environmental/genetic group made up of people who are at greater risk from exposure to carcinogens owing to pharmacogenetic polymorphisms; and (4) The exclusive genetic group, in whom genetic susceptibility is more important than either spontaneous or environmentally induced events. For this group mutant genes were passed on in either the sperm or ova by the patients. These individuals have a high risk of developing the cancer characteristic of the gene mutation type. It is of interest to note that in the majority of common cancers, affected patients have no family history of cancer and the genetic damage occurs in the organ where the cancer first arises.

To have confidence in any preventive approach, however, it is useful to know the role of genetic constitution and environmental exposure in the causation of cancer. Until recently, it was impossible to tell the difference between spontaneous and inherited cancers. However, by examining tumors with microarray technology, scientists have been able to develop a relatively simple way to tell them apart. The upsurge in molecular genetics has overshadowed environmental explanations by revealing genetic mechanisms underlying cancer. This has created much confusion among patients, researchers and policy makers. Current work on the human genome will no doubt

identify numerous genes that may affect susceptibility to tumor development.

In 1991 it was estimated that between 5 and 10% of cancers have a genetic family link (Easton 1991). A landmark paper published recently (Lichtenstein 2000) estimates the genetic predisposition to various cancers compared with the contribution from environmental factors. This study has several advantages over previous work that attempted to unravel the nature-nurture debate. The investigators examined as many as 44,788 pairs of twins, the study was population based and the outcomes were derived from complete data on incidence. The findings shows that inherited genetic factors make an important but a minor contribution to susceptibility and that the environment had the principal role in causing cancers.

The relative contribution of genetic and environment factors will be presented for each of the cancers below.

1. Prostate

Prostate cancer has become a major public health problem worldwide. In populations across the world rates are increasing, partly due to the widespread use of prostate specific antigen – the results of which are not always precise. False positive findings often lead to controversy regarding the screening process and this is complicated by its poorly understood natural history. Although numerous studies have been done on prostate cancer in recent decades several basic elements of the disease are still baffling. For example, it remains a mystery that among the more than one thousand species of mammals why only humans and dogs have any significant risk of dying of prostate cancer.

Among all cancers, heritable factors alone were estimated to have the largest effect (42%) with prostate cancer (Lichtenstein, 2000). Nevertheless, one of the chief causes of prostate cancer may be related to diet. A recent study shows that the consumption of fish is associated with significant lowering of the risk of prostate cancer (Terry, 2001). Diets low in meat and other fatty foods of animal

origin may prevent 10-20% of cases. It is suggested that diets high in a variety of vegetables and fruits may prevent between 10-20% of cases of cancer (Jansen 1995).

2. Breast

The primary reason for the escalating mortality of breast cancer in developing countries is late diagnosis. (Pinotti, 1995). The causal evidence on cancer of the breast is clearer than for the prostate. Hormonal events are central to its etiology even though some of the main determinants of risk are probably related to diet. Between 11% and 30% of breast cancer cases have been attributed to obesity (IARC 1990). Diets high in a variety of vegetables and fruits have been estimated to prevent 10-20% of cases (Jansen 1995). Heritable factors alone are estimated to contribute 27% to this cancer.

3. Cervix

Cervical cancer is both preventable and curable, if detected early. In developed countries 80% of cervical cancers are cured because of early detection. In contrast, in developing countries, 80% of cervical cancer cases are incurable at the time of detection. Infection with Human Papillomavirus (HPVs) is the most important non-dietary cause of cervical cancer. Risk is also increased by smoking tobacco. Diets high in vegetables and fruits possibly protect against this cancer. It is estimated that cessation of smoking, protection against HPVs and diets high in vegetables and fruits can reduce incidence of cervical cancer by up to 20% (Jansen 1995). There is no contribution of heritable factors by itself to cervical cancer (Lichtenstein, 2000).

4. Stomach

Stomach cancer is strongly related to diet. Helicobacter pylori infection is a non-dietary cause, but this infection may interact with dietary factors. Heritable factors are estimated to contribute 28% to this cancer (Lichtenstein, 2000). Diets high in a variety of vegetables and fruits, together with the use of freezing and refrigeration to preserve perishable food, and a low consumption of salt and salted foods may prevent up to 75% of the cases of stomach cancer.

5. Lung

Smoking is the most important cause of lung cancer. Tobacco use, together with specific occupational exposures is estimated to cause around 80% of the cases. (IARC 1990). It is estimated that diets high in vegetables and fruits may prevent up to 33% of lung cancer cases in both smokers and non-smokers. Heritable factors are estimated to contribute 26% to lung cancer (Lichtenstein, 2000).

6. Colon and rectum

The main causes of colorectal cancer are dietary factors,(Jansen 1995) although more is known about colon than about rectal cancer. Diets high in vegetables, and therefore high in fibre, low in meat, the avoidance of alcohol and regular physical activity may reduce the incidence of colorectal cancer by up to 75%. Heritable factors appear to make the second largest contribution (35%) to this cancer (Lichtenstein, 2000). Table 4 summarizes the contribution of various factors to the six most common cancers in the Caribbean.

RELATION TO LIFESTYLE

The major impact on cancer is likely to come through interventions focusing on healthy lifestyle behavior. Below are some of the key aspects to be considered.

(i) Body size

Overweight is the nutritional factor for which the evidence is most convincing and for which the quantitative impact on overall cancer rates is most important. Epidemiological studies have consistently shown that excess body mass is associated with increased risk of cancer particularly of the endometrium, breast and colon. It is important to note that excess risk of these cancers increases continuously with greater adiposity and is not limited to the standard cut-off point for obesity i.e. BMI >30. It is estimated that excess body weight (BMI > 25) accounts for approximately 5% of total cancer incidence (Bergstrom, 2001).

(ii) Fat

Fat is the most energy-dense constituent of the diet and there is no doubt that diets high in fat increase the risk of obesity and therefore are an indirect risk for obesity-related cancers through excess body weight.

The hypothesis that high fat intake is a major cancer risk factor has been at the center of much controversy. Studies have found a positive and significant correlation between fat intake and the incidence of breast cancer [Armstrong 1997). Various studies, however, generally found either weak associations between fat intake and cancer risk, or no association, particularly after statistical adjustment for total energy intake (Hunter 1996).

Although several studies did not find any relationship between fat intake and breast cancer, it is still possible that a weak relationship exists, but it is obscured by the effect of random dietary measurement error (Prentice 1990). It is often speculated that the inconsistencies in the findings relating fats to cancers reflect varying biological effects of different fatty acids such as the n-3 or n-6 some of which may be beneficial and some adverse for tumor growth. There is, however, no clear evidence that different types of fats: n-3 and n-6 polyunsaturated, monounsaturated (n-9) or saturated fatty acids are risk factors for breast cancer. Further, the scientific data do not support an association between trans fatty acids and cancer (Ip 1996).

This controversy about whether dietary fat consumption influences cancer risk does not seem likely to be resolved in the immediate future. It is therefore prudent at this time to recommend weight control focusing on limitation of excessive energy intake from any source and the adoption of adequate daily physical activity.

There is much speculation on the possible mechanisms in the relationship between fat intake and breast cancer. The evidence is far from being conclusive we do know that fat is a major source of estrogen especially in post-menopausal women. In addition to this extra hormonal influence on the body created by obesity, fat, like water, is a universal solvent. This fatty storehouse for chemical pollutants then maintains high toxin levels in the body, subjecting the cells long term to unwanted chemical influences.

(iii) Physical activity

The hypothesis that physical activity protects against cancer development is not new. Since 1922 investigators have examined cancer mortality rates among men with different occupations. (Sivertsen 1922). After that initial work it was only in the last three decades that several studies focused on this hypothesis (Physical activity and Health: 1996) There is now convincing evidence that regular physical activity protects against colon cancer and possibly against cancers of the breast and lung (Hardman, 2001). Physical activity stimulates immune function and favorably affects hormonal balance. It certainly protects against overweight and therefore against cancers for which the risk increases with obesity.

(iv) Fruits and vegetables

The most consistent finding in diet and cancer research is the association observed between consumption of fruits and vegetables and reduced risk of several cancers. The consistency of the results provided by studies conducted worldwide suggests that vegetables and fruits all contain a great number of constituents thought to protect against cancer. The role of fruits and vegetables is so dominant as a cancer prevention factor that they deserve some elaboration.

Recent studies have shown that the dose–response is important. A very low intake of fruits and vegetables e.g. less than 2 servings or 200g per day is related to increases in risk of breast cancer but there may be little additional benefit for higher intakes. [Smith-Warner 2001). Much promising work has been done with phytochemicals in vegetables. The yellow vegetables have been found to contain a combination of factors including carotenoids, calcium, selenium and other micronutrients which work in concert to produce a strong anticancer effect. The plant chemicals – phytates, protease inhibitors, isoflavonoids show good promise as inhibitors of cancer genes.

Many vegetables and fruits are high in dietary fibre, which may protect against cancers of the stomach, pancreas, colon, rectum and breast. The phytates and lignans in fibre directly lower the production of free radicals. High fibre levels also speed up the transit time of

potential carcinogens through the bowel. Micronutrients in vegetables and fruits likely to protect against cancers include the antioxidant vitamins and minerals – beta-carotene, vitamins C and E and selenium. Carotenoids other than beta-carotene also have antioxidant or other potentially anti-carcinogenic actions, or both; these include lutein (a xanthophyll pigment in green vegetables) and alpha-carotene (in orange vegetables). Some studies have suggested that intake of tomato products high in lycopene (the red pigment) is inversely related to prostate cancer Giovannucci,1998).

Green leafy vegetables and citrus fruits are also rich in folic acid. Folate plays an important role in DNA metabolism. Folate deficiency may contribute to carcinogenosis through increased DNA damage (Choi, 2000). Cruciferous vegetables contain several potentially anticarcinogenic bioactive microconstituents and their intake is inversely associated with bladder cancer incidence (Michaud, 1999). Anticarcinogenic flavonoids are also found in many fruits and vegetables.

Although plausible biological pathways have been identified, the lack of epidemiological evidence to support existing experimental evidence means that it is not possible to come to any definite judgement about the role of these compounds in cancer risk.

(v) Foods - smoked, salted, and pickled

Foods processed to its refined white stste is also a serious offender because the processing removes vital minerals, vitamins and the plant phytochemicals which are so crucial to the body's normal healthy cellular function.

Children are currently estimated to get a large part of their daily calorie requirement from fizzy drinks and sweets. This is a major problem since these foods contain only "empty calories" with virtually no nutritional value. To compound the problem it is estimated that 47% of children currently eat no vegetables whatsoever other than chips. This means that while children may be getting more than enough energy and calories to continue to function and become obese, the vital nutrients required for healthy growth , immune function and intracellular protection from cancer are inexorably

depleted, making their vulnerability to major degenerative diseases such as cancer much more heightened.

The foods for which a positive association with cancer risk has been found consistently are red and processed meat for colorectal cancer.

High salt intake and consumption of salt-preserved foods probably increases the risk of stomach cancer. Convincing evidence would require confirmation in prospective studies and evidence that this relationship was not confounded by Helicobacter pylori infection.

It is generally believed that char-grilling meats and fats, and superheating fats, creates dangerous free radicals and carcinogenic compounds such as poly cyclic aromatic hydrocarbons. For similar reasons concern is also expressed about the safety of smoked foods. But there is no convincing evidence that curing or smoking modifies the risk of any cancer, nor is there evidence of any probable causal relationship. However, diets high in cured meats possibly increase the risk of colorectal cancer. Similarly, diets high in meats cooked at high temperatures possibly increase the risk of stomach and colorectal cancers.

(vi) Smoking

Tobacco is the chief cause of lung cancer and is implicated in several others. It is probably the most important single cause of the upper aerodigestive tract and drinkers who smoke greatly increase the risk of these cancers. Cigarette smoke is estimated to contain over forty different carcinogenic and irritant chemicals. In addition the heat of the smoke and the cigarette end can cause direct burning and irritation to the lips and upper aerodigestive tract. This continual burning irritation can create ideal conditions for cancer to develop. Smoking of any sort should be stopped, whether it is cigarette, pipe or cigar smoking. Further, tobacco is a cause of cancer whether smoked, chewed or consumed in other ways.

(vii) Alcohol

There is sufficient evidence that alcohol is carcinogenic to humans (Jensen 1996). The role of alcohol in breast cancer development is the most recent. This effect is probably caused by alcohol’s ability to

raise hormone levels in the body (Dorgan, 2001). The evidence that alcohol increases the risk of mouth and pharyngeal, laryngeal and esophageal cancers is also convincing. Alcohol probably also increases the risk of colorectal cancer. The increase in risk appears to be primarily due to alcohol per se rather than specific alcoholic beverages. Whereas most of the excess risk occurs with high alcohol consumption, a small (about 10%) increase in risk of breast cancer has been observed with approximately one drink per day (Longnecker, 1994).

(viii) Sexual Behavior

Prostate cancer incidence and mortality rates vary widely according to geography and race. (Hsing, 2000). The association of prostate cancer with sexual history and particularly sexually transmitted disease has been suggested by some studies. But these relations are not firmly established. The situation has similarities to that observed for cervical cancer before the association of human papillomavirus.

A recent study (Rosenblatt, 2000) showed no relation between lifetime frequency of sexual intercourse and risk of prostate cancer and therefore support an infectious etiology for prostate cancer. If an infectious cause of prostate cancer is found, this will provide an excellent opportunity prevention and treatment. But such a finding will not be easy to demonstrate as prospective studies will be required to provide evidence for an association between sexual behavior or sexually transmitted disease. Further technical difficulties loom since the effects being measured appear to be moderate and the prevalence of sexually transmitted diseases will not be high in most populations likely to volunteer for long follow-up studies.

(ix) Holistic body-mind approaches

There is now great interest in the role of stress, depression, isolation and emotional repression in depressing our immune function and on how these things affect our ability to both resist and ultimately survive serious disease. This interest also arises from the dissatisfaction of approaches that treat only the symptoms of disease without addressing the underlying causes. The holistic approach recognizes that human beings are very complex and the body, mind

and spirit interact in their functions to have profound affects on our health and well being.

Conclusion:

The media image of Western success is a lure to copy their economic and cultural practices. The Caribbean has rapidly adapted to the Western lifestyle and the strong inherent health risks associated with it.

There is now clear evidence that factors related to diet, nutritional status, anthropometry and physical activity influence the incidence of various cancers. Current public health recommendations should therefore focus on the benefits which can be expected from a diet rich in vegetables and fruit, the avoidance of overweight and a physically active lifestyle.

Finally, in comparing genetic and environmental factors it is clear that cancer is mostly a preventable disease. The chief causes of cancer are use of tobacco and inappropriate diets. Adopting healthy lifestyles are therefore the key to reducing the incidence and mortality from cancers. Prevention benefits not only the individual, but also communities and national economies. For the Caribbean, this should be the logical and most rewarding approach, because the chief lifestyle interventions for cancer prevention will also have substantial impact on the other chronic diseases which are the main causes of death in the region.

Figure 1

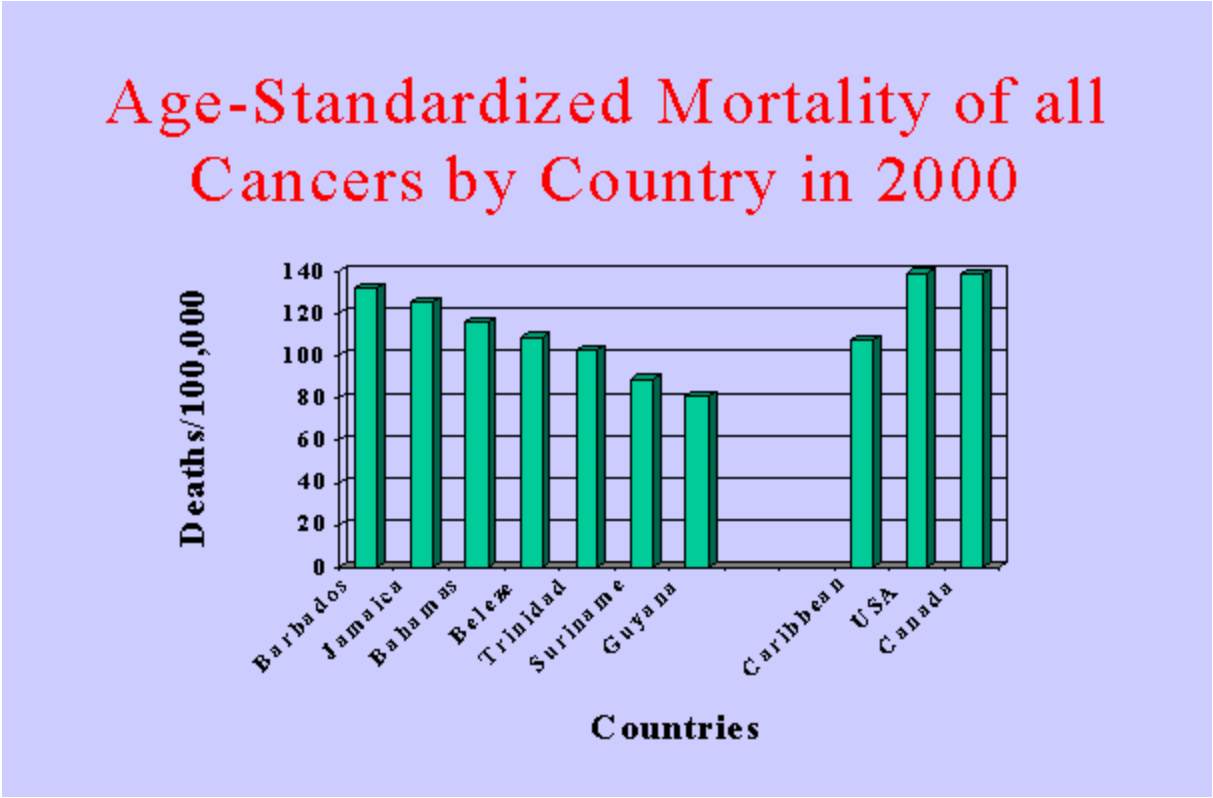


TABLE 1

AGE -STANDARDIZED MORTALITY RATES (PER 100,000) OF CANCERS IN 2000

	BARBADOS		JAMAICA		BAHAMAS		BELIZE		TRINIDAD & TOBAGO		SURINAME		GUYANA		U.S.A.	
Prostate	55.3		24.1		33.3		16.1		32.3		15.6		22.3		17.9	
Breast	25.5		22.0		23.0		11.7		20.6		9.9		11.1		21.2	
Cervix	13.6		18.4		9.3		16.7		15.0		18.1		20.6		3.3	
	M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**
Stomach	17.1	5.4	24.6	13.2	12.3	5.9	14.8	10.4	8.7	6.9	11.9	5.5	10.5	9.5	4.5	2.3

Lung	14.4	2.9	22.3	5.0	20.8	5.2	20.8	7.7	13.2	4.3	14.4	4.4	8.3	2.8	53.2	27.2
Colorectal	14.8	11.0	10.5	9.6	10.0	8.6	4.8	4.6	8.5	9.7	6.0	5.9	7.7	4.7	15.9	11.9

Source: Globocan 2000

Table 2. Comparison of Age-standardized Cancer Mortality Rates Relative to the USA.

CANCER SITE	PROSTATE Rank 1	BREAST Rank 2	CERVIX Rank 3	STOMACH Rank 4		LUNG Rank 5		COLORECTAL Rank 6	
				Male	Female	Male	Female	Male	Female
World	44	59	244	345	335	59	35	62	63
Caribbean	158	84	500	314	348	31	17	56	65
United States	100	100	100	100	100	100	100	100	100

Table 3 Percentage Increase in Mortality from Nutrition-Related Cancers

In Selected Caribbean Countries, compared with Canada and the USA

1960s-1990s

Country	% Increase in Nutrition-Related Cancers
Trinidad	4.3

Barbados	9.6
St. Vincent	12.9
Bahamas	10.1
Jamaica	5.7
St. Lucia	7.3
Belize	1.3
Guyana	1.7
Canada	4.6
USA	3.5

Source: World Health Organization

Table 4. Contribution of Various Factors to the Risk of Common Cancers

	LIFESTYLE FACTORS									GENETIC FACTORS	OTHER MAJOR FACTORS
	FAT	BODY WEIGHT	FIBRE	FRUITS & VEGETABLES	ALCOHOL	SMOKING	SMOKED, SALTED, PACKED FOODS	PHYSICAL ACTIVITIES	SEXUAL BEHAVIOR		
Prostate	+			-						++	
Breast	+	+++	-	--	++			-		++	++ (hormonal)
Cervix				-		+++			+++		++ (HPV)
Stomach			-	---			++			+	+++

Lung	+			--	+	+++		-		+	+++
Colorectal	+	+	-	--	++	+++		---		++	++

\+ Increased risk

\- Decreased risk

+++ Convincing evidence ---

++ Probable evidence --

\+ Possible evidence -

Fig 2A

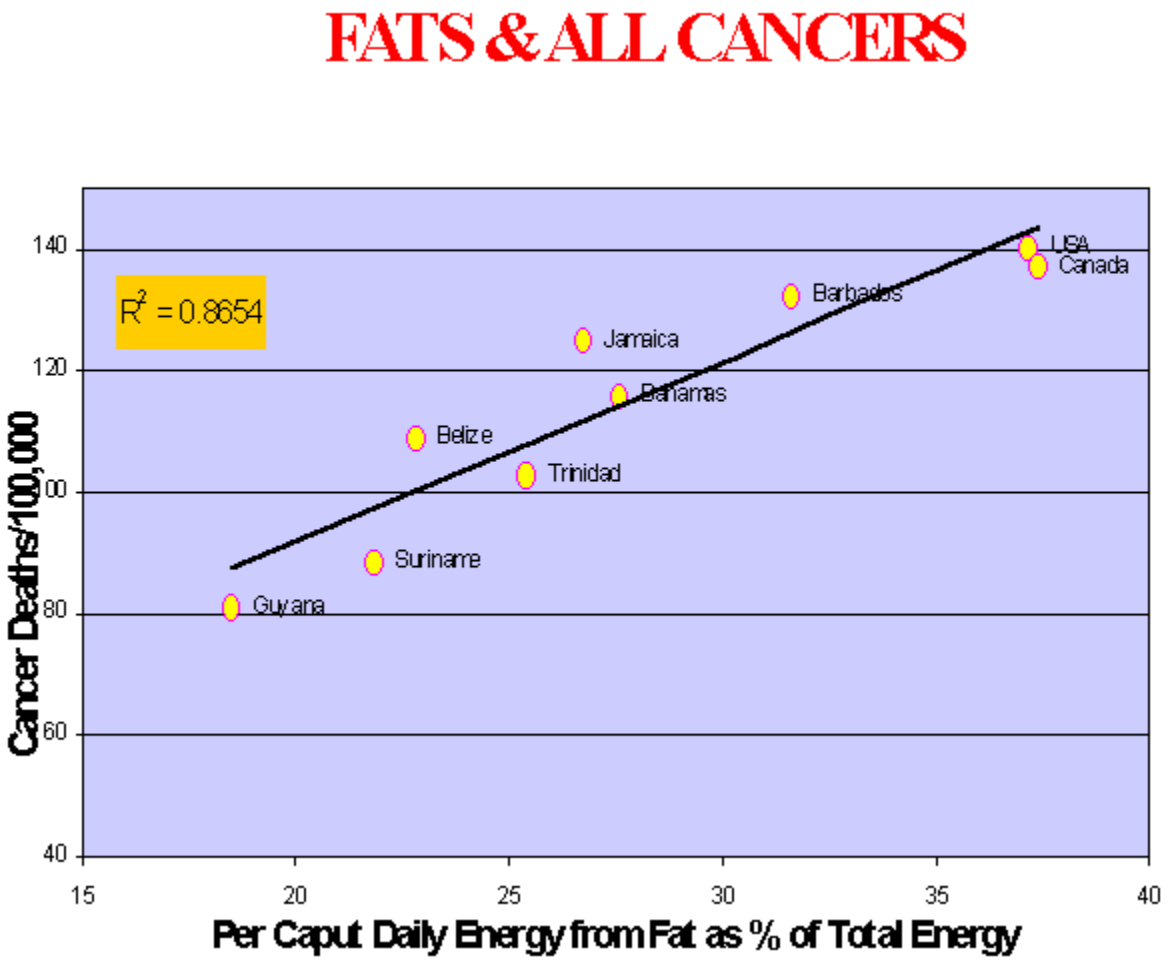


Fig 2B

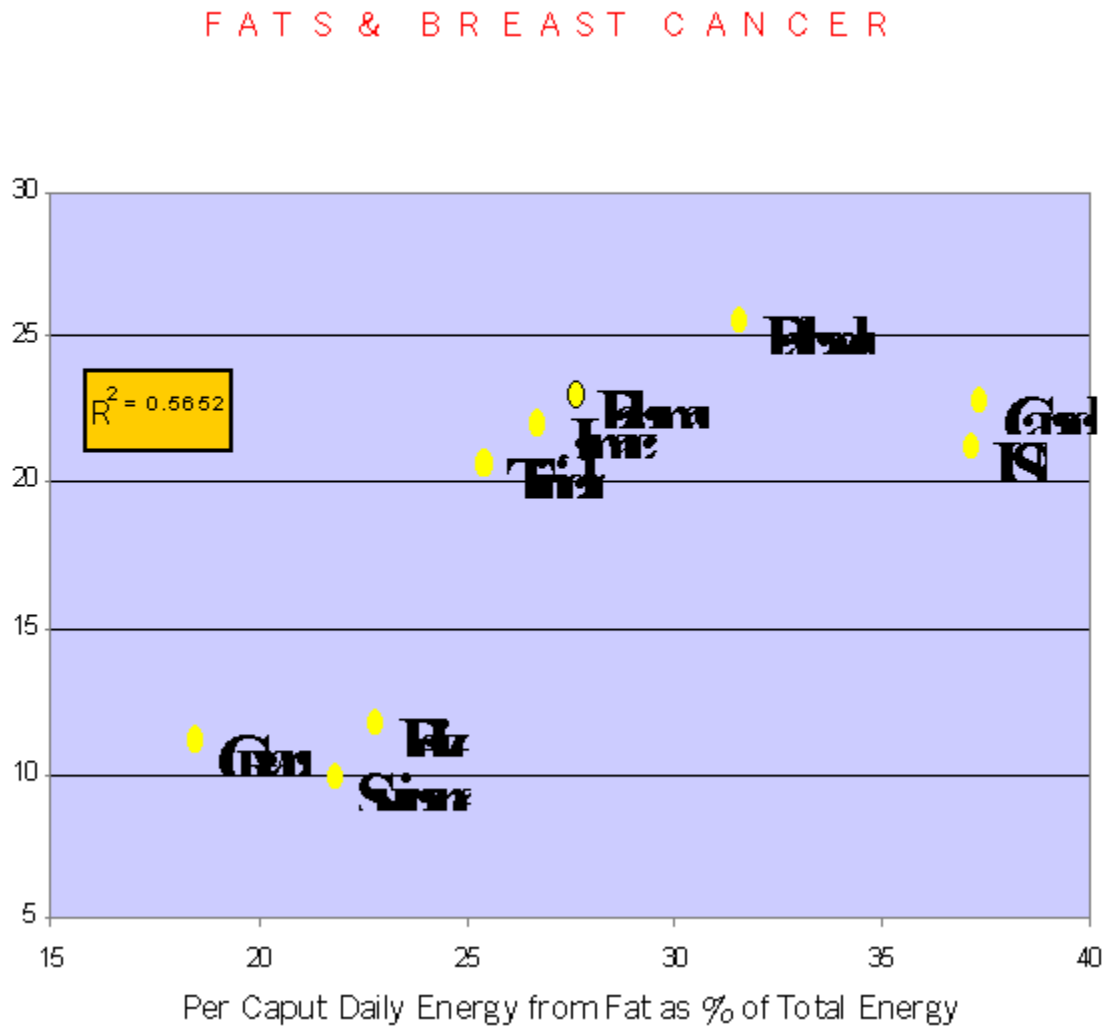

FATS & BREAST CANCER
30
25
20
15
10
5
15
20
25
30
35
40
R^2 = 0.5652
Per Caput Daily Energy from Fat as % of Total Energy

Fig 3A

PLANT FOODS AND ALL CANCERS

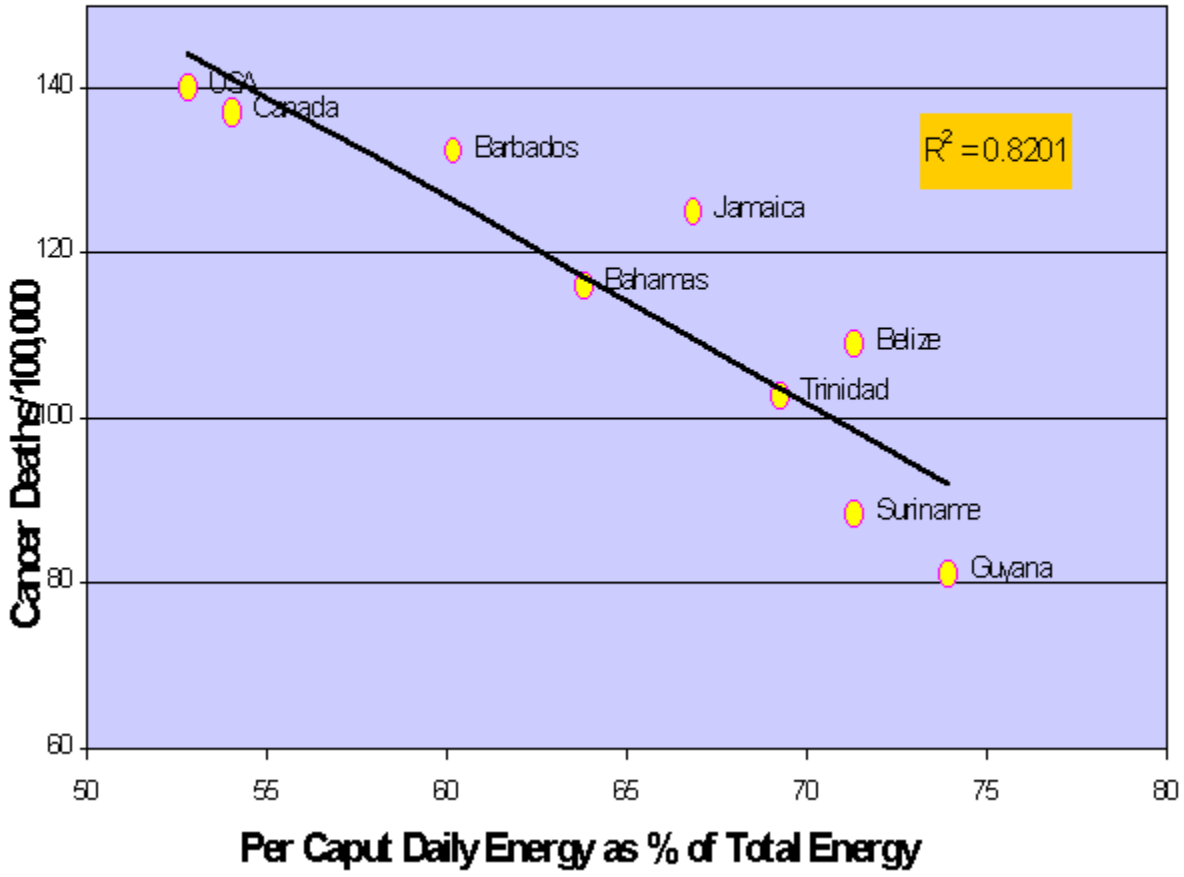
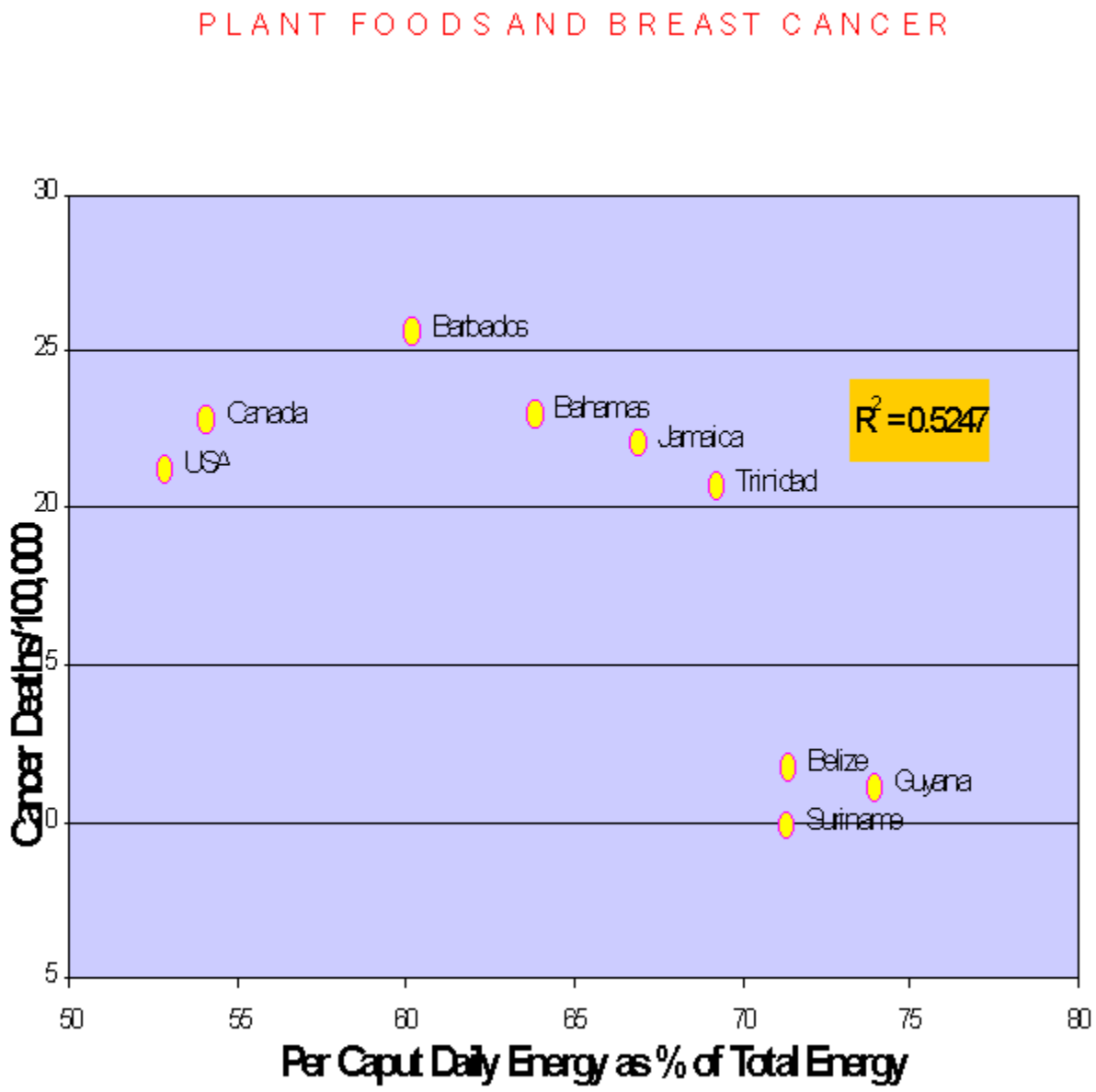


Fig 3B



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