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This information is current as of July 24, 2007

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Cancer Mortality Among Low-Risk Populations

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What can we learn by studying populations that develop chronic diseases at relatively low rates compared with the general population? Are there protective factors that minimize or delay an individual's risk of developing and dying from heart disease, cancer, diabetes? A number of epidemiological studies have examined relatively low rates of disease around the world.¹ These have been directed primarily at coronary heart disease.²⁻⁴ This approach is being applied more extensively to cancer.⁵ In studying cancer etiology, it is as important to identify populations at relatively low risk as it is to identify populations at relatively high risk. From those at low risk, clues to protective mechanisms emerge; from those at high risk, clues to causative mechanisms emerge. Based on these findings, interventions may be introduced to challenge apparent risk factors.

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I thank Devra M. Breslow, Editor/Manager of the U.C.L.A. Cancer Center Bulletin, for assisting me in the preparation of this article.

I gratefully acknowledge support from American Cancer Society grants PDT-51 and PDT-51A.

This paper presents a brief epidemiological review of the cancer mortality experience of the major low-risk populations in the United States. Low-risk here means a cancer mortality rate that is significantly less than that experienced by the general U.S. population. Ideally, an assessment of risk should include cancer incidence. Unfortunately cancer incidence has not been determined for nearly as many subgroups of the U.S. population as has cancer mortality. But cancer incidence can often be approximated by knowing cancer mortality and cancer survival rates.⁶ This discussion of low-risk is focused on subpopulations of U.S. whites because these have been most extensively studied and have the most relevance to white Americans. The findings are probably applicable to other racial groups as well. This approach is the converse of the more common one that examines persons at high-risk of cancer.⁷ It should be noted that these data are derived from observations of naturally occurring populations and not from controlled experimental studies on humans, the latter being impossible to conduct.

Low-risk, in addition to meaning lowrisk to cancer, is extended here to include low-risk to total mortality. In low-risk U.S. adult populations, cancer comprises 15 to 20 percent of all deaths and total cardiovascular disease comprises 75 to 80 percent of all non-cancer deaths. In some

CA-A CANCER JOURNAL FOR CLINICIANS

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parts of the world, such as Africa, India, and Latin America, cancer is poorly diagnosed and hence cancer rates appear to be very low, for the simple reason that the disease is under-reported. However, the total mortality rate, which is usually a more accurately compiled indicator in these same countries, is substantially higher than that in the U.S., chiefly due to high death rates from infectious diseases, malnutrition, and ill-defined causes.1 Consequently the residents of these countries avoid cancer simply by dying young. This is clearly not the way Americans want to avoid cancer. Aging is by far the most important risk factor in cancer mortality. The probability of death from cancer increases about fiftyfold from age 35 to age 85. Consequently all rates discussed here have been made comparable with respect to age by using a technique known as direct age-adjustment to the standard 1940 United States population.

In relatively primitive societies, such as the small principality of Hunza in West Pakistan, the village of Vilcabamba in Ecuador, and the highlands of Georgia in the Soviet Caucasus, it is often reported in the popular press that residents live to extremely old ages, often in excess of 100 years, and experience little or no cancer.^{8,9} Only upon closer inspection do

CA: A Cancer Journal for Clinicians

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we find that these areas do not maintain any formal birth or death records and do not have doctors qualified to diagnose cancer properly. Hence most of these extraordinary claims have no scientific validity.

In certain developed countries where disease records are kept and diagnostic capabilities are good, the cancer rate is very low for some cancer sites but high

VOL. 29, NO. 6 NOVEMBER/DECEMBER 1979

for others. In Japan, breast and colon cancers are relatively rare, but the frequency of stomach cancer is great. Consequently, the total cancer rate among Japanese is only five percent less than among U.S. whites.¹

Epidemiologic Evidence

One way to examine low-risk populations is to first identify the largest groups in the United States that have been studied in the greatest detail over the past 25 years and then examine their characteristics. The total age-adjusted death rate, life expectancy, and total age-adjusted cancer rate for each of these populations are shown on Tables 1 and 2.

The American Cancer Society "cancer prevention study" prospectively followed a cohort of 440,558 men and 562,671 women, initially 35 to 84 years old, who were enrolled between October, 1959 and February, 1960 by 68,116 American Cancer Society volunteer workers.^{10,11} This is the largest epidemiologic study of individuals ever conducted. The study area included 1,121 counties of all sizes and types in 25 states. The enrollees were essentially all white, generally not ill, and generally above average in socioeconomic status. Consequently the cohort as a whole was healthier than the general population. Among this cohort, there was an unusually healthy subgroup of 95,849 males and 381,369 females, initially 35 to 84 years old, who never smoked regularly. This cohort was followed for mortality from date of enrollment to September 30. 1963, for an average 46 months of followup. The published data have been modified with a life table correction to make them comparable with other data in this paper.¹²

The Dorn U.S. veterans study prospectively followed a cohort of 248,195 U.S. veterans who held active U.S. Government life insurance policies in 1953.^{13,14} Most of the enrollees were healthy white male veterans of World War I; 82 percent were white-collar or skilled workers. Again the cohort as a whole is healthier than U.S. white males. Among this cohort there was an unusually healthy subgroup of 54,344 men 35 to 84 years old who never smoked regularly. They were followed for mortality from July 1, 1954 to December 31, 1962.¹³ These nonsmoking men have the lowest total cancer rate shown in Table 2.

Adventist Population

The Seventh-Day Adventist religious group has been studied in great detail over the past 20 years.¹⁵⁻¹⁷ Seventh-Day Adventists are a conservative evangelical religious denomination with about 100,000 members in California and three million worldwide. By church proscription, they completely abstain from smoking and the use of alcoholic beverages. In addition, they generally avoid the use of coffee, tea, and cola beverages, hot condiments and spices, and highly refined foods. About half follow a lacto-ovovegetarian diet, which is free of any type of meat, poultry, or fish, but does contain milk products and eggs. Virtually all Adventists abstain from pork products and other biblically defined "unclean meats." A few percent are pure vegetarians. They make abundant use of fruits, whole grains, vegetables, and nuts. These dietary habits have been recommended by the church for over 100 years. In addition, Adventists emphasize quality education and family life and are deeply committed to their religion.

In 1958, investigators carefully identified approximately 47,000 Adventists living in California, who were followed for mortality during the next eight years.¹⁷ Causes of death were tabulated as recorded on death certificates. As expected, Adventists had extremely low mortality ratios for cancer sites that are related to cigarette smoking or alcohol consumption. However, they also showed significantly lower mortality rates for other major classes of cancers, those of the reproductive system, and leukemia.

For most of the cancer sites unrelated to smoking or drinking, the reduced risk

in Adventists occurs in sites that have the most evidence of being related to dietary practices. For both sexes, the risk of death from cancer of the colon, stomach, and pancreas is about 60 to 70 percent that of the general U.S. population. For females, the risk of postmenopausal deaths from cancers of the breast, ovary, and uterus is significantly below that of the general U.S. population. The investigators feel that a plausible factor to explain these findings is diet. Beef, and other animal fat, and low fiber consumption have been suggested as factors in developing cancer of the large bowel, breast, and other sites.¹⁷ The exact role, if any, of dietary factors on cancer induction remain to be determined by ongoing investigation.

Mormon Population

The most recent low-risk population to be studied are Mormons.¹⁸⁻²⁰ Mormons are interesting from an epidemiological standpoint because their "Word of Wisdom," a Church doctrine since 1833, advises against the use of tobacco, alcohol, coffee, tea, and addictive drugs and recommends a well-balanced diet. Furthermore, the Church emphasizes a strong family life and advocates good health

"The Utah cancer rate is the lowest among the states in the U.S."

practices in general.¹⁸ The Mormon Church, officially known as The Church of Jesus Christ of Latter-Day Saints, has approximately 2.5 million members in the United States and about four million members worldwide. Located mainly in the Rocky Mountain states, Mormons constitute about 70 percent of Utah's 1.3 million population; and there are almost 400,000 in California.¹⁹

CA-A CANCER JOURNAL FOR CLINICIANS

An indirect indication of the Mormon cancer rates is the fact that Utah whites have a cancer death rate about 75 percent that of U.S. whites.¹⁸ The Utah cancer rate is the lowest among the states in the United States. Direct evidence comes from an analysis of well-kept Church death records and membership statistics which shows that 360,000 California Mormons during 1968 to 1975 have a cancer mortality ratio of 66 percent for males and 81 percent for females compared with U.S. whites.¹⁹

The most striking findings pertain to the active Mormon males, known as High Priests and Seventies, who comprise about 20 percent of all adult Mormon males; no equivalent classification exists for active Mormon females.¹⁹ High Priests are the Church leaders, such as bishops, clerks and patriarchs; Seventies are adult missionaries who proselytize and bring new members into the Church. These Mormon men are most likely to adhere to the Word of Wisdom. However, they do not necessarily represent the optimum group of Mormons with respect to health habits and mortality. The 13,880 California active Mormon males at least 35 years of age have a total cancer death rate that is about 50 percent that of U.S. white males. Their remaining life expectancy at age 35 is 44.6 years (a total life expectancy of 79.6 years), eight years longer than that of U.S. white males in 1970.

There are several interesting features of these data. First, these cancer rates appear to be substantially lower than expected for essentially all cancer sites except prostate, lymphomas, and leukemias. In fact, for active California Mormon males at least 35 years of age, the mortality ratio is 25 percent for the "smoking-related" cancer sites of the entire buccal cavity, esophagus, lung, and bladder and 65 percent for all remaining cancer sites. For all California Mormon males at least 35 years of age, the ratio is 55 percent for the "smoking-related" sites and 73 percent for all other sites. The major mortality difference between the active Mormon males and Mormon males as a whole appears to be in the "smokingrelated" cancer sites.^{18,19} This is in line with the available data that indicate active Mormons abstain completely from tobacco and alcohol, whereas Mormon males as a whole smoke and drink about half as much as the general population.^{18,19}

Nonsmokers

Data on a representative national sample of nonsmokers in the U.S. have been obtained using a census survey.^{12,19,21} Information on deceased persons 35 to 84 years old in the United States in 1966 to 1968 comes from the National Mortality Survey, a follow-back survey of a representative sample of 19,526 death registration records, including 2,532 deaths among white males who never smoked cigarettes and 3,358 deaths among white females who never smoked cigarettes. By mail questionnaire, surviving family members and others named on the death certificate provided smoking histories and socioeconomic characteristics of the deceased person; the overall response rate was 92 percent.²¹ Then through the Current Population Survey conducted by the Bureau of the Census in August 1967, smoking and socioeconomic information comparable to that for the decedents was obtained for a representative national sample including 25,266 white males and 29,308 white females 35 to 84 years old.²¹ This sample represents about 10 million white males and 25 million white females who never smoked cigarettes. The resulting cancer rates can then be compared with rates for U.S. whites as a whole.²²

The mortality data for the above described epidemiologic studies, plus comparable data for U.S. whites and Swedes are summarized in Table 1 for total mortality and life expectancy and in Table 2 for cancer mortality. Sweden has been included, because contemporary Swedes have the longest life expectancy of any country in the world. Sweden is often cited to as a place where people enjoy excellent health and have an excellent

VOL. 29, NO. 6 NOVEMBER/DECEMBER 1979

		Total life expectancy (years)**		78.0	78.7		
CTANCY WEDESt	Females	Average annual age- adjusted death rate (deaths/ 1000) *	~	10.9	10.0		
D LIFE EXPE		Number of persons at least 35 years of age		40,652,869	2,090,000	÷	
Y RATE ANI VITH U.S. WH		Total life expectancy (years) **		71.5	74.7		79.0
BLE 1 L MORTALIT :OMPARED V	Males	Average annual age- adjusted death rate (deaths/ 1000) *		19.4	15.0		8.
TA STED TOTA COHORTS C		Number of persons at least 35 years of age		35,672,885	1,967,000		54,344
INUAL AGE-ADJU AL LOW-RISK U.S.		Methodology	-	mortality- census survey	mortality- census survey		prospective cohort study
AVERAGE AN FOR SEVER		Population	COUNTRIES	United States whites	Sweden	NONSMOKING COHORTS	U.S. veterans who "never smoked or occasional only"
		Y ears Observed		1970	1970		1954-62

CA-A CANCER JOURNAL FOR CLINICIANS

CA: A Cancer Journal for Clinicians

1960-63	ACS cohort from 25 states who "never smoked regularly"	prospective cohort study	95,849	11.7	4.77	381,369	7.6	80.7
1958-65	California Adventists	prospective cohort study	12,250	11.0	78.0	23,210	7.0	81.2
1968–75	California active Mormons	mortality - census survey	13,880	4.0	79.6			
1966-68	U.S. whites who "never smoked cigarettes" (representative sample)	mortality- census sample survey	10,000,000	15.1	74.6	25,000,000	Q Q	78.8
	НЕАLTHY СОНО	RTS						
1954–62	U.S. veterans	prospective cohort study	248,195	13.1	76.3			
1960-63	ACS cohort from 25 states	prospective cohort study	440,558	16.5	74.3	562,671	6.7	80.5
1968-75	California Mormons	mortality - census survey	56,361	12.9	76.5	68,708	8.6	79.9
• Age-adju • • Total life † Populatior	sted by the direct me expectancy obtained rs include only persor	thod to the 1940 U.S. d by adding 35 years to ns at least 35 years of a	population at le the remaining l ge.	est 35 years of Ife expectancy	age. for persons alr	ady 35 years of a	90	

VOL. 29, NO. 6 NOVEMBER/DECEMBER 1979

357

health care system. The data in the tables have been adopted from rates published in references 10 to 21 and are made as comparable as possible using age-adjustment to the 1940 U.S. population. However, several table values have been obtained by extrapolation from incomplete published data and are not given in the original references as shown here.

Conclusions

It is clear that several nonsmoking populations experience relatively low cancer rates and low total mortality rates. The precise reasons for the low-risk are not clear at this time. The most plausible explanation is that lack of smoking per se reduces the total cancer rate by a substantial amount. Furthermore, selection associated with being a questionnaire respondent apparently reduces the cancer rate by another 20 percent in men and 10 percent in women, based on the American Cancer Society and U.S. veteran cohort studies. The respondents in these cohort studies could be healthier than normal for several reasons: they probably are health conscious and follow several good habits in addition to not smoking; also, it is well known that very sick persons do not usually respond to questionnaire sur-

"If all Americans did not smoke, the mortality reduction that would occur has been estimated to be ... a reduction of 26 percent."

veys, thereby raising the average level of health of the respondents.

If all Americans did not smoke, the mortality reduction that would occur has been estimated to be 80,000 lung cancer deaths plus 22,000 other cancer deaths of the 1978 total of 390,000 cancer deaths—a reduction of 26 percent.²³ Another estimation is that about 33 percent of cancer deaths are preventable by applying all current knowledge, e.g., eliminating human exposure to known carcinogenic factors like cigarette smoking, high alcohol intake, excess sunlight, and certain occupational and industrial exposures.²⁴

Table 2 shows that representative U.S. white nonsmokers (males and females averaged together) have a total cancer rate of 24 percent less than that of all U.S. whites. This is in good agreement with the predicted 26 percent reduction above. The nonsmoking healthy American Cancer Society, Mormon and Adventist cohorts of males and females combined, as shown in Table 2, have an average total cancer rate reduction of 39 percent relative to U.S. whites. This is slightly more than the 33 percent reduction predicted above. What else are these groups doing, in addition to not smoking, to diminish their risk of cancer death?

It may be possible to lower the cancer mortality rate even below the Table 2 rates by minimizing several risk factors simultaneously. Some indication of this is the fact that 282 adult men and 386 adult women in Alameda County, California who followed seven good health habits experienced over a nine and onehalf year period only 52 percent of the total mortality rate of a representative sample of 6,928 Alameda County adults.²⁵ (This 52 percent is based on only 48 deaths, with 95 percent confidence limits from 38 percent to 69 percent.)

The actual preventability of cancer remains to be demonstrated. There is certainly an overwhelming amount of evidence pointing to the benefits of being a nonsmoker.²³ However, the precise effects of smoking cessation on current smokers are still unknown. One major study showed that British physicians who reduced their cigarette smoking as a whole by more than 50 percent over a 20-year period experienced a reduction in lung cancer mortality relative to the mortality of the general British population: from a ratio of 65 percent in 1955 to 35 percent in 1972.26 On the other hand, a recent randomized controlled trial of smoking

CA-A CANCER JOURNAL FOR CLINICIANS

			Age-adjuste	ed cancer deat	th rates (death:	s/1000)*	
			Males		Females	Both	Sexes
s	Population	Smoking- related cancer sites**	All other cancer sites	Total cancer	Total cancer	Total cancer t	% of rate of U.S. whites
N N CON	NTRIES ited States whites eden	1.45 .63	2.20 2.45	3.65 3.08	2.53 2.60	3.09 2.84	100% 92%
62 NON 50. U.S	ISMOKING COHORTS 5. veterans who "never oked or occasional only"	21	1.44	1.65			
-63 AC wh	S cohort from 25 states o "never smoked regularly"	.21	1.60	1.81	2.00	1.91	62%
-65 Cal -75 Cal	lifornia Adventists lifornia active Mormons	.20	1.70	1.90 1.80	1.70 2.06‡	1.80	58% 62%
-68 sm (re	S. whites who "never oked cigarettes" presentative sample)	.40	2.03	2.43	2.28	2.36	76%
-62 U.S	LTHY COHORTS 5. veterans	.76	1.74	2.50			
-63 AC	S cohort from 25 states lifornia Mormons	.97 .80	1.83 1.61	2.80	2.10 2.06	2.45	79% 72%

cessation among middle-aged British men surprisingly showed no difference in total mortality rates between intervention group and control group after eight years of followup.²⁷ In view of these data, it is both impor-

In view of these data, it is both important to realize the benefits of not smok-

"Some carcinogens that have been given a great deal of attention by the media... are not likely to have an important impact on reducing cancer mortality."

ing and to ascertain what factors, in addition to lack of smoking, account for the low cancer mortality experience among various low-risk populations, and to discover how to apply these findings to persons at higher risk of cancer. Some carcinogens that have been given a great deal of attention by the media in recent years are not likely to have an important impact on reducing cancer mortality. These factors include hair dyes, food additives, saccharin, menopausal estrogens, and low-level ionizing radiation. Even if these factors caused most of the types of cancer with which they have been most strongly linked, primarily cancers of the bladder and endometrium and childhood leukemia, they would have little impact on total cancer mortality. This is because cancers of the bladder and endometrium and childhood leukemia comprise less than four percent of all cancer deaths. As of now, there is no good evidence that the above factors have caused an increase in the cancer death rate in the general population.

For the purposes of public health, it is imperative that research be directed first and foremost at factors that are likely to have the greatest impact on cancer mortality. These factors now appear to include personal health habits, diet, socioeconomic status, and certain host factors related to the aging process. The potential for identifying lower risk exists if sufficiently large and healthy population groups can be studied with respect to the important risk factors. Interpreting low risk for personal health is genuine cancer control.

References

1. World Health Statistics Annual, 1970: Vital Statistics and Causes of Death. Geneva, World Health Organization, 1973, vol 1.

2. Keys A (ed): Coronary heart disease in seven countries. American Heart Association Monograph No 29, 1970. Also Circulation, vols 41, 42, 1970.

 The Framingham study—an epidemiological investigation of cardiovascular disease. Sections 1-32. National Heart and Lung Institute. Washington, DC, US Government Printing Office, 1968-1977.
Tibblin G, Keys A, Werko L (eds): Pre-

4. Tibblin G, Keys A, Werko L (eds): Preventive Cardiology. Stockholm, Almqvist & Wiksell, 1972.

5. Hoover R, Mason TJ, McKay FW, Fraumeni JF: Cancer by county: new resource for etiologic clues. Science 189:1005-1007, 1975. 6. Enstrom JE, Austin DF: Interpreting cancer survival rates. Science 195:847-851, 1977.

7. Fraumeni JF (ed): Persons at High Risk of Cancer: An Approach to Cancer Etiology and Control. New York, Academic Press, 1975.

8. Leaf A: Getting old. Sci Am 229:45-52, 1973.

9. Stefansson V: Cancer: Disease of Civilization? An Anthropological and Historical Study. New York, Hill & Wang, 1960.

10. Hammond EC: Smoking in relation to the death rates of one million men and women. Natl Cancer Inst Monogr 19:127-204, 1966.

11. Hammond EC: Life expectancy of American men in relation to their smoking habits. J Natl Cancer Inst 43:951-962, 1969.

CA-A CANCER JOURNAL FOR CLINICIANS

12. Enstrom JE: Rising lung cancer mortality among nonsmokers. J Natl Cancer Inst 62:755-760, 1979.

 Kahn HA: The Dorn study of smoking and mortality among US veterans report on eight and one-half years of observation. Natl Cancer Inst Monogr 19:1-126, 1966.
Rogot E: Smoking and life expectancy among US veterans. Am J Public Health 68:1023-1025, 1978.
Wynder EL, Lemon FR, Bross IJ: Can-

15. Wynder EL, Lemon FR, Bross IJ: Cancer and coronary artery disease among Seventh-Day Adventists. Cancer 12:1016-1028, 1959.

16. Lemon FR, Kuzma JW: A biologic cost of smoking. Decreased life expectancy. Arch Environ Health 18:950-955, 1969.

17. Phillips RL: Role of life-style and dietary habits in risk of cancer among Seventh-Day Adventists. Cancer Res 35:3513-3522, 1975.

18. Enstrom JE: Cancer mortality among Mormons. Cancer 36:825-841, 1975.

19. Enstrom JE: Cancer and total mortality among active Mormons. Cancer 42:1943-1951 1978 and data to be published

1951, 1978 and data to be published. 20. Lyon JL, Klauber MR, Gardner JW, Smart CR: Cancer incidence in Mormons and non-Mormons in Utah, 1966-1970.

CA: A Cancer Journal for Clinicians

N Engl J Med 294:129-133, 1976.

21. Godley FH: Cigarette smoking, social factors, and mortality: new estimates from representative national samples. Unpublished thesis, University of Maryland, 1974.
22. US Public Health Service. Vital Statistics of the United States-1970. Rockville, Maryland, National Center for Health Statistics, 1974.
23. US Public Health Service. Smoking and

23. US Public Health Service. Smoking and Health: A Report of the Surgeon General. Washington, DC, US Department of Health, Education, and Welfare, 1979.

24. Schneiderman MA: Environmental factors and cancer prevention, in Nieburgs HE (ed): Prevention and Detection of Cancer. New York, Marcel Dekker, Inc, 1978, part 1, vol 2, pp 1667-1877.

25. Breslow L, Enstrom JE: Persistence of health habits and their relationship to mortality (submitted for publication).

 26. Doll R, Peto R: Mortality in relation to smoking: 20 year's observations on male British doctors. Br Med J 2:1525-1536, 1976.
27. Rose G, Hamilton PJS: A randomized

27. Rose G, Hamilton PJS: A randomized controlled trial of the effect on middle-aged men of advice to stop smoking. J Epidemiol Community Health 32:275-281, 1978.

VOL. 29, NO. 6 NOVEMBER/DECEMBER 1979