

Association between Coronary Heart Disease and Cancers of the Breast, Prostate, and Colon¹

Alfred I. Neugut,² David J. Rosenberg,³ Habibul Ahsan, Judith S. Jacobson, Nurul Wahid, Michael Hagan, Mirza I. Rahman,⁴ Zareen R. Khan, Lisa Chen, Ariel Pablos-Mendez, and Steven Shea

Department of Medicine, College of Physicians and Surgeons, Columbia University, New York, New York 10032 [A. I. N., D. J. R., N. W., A. P.-M., S. S.], and Division of Epidemiology, Columbia School of Public Health, New York, New York 10032 [A. I. N., H. A., J. S. J., M. H., M. I. R., Z. R. K., L. C., A. P.-M., S. S.]

Abstract

Coronary heart disease (CHD) and cancers of the breast, prostate, and colon are more common in industrialized countries than in the developing world, and to some degree, these conditions appear to share risk factors. To investigate whether there is an association between these cancers and a prior history of CHD, a hospital-based case-control study was conducted at Columbia-Presbyterian Medical Center in New York. The study was based on 252 breast cancer cases, 256 colorectal cancer cases, and 322 benign surgical controls, all of whom underwent biopsy or surgery between January 1989 and December 1992, and on 319 prostate cancer cases and 189 benign prostatic hypertrophy controls diagnosed between January 1984 and December 1986 (prior to widespread use of prostate-specific antigen screening). Medical records were reviewed on each, focusing on the preoperative anesthesia and surgical clearances. No association was found between a history of CHD and breast or colorectal cancer, but an elevated risk was found for prostate cancer (odds ratio, 2.00; 95% confidence interval, 1.18–3.39), using unconditional logistic regression with adjustment for appropriate confounders. No association was found between cigarette smoking and any of the three cancers. Aspirin use was protective for colorectal cancer (odds ratio, 0.35; 95% confidence interval, 0.17–0.73) but had no association with breast or prostate cancer. The study suggests that

individuals with CHD are at elevated risk for prostate cancer but not breast or colorectal cancer. Etiological risk factors associated with CHD should be investigated with regard to prostate cancer. Patients with CHD may represent a high-risk group for prostate cancer and potential future targets for prostate cancer screening interventions.

Introduction

Both atherosclerotic heart disease and several common cancers are known to have higher mortality rates in industrialized and affluent populations than in developing or less affluent countries (1–3). Migrant studies suggest that these differences in risk reflect lifestyle and health-related behaviors rather than genetic and endogenous factors (4–7). Secular changes, such as are occurring currently in Japan with regard to breast, prostate, and colon cancer, also support an environmental etiology (6).

CHD⁵ has been shown to have some risk factors in common with breast cancer, prostate cancer, and especially colorectal cancer. Physical activity is protective against CHD, colorectal cancer, breast cancer, and possibly prostate cancer, whereas obesity appears to be a risk factor for colorectal and breast cancers and probably prostate cancer (8–15). Certain components of diet, such as saturated fat ingestion, are risk factors for CHD, colorectal cancer, and prostate cancer (16–18), although not as clearly for breast cancer. Cigarette smoking, which has long been known to increase risk for CHD, increases the risk of colorectal adenomatous polyps (19–30) and may increase the risk of colorectal carcinoma (19, 28, 29, 31). Aspirin use appears to prevent CHD and colorectal cancer (32–35), although not breast or prostate cancer (36, 37).

Given their common geographic and risk factor associations, these conditions may be expected to occur in the same individuals, in the same way that having breast or colorectal cancer raises an individual's risk for the other cancer (38–40). Two autopsy studies found that atherosclerosis and colorectal adenomatous polyps tended to occur in the same individuals more often than expected (41, 42); however, Kune *et al.* (43) found no association between CHD and colorectal cancer. Audigier *et al.* (44) screened with sigmoidoscopy recent myocardial infarction patients and controls selected from a hospital digestive diseases unit and found no difference in the distribution of adenomatous polyps. A pilot study by our group (45) also found no association between CHD and colorectal neoplasia or cancer overall, although associations in some subgroups were possible.

A cross-sectional study in 1974 (46) found a relative risk of 2.0 ($P < 0.05$) for the association between prostate cancer

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² To whom requests for reprints should be addressed, at Division of Oncology, Columbia-Presbyterian Medical Center, 630 West 168th Street, New York, NY 10032.

³ Present address: Department of Medicine, Lenox Hill Hospital, New York, NY 10021.

⁴ Present address: Department of Family Practice and Epidemiology and Biostatistics, MetroHealth Medical Center, Case Western Reserve University, Cleveland, OH 44106.

⁵ The abbreviations used are: CHD, coronary heart disease; BPH, benign prostatic hypertrophy; OR, odds ratio; CI, confidence interval.

Table 1 Characteristics of the study population: comparison of cases and controls for three case-control analyses, Columbia-Presbyterian Medical Center, New York, January 1989 through December 1992 (breast cancer and colorectal cancer) and January 1984 through December 1986 (prostate cancer)

	Colorectal cancer		Breast cancer		Prostate cancer	
	Cases	Controls	Cases	Controls ^a	Cases	Controls
Total number	256	322	252	176	319	189
Women (%)	58.6	54.7	100	100	0	0
Mean age (+/SD)	71.6 (11.5)	66.5 (13.6)	59.2 (12.5)	64.9 (14.8)	69.6 (9.1)	68.1 (9.0)
White (%)	59.0	62.4	69.8	60.8	67.4	72.5
Current smoker (%)	32.0	27.8	30.2	21.7	25.7	24.1
Aspirin (%)	4.3	10.3	5.9	9.1	11.9	7.4
Prior CHD (%)	18.8	14.0	8.3	11.4	21.3	12.7
Postmenopausal (%)			72.0	71.8		

^aThe breast cancer controls were the same as the female colorectal cancer controls.

and heart disease. A study of 40 prostate cancer cases and 64 controls with BPH found no association between heart disease and prostate cancer (47). The Lipid Research Clinics Prevalence Study (48) followed 1776 adults and identified 100 subjects who developed prostate cancer, of whom 54 were incident, yielding a relative risk of 1.9, which was not statistically significant. We know of no specific studies investigating the possible association between CHD and breast cancer risk.

The present study investigates the association between CHD and breast, prostate, and colorectal cancer. Aspirin use and cigarette smoking were also assessed. In addition to generating future etiological hypotheses, an association between CHD and a specific cancer would suggest a new high-risk group for future cancer screening interventions.

Materials and Methods

The study used a hospital-based case-control design with three case groups: women with breast cancer, men and women with colorectal cancer, and men with prostate cancer. Both cases and controls were identified by review of hospital discharge files for the time period under study. Patients with a prior history of cancer were excluded. To assure completeness of medical chart information on history of CHD, aspirin use, and other covariates, study subjects included only those who had a surgical or biopsy procedure.

Eligible breast and colorectal cancer cases had to be diagnosed and to undergo a surgical procedure for cancer between January 1989 and December 1992 at Columbia-Presbyterian Medical Center. The controls for these two case groups consisted of patients who underwent surgery for a benign condition at Columbia-Presbyterian Medical Center during the same time interval. Eligible surgical conditions included herniorrhaphy, BPH, fractures, accidents, cataracts, and lumbar disc disease. These conditions were chosen because they are not known to have any significant association with cigarette smoking, aspirin use, coronary heart disease, or gastrointestinal tract disorders.

For the prostate cancer case-control comparisons, cases consisted of men who were pathologically diagnosed with prostate cancer between January 1984 and December 1986, and controls consisted of men pathologically diagnosed with BPH during the same time frame. This time frame was chosen because it preceded the widespread introduction of prostate-specific antigen screening. Clinically diagnosed prostate cancer may represent a different entity from screen detected prostate cancer, with different etiological factors. However, even in the pre-prostate-specific antigen era, a diagnosis of prostate cancer may have been a result of referral and diagnostic biases. We

chose men with BPH as controls for the prostate cancer cases because, like the cases, they had come to the Medical Center for urological treatment and had undergone urological diagnostic procedures.

Each subject's medical record was reviewed for demographic information, history of prior angina or myocardial infarction, chronic use of aspirin or other nonsteroidal anti-inflammatory drugs, smoking history, and parity (for women). The preoperative assessments by the surgeon and anesthesiologist included information regarding prior history of CHD, smoking, and medication usage. The major analyses were conducted using unconditional logistic regression, controlling for relevant covariates, including as indicated in the tables, age, gender, ethnicity, aspirin use, history of CHD, and diabetes.

CHD was defined as a history of myocardial infarction, coronary artery bypass graft, positive coronary angiogram, or positive exercise stress test. Angina was classified as CHD in the absence of a positive coronary diagnostic test only when the case or control was taking antianginal medications (nitrates, β -blockers, or calcium channel blockers).

Ascertainment of the exposure variables was based on review of the medical record for the hospital admission for which the biopsy or surgical procedure was performed. Records of prior and subsequent admissions were not reviewed.

The hospital's computer database identified 319 eligible breast cancer cases, 342 eligible colorectal cancer cases (136 males and 206 females), 376 eligible prostate cancer cases, 455 eligible surgical controls, and 250 eligible BPH controls. Medical records and information on CHD, smoking, and medication history were successfully obtained on 252 breast cancer cases (79%), 256 colorectal cancer cases (75%), and 322 surgical controls (71%). Of the controls, 36 had herniorrhaphy, 59 had BPH, 36 had cataracts, 98 had fractures or other traumatic conditions, 32 had disc problems, and 61 had other miscellaneous surgical conditions. For the prostate cancer analyses, medical records were obtained on 319 prostate cancer cases (85%) and 189 BPH controls (76%).

Results

Table 1 compares the case and control groups on a variety of factors. The colorectal cancer cases were somewhat older, on the average, than the controls, whereas the breast cancer controls were somewhat older than the cases. The colorectal cancer cases included more females than the controls, probably because the cases were older. The breast cancer cases had a higher proportion of whites than the breast cancer controls. Otherwise, the case and control groups were similar in demographic characteristics.

Table 2 Adjusted ORs (95% CIs) for the association between history of coronary heart disease, aspirin use, and cigarette smoking and colorectal cancer, breast cancer, and prostate cancer: Columbia-Presbyterian Medical Center

	Colon cancer		Breast cancer		Prostate cancer	
	OR	95% CI	OR	95% CI	OR	95% CI
CHD ^a	1.18	0.73–1.90	1.00	0.49–2.04	2.00	1.18–3.39
Aspirin use ^b	0.35	0.17–0.73	0.80	0.35–1.80	1.60	0.82–3.11
Cigarette smoking ^b	1.20	0.83–1.75	1.11	0.76–1.63	1.06	0.66–1.68

^a Adjusted for age, gender (colorectal cancer only), race, menstrual status (breast cancer only), aspirin use, and diabetes (prostate cancer only).

^b Adjusted for age, gender (colorectal cancer only), race, menstrual status (breast cancer only), history of coronary heart disease, and diabetes (prostate cancer only).

Table 2 shows the main results of the study. No association was found between CHD and either breast or colorectal cancer, but a significant association was found between CHD and prostate cancer, with an OR of 2.00 (95% CI, 1.18–3.39).

No association was observed between current aspirin use and breast cancer or prostate cancer, but aspirin use was protective against colorectal cancer (OR, 0.35; 95% CI, 0.17–0.73). Cigarette smoking as a risk factor for breast cancer, colorectal cancer, and prostate cancer was also explored, and no significant associations were found.

The association between CHD and prostate cancer was investigated further (Table 3). An increased risk from CHD was observed when subjects were stratified by age (\geq or $<$ 70) with elevated ORs for both groups. Prostate cancer incidence is known to be higher among blacks. The association between CHD and prostate cancer among blacks was 1.50 (95% CI, 0.45–4.98) with an OR of 2.05 (95% CI, 1.12–3.71) for whites. Likewise, although the numbers were smaller, there was an OR of 3.55 for the CHD-prostate cancer association in Hispanics (95% CI, 0.32–38.85).

Discussion

Breast cancer, colorectal cancer, prostate cancer, and CHD are all recognized as major diseases of Western industrialized society. Certain risk factors are common to two or more of these diseases, including cigarette smoking, aspirin use, physical activity, obesity, and certain dietary factors. Two prior studies of the association between colorectal cancer and CHD found no association (43, 45), as did one study of CHD and colorectal adenomatous polyps (45), whereas two autopsy studies found an association between CHD and colorectal adenomas (41, 42). Of three studies of CHD and prostate cancer (46–48), only one found a statistically significant association (46). No previous study has explored the association between CHD and breast cancer.

The current study found no association between CHD and either breast cancer or colorectal cancer. However, it did find a consistent association between CHD and prostate cancer. Why would there be an association between CHD and prostate cancer? One of the consistent risk factors identified for prostate cancer incidence is dietary fat ingestion (15, 18). It is possible that dietary fat and obesity link prostate cancer to CHD. Furthermore, some evidence suggests physical activity may be protective against prostate cancer (8, 11, 13–15) as it is for CHD, although if this were the case, one would expect CHD to be associated with colorectal cancer as well.

The study confirms the numerous reports that aspirin use reduces the risk of colorectal cancer (32–35) but not breast or prostate cancer (36, 37). The aspirin analysis uses the same methodology as, and thus constitutes a “positive control” for, the CHD analyses.

Table 3 Crude and adjusted OR (95% CI) for the association between history of coronary heart disease and prostate cancer: Columbia-Presbyterian Medical Center

	Crude	Adjusted ^a
Age		
≤69	2.08 (0.94–4.67)	2.13 (0.94–4.82)
>69	1.70 (0.88–3.26)	1.81 (0.92–3.56)
Race		
White	2.03 (1.19–3.70)	2.05 (1.12–3.71)
Black	1.53 (0.46–5.05)	1.50 (0.45–4.98)
Hispanic	2.86 (0.28–29.7)	3.55 (0.32–38.85)

^a Age strata are adjusted for race; race strata are adjusted for age. Also adjusted for aspirin use and cigarette smoking.

This study has several limitations. It is, for example, hospital based rather than population based. However, cases and controls are comparable in that they had surgery or biopsy at the same hospital. On the other hand, the results may not be generalizable to all populations.

Because several hypotheses were tested simultaneously, the positive findings may represent chance. However, the aspirin effect has been consistently described previously, and furthermore, the CHD/prostate cancer association was consistent across different subgroups (Table 3).

The use of medical records to obtain exposure data is always questionable. However, both cases and controls were surgical patients, with charts that included information on the two major exposures of interest: prior history of CHD and aspirin usage. Information regarding these two variables was recorded in >95% of the charts reviewed.

Limiting the study to surgical patients may have had some effect on the results observed. We may have excluded patients who did not have surgery because they had severe CHD. If so, we have underestimated the prevalence of prior exposure to CHD. Because controls also underwent surgery, they should not have differed from the cases in exposure to CHD unless it was associated with risk. However, there remains the possibility that an association was missed or inflated because of this bias.

Another possible bias stems from the frequent prescription of aspirin following angina or myocardial infarction. If aspirin prevents colorectal cancer, a history of myocardial infarction would be more prevalent among controls than among colorectal cancer cases. Various studies of aspirin and colorectal cancer, particularly the analysis of the Physicians Health Study done by Gann and associates (49), suggest that this effect would require several years to be apparent. Nonetheless, it may have attenuated and obscured a possible association between CHD and colorectal cancer in particular. The lack of evidence that aspirin prevents breast or prostate cancer makes it unlikely that a similar bias was operating in these analyses.

In summary, although some evidence would suggest that CHD should be associated with breast and colorectal cancer in the same individuals, most notably their similar high incidence rates in industrialized and affluent nations, the current study has found no association. An association was observed between CHD and prostate cancer, in both blacks and whites. Aspirin appeared to be protective against colorectal cancer but not prostate or breast cancer, consistent with prior studies. Although further research is, as always, indicated, the current study would suggest that patients with CHD are at elevated risk of prostate cancer but not breast or colorectal cancer. Although this association may be due to chance, CHD risk factors and medications should be further investigated in relation to prostate cancer incidence (50, 51), and CHD survivors may represent a high-risk group for future prostate cancer screening interventions.

References

- 1993 World Health Statistics Annual. Geneva: WHO, 1994.
- Parkin, D. M., Muir, C. S., Whelan, S. L., *et al.* Cancer Incidence in Five Continents, Vol 6. Lyon, France: IARC, 1992.
- Kurihara, M., Aoki, K., and Hisamichi, S. (eds). Cancer Mortality Statistics in the World, 1960–1985. Nagoya, Japan: University of Nagoya Press, 1989.
- Staszewski, J., and Haenszel, W. Cancer mortality among the Polish-born in the United States. *J. Natl. Cancer Inst.*, 35: 291–297, 1965.
- Haenszel, W., and Kurihara, M. Studies of Japanese immigrants. I. Mortality from cancer and other diseases among Japanese in the United States. *J. Natl. Cancer Inst.*, 40: 43–68, 1968.
- Wynder, E. L., Fujita, Y., Harris, R. E., Hirayama, T., and Hiyama, T. Comparative epidemiology of cancer between the United States and Japan. *Cancer (Phila.)*, 67: 746–773, 1991.
- Lilienfeld, A. M., Levin, M. L., and Kessler, I. I. Cancer in the United States. Cambridge, MA: Harvard University Press, 1972.
- Shephard, R. J. Exercise and cancer: linkages with obesity? *Crit. Rev. Food Sci. Nutr.*, 36: 321–339, 1996.
- Friedenreich, C. M., and Rohan, T. E. A review of physical activity and breast cancer. *Epidemiology*, 6: 311–317, 1995.
- Giovannucci, E., Ascherio, A., Rimm, E. B., Colditz, G. A., Stampfer, M. J., and Willett, W. C. Physical activity, obesity, and risk for colon cancer and adenoma in men. *Ann. Int. Med.*, 122: 327–334, 1995.
- Thune, I., and Lund, E. Physical activity and the risk of prostate and testicular cancer: a cohort study of 53,000 Norwegian men. *Cancer Causes Control*, 5: 539–556, 1994.
- McFarland, G. J., and Lowenfels, A. B. Physical activity and colon cancer. *Eur. J. Cancer Prev.*, 3: 393–398, 1994.
- Lee, I. M., and Paffenbarger, R. S., Jr. Physical activity and its relation to cancer risk: a prospective study of college alumni. *Med. Sci. Sports Exercise*, 26: 831–837, 1994.
- LeMarchand, L., Kolonel, L. N., and Yoshizawa, Z. N. Lifetime occupational physical activity and prostate cancer risk. *Am. J. Epidemiol.*, 133: 103–111, 1991.
- Whittemore, A. S., Kolonel, L. N., Wu, A. H., John, E. M., Gallagher, R. P., Howe, G. R., Burch, J. D., Hankin, J., Dreanon, D. M., West, D. W., *et al.* Prostate cancer in relation to diet, physical activity, and body size in blacks, whites and Asians in the United States and Canada. *J. Natl. Cancer Inst.*, 87: 652–661, 1995.
- Willett, W. C., Stampfer, M. J., Colditz, G. A., Rosner, B. A., Hennekens, C. H., and Speizer, F. E. Dietary fat and the risk of breast cancer. *N. Engl. J. Med.*, 316: 22–28, 1987.
- Willett, W. C. *Nutritional Epidemiology*. New York: Oxford University Press, 1990.
- Kolonel, L. Nutrition and prostate cancer. *Cancer Causes Control*, 7: 83–94, 1986.
- Boutron, M. C., Faivre, J., Dop, M. C., Quipourt, V., and Senesse, P. Tobacco, alcohol and colorectal tumors, a multistep process. *Am. J. Epidemiol.*, 141: 1038–1046, 1995.
- Lee, W. C., Neugut, A. I., Garbowski, G. C., Forde, K. A., Treat, M. R., Wayne, J. D., and Fenoglio-Preiser, C. Cigarettes, alcohol, coffee and caffeine as risk factors for colorectal adenomatous polyps. *Ann. Epidemiol.*, 3: 239–244, 1993.
- Jacobson, J. S., Neugut, A. I., Murray, T., Garbowski, G. C., Forde, K. A., Treat, M. R., Wayne, J. D., Santos, J., and Ahsan, H. Cigarette smoking and other risk factors for recurrent colorectal adenomatous polyps. *Cancer Causes Control*, 5: 215–220, 1994.
- Monnet, E., Allemand, H., Farina, H., and Carayon, P. Cigarette smoking and the risk of colorectal adenoma in men. *Scand. J. Gastroenterol.*, 26: 758–762, 1991.
- Kikendall, J. W., Bowen, T. E., Burgess, M. B., Magnetti, C., Woodward, J., and Langenberg, P. Cigarettes and alcohol as independent risk factors for colonic adenomas. *Gastroenterology*, 97: 660–664, 1989.
- Zahm, S. H., Cocco, P., and Blair, A. Tobacco smoking as a risk factor for colon polyps. *Am. J. Publ. Health*, 81: 846–849, 1991.
- Cope, G. F., Wyatt, J. I., Pinder, I. F., Lee, P. N., Heatley, R. V., and Kelleher, J. Alcohol consumption in patients with colorectal adenomatous polyps. *Gut*, 32: 70–72, 1991.
- Olsen, J., and Tornberg, O. Coffee, tobacco, and alcohol as risk factors for cancer and adenoma of the large intestine. *Int. J. Epidemiol.*, 22: 398–402, 1993.
- Martinez, M. E., McPherson, R. S., Annegers, J. F., and Levin, B. Cigarette smoking and alcohol consumption as risk factors for colorectal adenomatous polyps. *J. Natl. Cancer Inst.*, 87: 274–278, 1995.
- Giovannucci, E., Rimm, E. B., Stampfer, M. J., Colditz, G. A., Ascherio, A., Kearney, J., and Willett, W. C. A prospective study of cigarette smoking and risk of colorectal adenoma and colorectal cancer in U. S. men. *J. Natl. Cancer Inst.*, 86: 183–191, 1994.
- Giovannucci, E., Colditz, G. A., Stampfer, M. J., Hunter, D., Rosner, B. A., Willett, W. C., and Speizer, F. E. A prospective study of cigarette smoking and risk of colorectal adenoma and colorectal cancer in U. S. women. *J. Natl. Cancer Inst.*, 86: 192–199, 1994.
- Longnecker, M. P., Chen, M. J., Probst-Hensch, N. M., Harper, J. M., Lee, E. R., Frankl, H. D., and Haile, R. W. Alcohol and smoking in relation to the prevalence of adenomatous colorectal polyps detected on sigmoidoscopy. *Epidemiology*, 7: 275–280, 1996.
- Neugut, A. I. Re: Tobacco, alcohol, and colorectal tumors: a multi-step process. *Am. J. Epidemiol.*, 142: 1346, 1995.
- Greenberg, E. R., Baron, J. A., Freeman, D. H., Jr., Mandel, J. S., and Haile, R. Reduced risk of large bowel adenomas among aspirin users. *J. Natl. Cancer Inst.*, 85: 912–916, 1993.
- Suh, O., Mettlin, C., and Petrelli, N. J. Aspirin use, cancer and polyps of the large bowel. *Cancer (Phila.)*, 72: 1171–1177, 1993.
- Thun, M. J., Namboodiri, M. M., and Heath, C. W., Jr. Aspirin use and reduced risk of fatal colon cancer. *N. Engl. J. Med.*, 325: 1593–1596, 1991.
- Neugut, A. I. Nonsteroidal anti-inflammatory drugs and colorectal cancer: an epidemiologist's perspective. *Prev. Med.*, 24: 125–127, 1995.
- Thun, M. J., Namboodiri, N. M., Calle, E. E., Flander, W. D., and Heath, C. W., Jr. Aspirin use and risk of fatal cancer. *Cancer Res.*, 53: 1322–1327, 1993.
- Schreinemachers, D. M., and Everson, R. B. Aspirin use and lung, colon and breast cancer incidence in a prospective study. *Epidemiology*, 5: 138–146, 1994.
- Neugut, A. I. Breast cancer and colorectal neoplasia: double jeopardy or not? *Am. J. Gastroenterol.*, 88: 1989–1991, 1993.
- Neugut, A. I., Murray, T. I., Lee, W. C., and Robinson, E. The association of breast cancer and colorectal cancer in men: an analysis of SEER program data. *Cancer (Phila.)*, 68: 2069–2073, 1991.
- Schatzkin, A., Baranovsky, A., and Kessler, L. G. Diet and cancer: evidence from associations of multiple primary cancers in the SEER program. *Cancer (Phila.)*, 62: 1451–1457, 1988.
- Correa, P., Strong, J. P., Johnson, W. D., Pizzolatto, P., and Haenszel, W. Atherosclerosis and polyps of the colon. Quantification of precursor coronary heart disease and colon cancer. *J. Chronic Dis.*, 35: 313–320, 1982.
- Stemmermann, G. N., Heilbrun, L. K., Nomura, A., Yano, K., and Hayashi, T. Adenomatous polyps and atherosclerosis: an autopsy study of Japanese men in Hawaii. *Int. J. Cancer*, 38: 789–794, 1986.
- Kune, G. A., Kune, S., and Watson, L. F. Colorectal cancer risk, chronic illnesses, operations and medications: case-control results from the Melbourne Colorectal Cancer Study. *Cancer Res.*, 48: 4399–4404, 1988.
- Audigier, J. C., Barthelemy, C., Etaix, J. P., Duranton, B., Verneyre, H., and Fraisse, H. Infarctus du myocarde et polypes rectocoliques. (in French). *Gastroenterol. Clin. Biol.*, 10: 458–461, 1986.

45. Neugut, A. I., Jacobson, J. S., Sherif, G., Ahsan, H., Garbowski, G. C., Wayne, J., Forde, K. A., and Treat, M. R. Coronary artery disease and colorectal neoplasia. *Dis. Colon Rect.*, *38*: 873–877, 1995.
46. Henderson, B. E., Bogdanoff, E., Gerkins, V. R., SooHoo, J., and Arthur, M. Evaluation of cancer risk factors in a retirement community. *Cancer Res.*, *34*: 1045–1048, 1974.
47. Checkoway, H., DiFerdinando, G., Hulka, B. S., and Micky, D. D. Medical, lifestyle and occupational risk factors for prostate cancer. *Prostate*, *10*: 79–88, 1987.
48. Thompson, M. M., Garland, C., Barrett-Connor, E., Khaw, K. T., Friedlander, N. J., and Wingard, D. L. Heart disease risk factors, diabetes, and prostatic cancer in an adult community. *Am. J. Epidemiol.*, *129*: 511–517, 1989.
49. Gann, P. H., Manson, J. E., Glynn, R. J., Buring, J. E., and Hennekens, C. H. Low-dose aspirin and incidence of colorectal tumors in a randomized trial. *J. Natl. Cancer Inst.*, *85*: 1220–1224, 1993.
50. Steenland, K., Nowlin, S., and Palu, S. Cancer incidence in the National Health and Nutrition Survey. I. Follow-up data: diabetes, cholesterol, pulse and physical activity. *Cancer Epidemiol. Biomark. Prev.*, *4*: 807–811, 1995.
51. Connor, J., Sawczuk, I. S., Benson, M. C., Tomashefsky, P., O'Toole, K. M., Olsson, C. A., and Buttyan, R. Calcium channel antagonists delay regression of androgen-dependent tissues and suppress gene activity associated with cell death. *Prostate*, *13*: 119–130, 1988.