A Different Perspective on Breast Cancer Risk Factors: Some Implications of the Nonattributable Risk

Herbert Seidman, M.B.A.
Steven D. Stellman, Ph.D.
Margaret H. Mushinski, M.A.

Introduction

Since the late 1940s, breast cancer has been the leading cause of cancer death among American women. It is estimated that in 1982, 37,000 deaths from this disease will be recorded, and that 112,000 new cases will be diagnosed.[1]

The epidemiology of breast cancer has been the subject of investigation since before the 1930s,[2] and studies have proliferated since the 1960s. By the end of 1979, close to 400 articles had been written on the subject, including a number of comprehensive reviews.[3-6] This massive amount of investigation has established a number of widely accepted risk factors for this disease, which have been documented with a fair degree of consistency. These include a family history of breast cancer; nulliparity; late age at first live birth; early age at menarche; late age at menopause; history of benign breast disease; high socioeconomic status; high-dose radiation exposure; and being single, Jewish, or obese.[3-22]

Mr. Seidman is Assistant Vice President for Epidemiology and Statistics of the American Cancer Society in New York, New York.

Dr. Stellman is Assistant Vice President for Epidemiology of the American Cancer Society in New York, New York.

Ms. Mushinski is Senior Epidemiologic Research Associate of the American Cancer Society in New York, New York.

In addition, many experts have believed that a diet high in animal fats and perhaps dairy products or a diet low in fiber is associated with an elevated risk of breast cancer.[23-29] For many reasons, epidemiologic confirmation of this hypothesis has been difficult to obtain.[30]

More recently, several heretofore unrecognized associations between certain factors and breast cancer development have been uncovered and await further confirmation. These include alcohol consumption, long-term estrogen replacement therapy, tonsillectomy, and abortion during first trimester of pregnancy.[31-37] Controversy still surrounds the estimates of the risk of breast cancer related to long-term use of oral contraceptives, hair dyes, and some antihypertensive medication.[38-59]

The variety of factors and multitude of possible combinations make it extremely difficult to identify specific factors that predict the development of this disease in individuals. For example, most of the identified risk factors can be indicated in a number of different forms or combinations: being single as a reflection of nulliparity; consuming a high-fat diet as a reflection or extension of high socioeconomic status; use of hair dye as an indicator of social class; diets high in animal fats or milk reflecting a low intake of fiber; high parity indicating early age at first birth. Sorting out these independent and possibly confounding factors is one of the many

Downloaded from caonline.amcancersoc.org by on September 22, 2009 (©American Cancer Society, Inc.)

difficult tasks faced by epidemiologists.

While epidemiologic studies continue to be conducted and models and mechanisms of pathogenesis are being explored, the fact remains that one out of 11 U.S. women will develop breast cancer during her lifetime.[60] The magnitude of the problem with its psychological and clinical ramifications makes it imperative that we accelerate our efforts in developing practical means of identifying high-risk women and providing them with some assistance. This paper will describe the proportion of the total breast cancer burden carried by high-risk women and alert clinicians to the fact that even women without the "accepted" risk factors are at risk of developing the disease.

Materials and Methods

We undertook an analysis of the contribution each common risk factor made to the total risk experienced by more than 570,000 white American women enrolled in the American Cancer Society's large-scale prospective study begun in 1959.

Study enrollment was made according to "households." Participation was restricted to persons 30 years old or older who lived in a household in which at least one person 45 or older was also enrolled in the study. Participants completed a baseline questionnaire between October 1959 and February 1960. In addition to demographic questions, questions were asked pertaining to occupation, dietary habits, medical and family histories, breast disease, operations, parity, and lactation experiences. (For a more detailed description of the questions asked on the original questionnaire, see reference 61.)

Follow-up information was obtained from nearly all subjects (more than 98 percent of the subjects enrolled were traced for 12 years). Supplementary data were collected from questionnaires mailed to women in 1961, 1963, 1965, and 1972. These included information on whether they had had a breast operation during the intervening years and the reason for and date of operation. Many analyses of these data have been published.[14, 61–67]

A total of 571,716 white women aged 30 and over were enrolled in the study and followed for six years. Of this group, 9,429 reported breast cancer at entry and are excluded. The current analysis is further restricted to 365,812 white women aged 30 to 84, or 64 percent of those originally enrolled. Because women aged 85 years or older represented only 0.7 percent of the total women, and because their contribution to the rates of breast cancer was minimal, they were dropped from the calculations. Also excluded from the sample were women for which any of the following conditions obtained:

- positive history of breast cancer prior to entry into study
- height or weight data missing
- loss of 10 or more pounds during the year prior to study entry
- alcoholic beverage information omitted
- insufficient data provided on menarche or childbirth histories
- religion, education, or marital status not stated
- menopause information missing for women 50 years old or older
- history of a surgical menopause.

Of the study group, a total of 3,130 new cases of breast cancer were reported for the women during the six-year study period; 14 percent of these were determined through death certificates only.

The women were grouped into five age categories for analyses: 30 to 44, 45 to 54, 55 to 64, 65 to 74, and 75 to 84. The data were collapsed into two groups (30 to 54 and 55 to 84) for presentation of results because of the well-known differential in risk for premenopausal and postmenopausal women.[68–69] Incidence rates were standardized for age to the distribution of the total study group within the age intervals 30 to 54 and 55 to 84. Frequencies of cancer in various risk indicator groups were computed directly.

The majority of the women (64 percent) were between the ages of 30 and 54, with close to two thirds of these in the 45-to-54 age group. (Because of the enrollment criteria, described above, there was a large proportion of the population enrolled at ages 45 to 49 compared with ages

Downloaded from caonline.amcancersoc.org by on September 22, 2009 (©American Cancer Society, Inc.)

TABLE 1
HIGH-RISK AND LOW-RISK CATEGORIES USED IN ACS BREAST CANCER RISK FACTOR STUDY

High Risk	Low Risk
History of breast cancer in mother and/or sister	No history of breast cancer in mother and/or sister
History of breast surgery for a nonmalignant breast condition*	No breast surgery
Jewish	Non-Jewish
Menopause at age 50 or older	Menopause before age 50
Menarche before age 12	Menarche at age 12 or older
Never married	Ever married
First live birth at 30 years of age or older, or no live birth	First live birth before age 30
College graduate**	Did not graduate from college
Daily alcohol consumption (wine, beer, or hard liquor)	No daily alcohol consumption
Relative weight index 110 or more***	Relative weight index less than 110

*As an indicator of benign breast disease.
**As an indicator of socioeconomic status.
***Defined as 10 percent or more above average weight for a given woman's height and age.

Downloaded from caonline.amcancersoc.org by on September 22, 2009 (©American Cancer Society, Inc.)

40 to 44.) Among the women aged 55 to 84, the majority (63 percent) were between the ages of 55 and 64.

Of the many risk factors known to be related to the development of breast cancer, 10 were chosen for the current analysis. With the exception of alcohol consumption, these are factors that most investigators consider major predictors of breast cancer risk. These factors were treated as dichotomous variables; women were classified as being in a high-risk or low-risk group according to the presence or absence of the risk factor (Table 1).

A combination of dietary factors was originally included in the risk factor analyses, but was discarded once it was shown that the combination did not discriminate well enough between groups. That is, when high risk was defined using an index composed of the regular consumption of fried foods, eggs, meat, or poultry; use of fat for cooking; and/or daily milk consumption, close to 70 percent of women in both age groups fell into this risk category, and there was very little difference in risk estimates between these women and others. Other combinations of dietary information yielded similar results. Thus, it was decided not to consider diet as a risk factor for this analysis.

Results

Table 2 shows the number of women in each of two broad age groups, 30 to 54 and 55 to 84, according to the number of risk factors observed. More than 25 percent fell into the no-risk-factor category, according to our definition. About two thirds of the women had either one or two risk factors, and the remainder had three or more. The average number of risk factors per woman in the younger group was 1.4 and in the older group was 1.3.

Table 2 shows the relative and attributable risk for each group of women. The relative risk (RR) is the ratio of the age-standardized incidence rate in a given group, divided by the incidence among the group having no risk factors. As expected, the RR increases with the number of risk factors (one, two, three, and four or more); the RR is higher in the older group than in the younger group, because the specific risk factors are different (see below).

The second figure given in Table 2 is the so-called attributable risk percent, AR%, the proportion of breast cancers in the entire population that are associated with the given risk factors. It is calculated as: $AR\% = P_e \cdot (RR \cdot - 1) \div [P_e \cdot (RR \cdot - 1) + 1] \times 100\%$ where P_e is the proportion of that group "exposed" to or possessing the risk factor, RR is the relative risk for breast cancer in the group being considered, † = specific subcategories of risk factors, and * = total of one or more risk factors.

Despite our efforts to determine risk factors for breast cancer, we have not appreciably increased our ability to identify substantial numbers of truly high-risk women.

Thus, for example, the largest identifiable contribution to the total breast cancer incidence in women 55 to 84 years old comes from women with exactly two risk factors (10.4 percent of all breast cancers in this age group), even though numerically there are more women with only one risk factor.

In the 30-to-54-year-old women, the largest attributable risk is 7.9 percent, also in the two-risk-factor group. This means that 7.9 percent of all breast cancers in 30-to-54-year-old women can be identified or attributed to the small group of women (22.8 percent) who possess exactly two risk factors (regardless of which factors they are). It means as well that if all risk factors were absent in this group of women, the total number of breast cancers in the 30-to-54-year-old group might be reduced by 7.9 percent.

Another interesting interpretation of the AR is that 7.9 percent of breast cancers in the 35-to-54 age group would be *prevented* if all the risk factors in this small group of double-risk-factor women were

Downloaded from caonline.amcancersoc.org by on September 22, 2009 (©American Cancer Society, Inc.)

TABLE 2
INCIDENCE RATE, RELATIVE RISK, AND ATTRIBUTABLE RISK FOR BREAST CANCER ACCORDING TO NUMBER OF RISK FACTORS

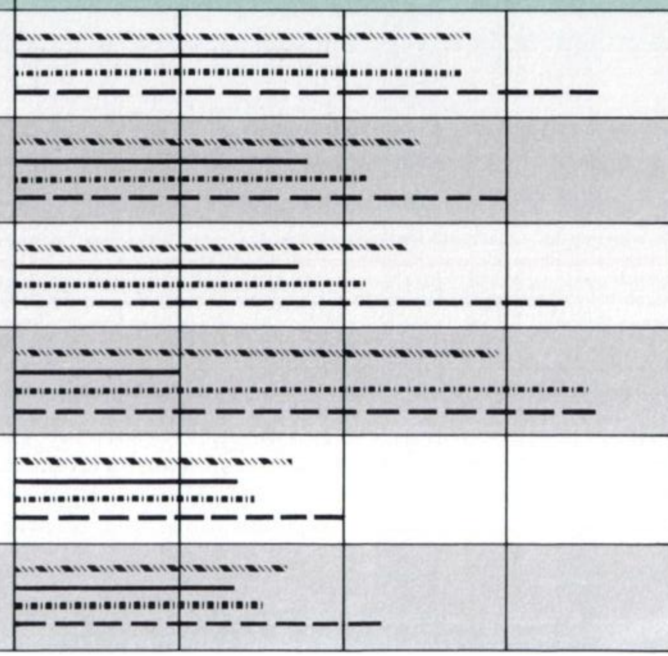
Number of Risk Factors	Number of Women	Percent of Women	Cases of Breast Cancer	Annual* Incidence (per 10^5)	RR	AR
Ages 30–54						
None	68,024	29.1	387	112.9	1.00	0.0
One	89,872	38.4	601	134.8	1.19	5.7
Two	53,248	22.8	423	163.0	1.44	7.9
Three	17,961	7.7	176	209.9	1.86	5.2
Four or more	4,618	2.0	58	279.1	2.47	2.3
Total, one or more	165,699	70.9	1,258	155.3	1.38	21.1
Total	233,723	100.0	1,645	142.8		
Ages 55–84						
None	33,539	25.4	264	120.2	1.00	0.0
One	48,818	36.9	500	154.6	1.29	7.6
Two	32,715	24.8	419	191.6	1.59	10.4
Three	13,036	9.9	230	263.5	2.19	8.4
Four or more	3,981	3.0	72	264.1	2.20	2.6
Total, one or more	98,550	74.6	1,221	186.4	1.55	29.0
Total	132,089	100.0	1,485	169.6		

*Adjusted by the direct method to age distribution of total study women.

Key RR = Relative Risk
AR = Attributable Risk Percent

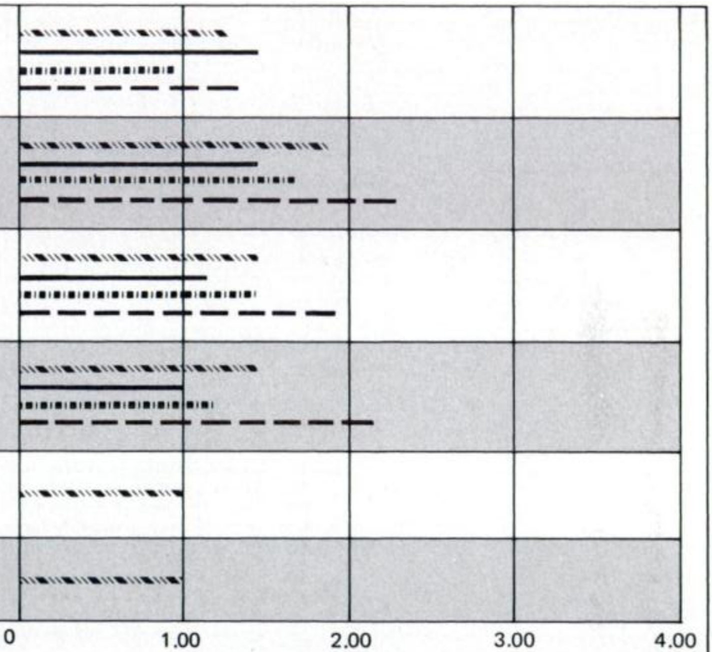
Downloaded from caonline.amcancersoc.org by on September 22, 2009 (©American Cancer Society, Inc.)

TABLE 3 BREAST CANCER RISK FACTORS, WHITE FEMALES RATIO OF BREAST CANCER INCIDENCE RATES TO RATES FOR WOMEN WITH NO RISK FACTORS				
Risk Factors	**Age**	**Percent of Total Women**	**Average Number of Additional Risk Factors**	**Relative Risk**
Family History of Breast Cancer	30–54	3.6	1.2	
	55–84	5.1	1.3	
History of Breast Operation	30–54	2.2	1.2	
	55–84	1.8	1.4	
No Live Birth by Age 30	30–54	26.4	1.0	
	55–84	26.8	1.1	



Downloaded from caonline.amcancersoc.org by on September 22, 2009 (©American Cancer Society, Inc.)

Menopause After Age 50	30-54	2.7	0.5	
	55-84	26.8	1.1	
Menarche Before Age 12	30-54	14.6	1.1	
	55-84	10.5	1.2	
No Risk Factors		29.1	0.0	
	55-84	25.4	0.0	



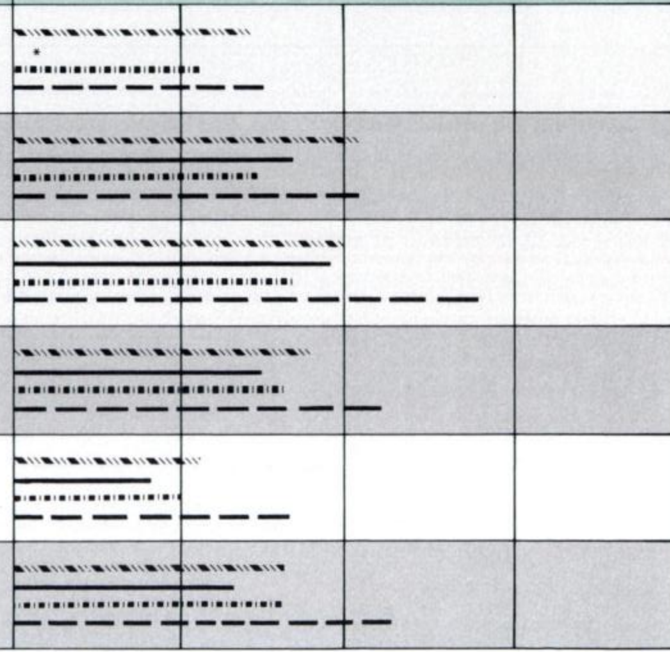
Key: All Women Having This Risk Factor
This Risk Factor Alone
This Risk Factor Plus One Other
This Risk Factor Plus Two or More Other

Note: Incidence rates are standardized to the age distribution of total study group.

Downloaded from caonline.amcancersoc.org by on September 22, 2009 (©American Cancer Society, Inc.)

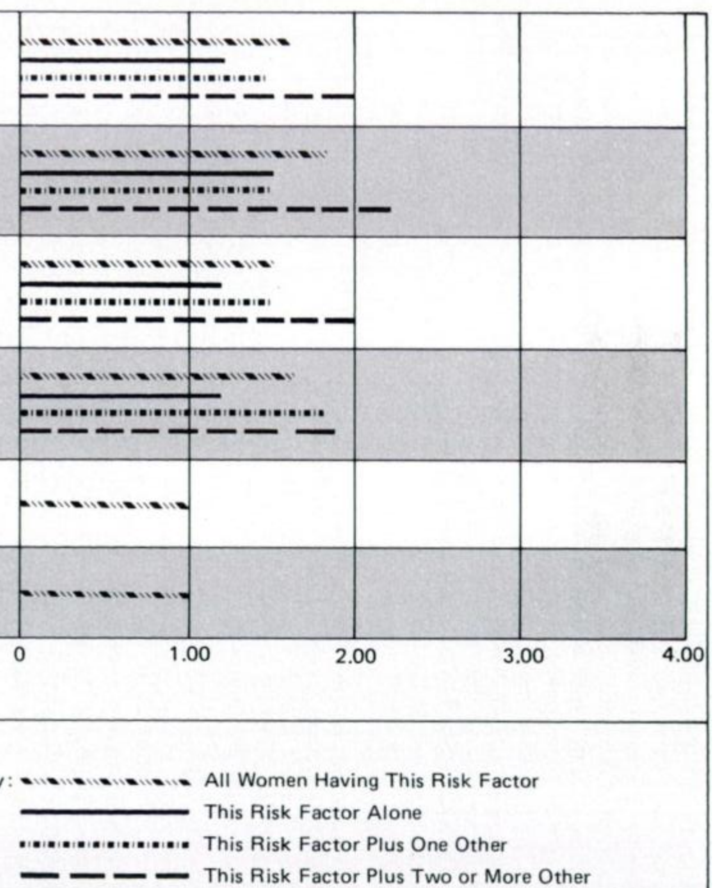
TABLE 3 (continued)
BREAST CANCER RISK FACTORS, WHITE FEMALES
RATIO OF BREAST CANCER INCIDENCE RATES TO RATES FOR WOMEN WITH NO RISK FACTORS

Risk Factors	Age	Percent of Total Women	Average Number of Additional Risk Factors	Relative Risk
Never Married	30–54	1.2	2.1	*
	55–84	1.3	2.3	
Jewish	30–54	4.2	1.1	
	55–84	2.6	1.3	
Relative Weight Index 110 or Over	30–54	20.2	0.8	
	55–84	23.7	0.9	



Downloaded from caonline.amcancersoc.org by on September 22, 2009 (©American Cancer Society, Inc.)

College Graduate	30–54	15.6	1.2
	55–84	12.3	1.4
Alcohol Daily	30–54	24.7	0.9
	55–84	17.7	1.2
No Risk Factors	30–54	29.1	0.0
	55–84	25.4	0.0



*Too few cases to calculate.

Note: Incidence rates are standardized to the age distribution of total study group.

Downloaded from caonline.amcancersoc.org by on September 22, 2009 (©American Cancer Society, Inc.)

eliminated. This is a less useful concept, however, since some risk factors represent "exposures" that can be modified or eliminated (such as diet, alcohol consumption, and excess weight), while others may not be subject to such control (age at menarche, family history, etc.).

What is of primary importance is that the ARs are additive (see Table 2). The total AR in the 30-to-54-year-old group is 21.1 percent, while in the 55-to-84-year-old group, it is 29.0 percent. This means that, given our current understanding of breast cancer risk factors, we are unable to identify or account for the "causes" of more than about one quarter of all cases.

Table 3 shows the RR for breast cancer in women with specific risk factors as defined above. Since close to one third of the women in our study population had more than one risk factor, we calculated incidence rates and RRs in subgroups of women with various combinations of factors. The RR associated with each labeled risk factor is shown for four groups of women:

- those who possess that factor, regardless of any other factors they may have
- those who possess that factor only, and no other factors
- those with that factor and exactly one other factor
- those with the given risk factor and at least two other factors.

The most remarkable feature of the graph is its *lack* of remarkability—that is, the majority of factors are associated with risks of 1.8 or less.

The largest RR seen is 3.5. This RR was found for one risk factor in each in both of the age groups considered—i.e., women aged 30 to 54 with a family history of breast cancer and two or more other risk factors, and women aged 55 to 84 with a history of a breast operation (as an index of benign breast disease) and at least two other factors. This latter risk factor appears to be the strongest of those we considered, because an RR of 3.4 was also found for it in association with only one other risk factor among the older women, and an RR of 3.3 was seen among the younger women with two or more other risk factors.

History of breast operation more than doubled the risk in younger women and nearly tripled it in older women. However, because about one in 50 women possesses this risk factor, it accounts for at most only about three percent of the total number of breast cancer cases.

Family history of breast cancer produces the next highest RR in both age groups; the incidence of breast cancer is about triple the rate in the four to five percent of women with a family history, compared with women with no risk factors. Surveillance is greatest in these two groups of women with the highest RRs (family history and history of breast operation), which may lead to a better approximation of their actual breast cancer risk. Because these factors are those that are mostly genetically determined and thus not subject to preventive measures, these women should indeed receive a great deal of monitoring.

It looks as if the clinician must consider every female patient of 35 or older as one at substantial risk of developing breast cancer.

Discussion

Many advances have been made in our understanding and treatment of cancer. Many people have quit or never started smoking, and screening for cervical cancer has become a routine part of a woman's annual checkup. Nonetheless, major difficulties still obstruct our goal of more widespread prevention. Even when epidemiologists uncover major risk factors for some cancers, such as those associated with smoking exposure, inertia and indifference often reduce the potential success of control efforts.

In the case of breast cancer, the risk factors neither present as great a potential for control nor are as clear-cut as those for lung or cervical cancer. Investigators con-

Downloaded from caonline.amcancersoc.org by on September 22, 2009 (©American Cancer Society, Inc.)

sistently have reported excess risks for women with a family history of breast cancer, nulliparity, late age at first birth, and benign breast disease. These are factors over which a woman has little or no control. A factor over which the high-risk women have some control is excessive relative weight (particularly among older women).

The results of this analysis seem to correspond more with earlier reports than recent ones stating that certain risk factors hold "the key" to the understanding of the etiology of breast cancer.[70, 71] That is, when we considered the risk factors alone or in combination, they explained only 21 percent of the breast cancer risk among women aged 30 to 54 and 29 percent among women aged 55 to 84. Different choices and definitions of the risk factors lead to somewhat different specific figures but to the same general results. Further effort might delineate combinations of specific factors that could lead to even greater risks, but such specific combinations occur in relatively few women.

Despite our efforts to determine risk factors for breast cancer, we have not appreciably increased our ability to identify substantial numbers of truly "high-risk" women. From the point of view of the clinician, all women should be treated as being at appreciable risk for breast cancer; which is not to say that it may not be useful to single out specific women as at especially "high risk." From the point of view of prevention, even small identifiable attributable risks, such as we have delineated here, represent significant numbers of cases of breast cancer.

The fact that three quarters of all breast cancer cannot yet be attributed to any known specific causes is reason to increase our efforts to identify and quantify risk factors, and to seek effective means of intervention and control.

Since the principles of prevention of breast cancer are complicated and still in an embryonic stage, women are fortunate that early detection has proved so beneficial. Early detection of breast lesions has led to both increased survival rates and better quality of life for women with the disease. Even if more data are amassed to provide a better description of the truly high-risk woman, it seems likely that such women will constitute only a small proportion of total breast cancer cases. Women should be taught breast self-examination and encouraged to have periodic mammograms.

If the state of our knowledge does not permit us to claim means of reducing the incidence of breast cancer, at least we can claim means of providing better outcomes through earlier detection to those in whom the disease was not prevented. Such news should provide all women with the comfort of knowing that they can take an active role in their health.

References

1. American Cancer Society: Cancer Facts and Figures, 1982. New York, American Cancer Society Inc, 1982.

2. Lane-Claypon JE: A further report on cancer of the breast, with special reference to its associated antecedent conditions, in Reports of the Ministry of Health: Public Health and Medical Subjects No. 32. London, British Ministry of Health, 1926.

3. MacMahon B, Cole P, Brown J: Etiology of human breast cancer: a review. JNCI 50:21–42, 1973.

4. Wynder EL, MacCornack FA, Stellman SD: The epidemiology of breast cancer in 785 United States Caucasian women. Cancer 41:2341–2354, 1978.

5. Kelsey JL: A review of the epidemiology of human breast cancers. Epidemiol Rev 1:74–109, 1979.

6. Miller AB, Bulbrook RD: The epidemiology and etiology of breast cancer. N Engl J Med 303:1246–1248, 1980.

7. Anderson DE: Some characteristics of familial breast cancer. Cancer 28:1500–1504, 1971.

8. Lilienfeld AM: The epidemiology of breast cancer. Cancer Res 23:1503–1513, 1963.

9. Petrakis NL: Genetic factors in the etiology of breast cancer. Cancer 39:2709–2715, 1977.

Downloaded from caonline.amcancersoc.org by on September 22, 2009 (©American Cancer Society, Inc.)

10. Slaber EJ, Trichopoulos D, MacMahon B: Lactation and reproductive histories of breast cancer patients in Boston, 1965–1966. JNCI 43:1013–1024, 1969.
11. Wynder EL, Bross IDJ, Hirayama T: A study of the epidemiology of cancer of the breast. Cancer 13:559–601, 1960.
12. Staszewski J: Age at menarche and breast cancer. JNCI 47:935–940, 1971.
13. Trichopoulos D, MacMahon B, Cole P: Menopause and breast cancer risk. JNCI 48:605–613, 1972.
14. Lew EA, Garfinkel L: Variations in mortality by weight among 750,000 men and women. J Chronic Dis 32:563–576, 1979.
15. De Waard F: Breast cancer incidence and nutritional status with particular reference to body weight and height. Cancer Res 35:3351–3356, 1975.
16. De Waard F, Baanders-van Halewijn EA: A prospective study in general practice on breast cancer risk in postmenopausal women. Int J Cancer 14:153–160, 1974.
17. MacKenzie I: Breast cancer following multiple fluoroscopies. Br J Cancer 19:1–8, 1965.
18. Wanebo CK, Johnson KG, Sato H, et al: Breast cancer after exposure to the atomic bombings of Hiroshima and Nagasaki. N Engl J Med 279:667–671, 1968.
19. Myrden JA, Hiltz JE: Breast cancer following multiple fluoroscopies during artificial pneumothorax treatment of pulmonary tuberculoses. Can Med Assoc J 100:1032–1034, 1969.
20. Jablon S, Kato H: Studies of the mortality of A-bomb survivors: 5. Radiation dose and mortality, 1950–1970. Radiat Res 50:649–698, 1972.
21. McGregor DH, Land CE, Choi K, et al: Breast cancer incidence among atomic bomb survivors, Hiroshima and Nagasaki, 1950–1969. JNCI 59:799–811, 1977.
22. Shore RE, Hempelmann LH, Kowaluk E, et al: Breast neoplasms in women treated with x-rays for acute postpartum mastitis. JNCI 59:813–822, 1977.
23. Alcantara EN, Speckman EW: Diet, nutrition, and cancer. Am J Clin Nutr 29:1035–1047, 1976.
24. Armstrong B, Doll R: Environmental factors and cancer incidence and mortality in different countries, with special reference to dietary practices. Int J Cancer 15:627–631, 1975.
25. Carroll KK, Gammal EB, Plunkett ER: Dietary fat and mammary cancer. Can Med Assoc J 98:590–594, 1968.
26. Miller AB: Role of nutrition in the etiology of breast cancer. Cancer 39:2704–2708, 1977.
27. Gaskill SP, McGuire WL, Osborne CK, et al: Breast cancer mortality and diet in the United States. Cancer Res 39:3628–3637, 1979.
28. Miller AB, Kelly A, Choi NW, et al: A study of diet and breast cancer. Am J Epidemiol 107:499–509, 1978.
29. Hankin JH, Rawlings V: Diet and breast cancer: a review. Am J Clin Nutr 31:2007–2016, 1978.
30. Graham S, Marshall J, Mettlin C, et al: Diet in the epidemiology of breast cancer. Am J Epidemiol 116:68–75, 1982.
31. Rosenberg L, Slone D, Shapiro S, et al: Breast cancer and alcoholic beverage consumption. Lancet 1:267–270, 1982.
32. Hoover R, Gray L, Cole P, et al: Menopausal estrogens and breast cancer. N Engl J Med 295:401–405, 1976.
33. Ross RK, Paganini-Hill A, Gerkins VR, et al: A case-control study of menopausal estrogen therapy and breast cancer. JAMA 243:1635–1639, 1980.
34. Brinton LA, Hoover RN, Szklo M, et al: Menopausal estrogen use and risk of breast cancer. Cancer 47:2517–2522, 1981.
35. Jick H, Walker AM, Watkins RN, et al: Replacement estrogens and breast cancer. Am J Epidemiol 112:586–594, 1980.
36. Lubin JH, Burns PE, Blot WJ, et al: Risk factors for breast cancer in women in northern Alberta, Canada, as related to age at diagnosis. JNCI 68:211–217, 1982.
37. Pike MC, Henderson BE, Casagrande JT, et al: Oral contraceptive use and early abortion as risk factors for breast cancer in young women. Br J Cancer 43:72–76, 1981.
38. Trapido EJ: A prospective cohort study of oral contraceptives and breast cancer. JNCI 67:1011–1015, 1981.
39. Vessey MP, Doll R, Jones K, et al: An epidemiologic study of oral contraceptives and breast cancer. Br Med J 1:1757–1760, 1979.
40. Arthes FG, Sartwell PE, Lewison EF: The pill, estrogens, and the breast: epidemiologic aspects. Cancer 28:1391–1394, 1971.
41. Henderson BE, Powell D, Rosario I, et al: An epidemiologic study of breast cancer. JNCI 53:609–614, 1974.
42. Fasal E, Paffenbarger RS: Oral contraceptives as related to cancer and benign lesions of the breast. JNCI 55:767–773, 1975.
43. Kelsey J, Holford TR, White C, et al: Oral contraceptives and breast disease. Am J Epidemiol 107:236–244, 1978.
44. Vessey MP, Doll R, Sutton PM: Oral contraceptives and breast neoplasia: a retrospective study. Br Med J 3:719–724, 1972.
45. Paffenbarger RS, Fasal E, Simmons ME, et al: Cancer risk as related to use of oral

Downloaded from caonline.amcancersoc.org by on September 22, 2009 (©American Cancer Society, Inc.)

contraceptives during fertile years. Cancer 39:1887–1891, 1971.
46. Lees AW, Burns PE, Grace M: Oral contraceptives and breast disease in premenopausal northern Albertan women. Int J Cancer 22:700–707, 1978.
47. Shore RE, Pasternak BS, Thiessen EU, et al: A case-control study of hair dye use and breast cancer. JNCI 62:277–283, 1979.
48. Kinlen LJ, Harris R, Garrod A, et al: Use of hair dyes by patients with breast cancer: a case-control study. Br Med J 2:366–368, 1977.
49. Hennekens CH, Speizer FE, Rosner B, et al: Hair dyes and human cancer, abstracted. Am J Epidemiol 108:240–241, 1978.
50. Shafer N, Shafer RW: Potential of carcinogenic effects of hair dyes. NY State J Med 76:394–396, 1976.
51. Boston Collaborative Drug Surveillance Program: Reserpine and breast cancer. Lancet 2:669–671, 1974.
52. Armstrong B, Stevens N, Doll R: Retrospective study of the association between use of Rauwolfia derivatives and breast cancer in English women. Lancet 2:672–675, 1974.
53. Heinonen OP, Shapiro S, Tuominen L, et al: Reserpine use in relation to breast cancer. Lancet 2:675–677, 1974.
54. Williams RR, Feinleib M, Connor RJ, et al: Case-control study of antihypertensive and diuretic use by women with malignant and benign breast lesions detected in a mammography screening program. JNCI 61:327–335, 1978.
55. Laska EM, Siegel C, Meisner M, et al: Matched-pairs study of reserpine use and breast cancer: Lancet 2:296–300, 1975.
56. Lilienfeld AM, Chang L, Thomas DB, et al: Rauwolfia derivatives and breast cancer. Johns Hopkins Med J 139:41–50, 1976.
57. O'Fallon WM, Labarthe DR, Kurland LT: Rauwolfia derivatives and breast cancer: a case-control study in Olmstead County, Minnesota. Lancet 2:292–296, 1975.
58. Armstrong B, Skegg D, White G, et al: Rauwolfia derivatives and breast cancer in hypertensive women. Lancet 2:8–12, 1976.
59. Labarthe DR, O'Fallon WM: Reserpine and breast cancer: a community-based longitudinal study of 2,000 hypertensive women. JAMA 243:2304–2310, 1980.
60. Seidman H: Statistical and epidemiological data on cancer of the breast. New York, American Cancer Society Inc, 1979.
61. Seidman H: Screening for breast cancer in younger women: life expectancy gains and losses. CA 27:66–87, 1977.
62. Hammond EC: Some preliminary findings on physical complaints from a prospective study of 1,064,004 men and women. Am J Public Health 54:11–23, 1964.
63. Hammond EC: Smoking in relation to the death rates of one million men and women. NCI Monogr 19:127–204, 1966.
64. Hammond EC, Garfinkel L: The influence of health on smoking habits. NCI Monogr 19:269–285, 1966.
65. Hammond EC, Garfinkel L: Coronary heart disease, stroke, and aortic aneurysm: factors in the etiology. Arch Environ Health 19:167–182, 1969.
66. Hammond EC, Garfinkel L, Seidman H, et al: "Tar" and nicotine content of cigarette smoke in relation to death rates. Environ Res 12:263–274, 1976.
67. Hammond EC, Selikoff IJ, Seidman H: Asbestos exposure, cigarette smoking, and death rates. Ann NY Acad Sci 330:473–490, 1979.
68. De Waard F, Baanders-van Halewijn EA, Huizinga J: The bimodal age distribution of patients with mammary carcinoma: evidence for existence of two types of human breast cancer. Cancer 17:141–151, 1964.
69. Stavraky K, Emmons S: Breast cancer in premenopausal and postmenopausal women. JNCI 53:647–654, 1974.
70. Wynder EL: Identification of women at high risk for breast cancer. Cancer 24:1235–1240, 1969.
71. Henderson BE, Pike MC, Ross RK: Epidemiology of breast cancer, in Feig SA, Mclelland R (eds): Breast Carcinoma: Current Diagnosis and Treatment. New York, Masson Publishers, 1982.

Downloaded from caonline.amcancersoc.org by on September 22, 2009 (©American Cancer Society, Inc.)