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Introduction

Case-control studies, in which past exposure information for persons with a particular disease is compared to that of persons without the disease, are particularly useful for investigating potential risk factors for diseases that are relatively rare. To this end, the methods used to ascertain exposure status are critical to the validity of a case-control study. When these methods rely on self-reports of past exposure, there is the potential for recall bias to occur. According to Lippmann and Mackenzie, recall bias "refers to the unequivalence in responses of cases and controls to queries about exposures if the outcome event that defines study groups itself stimulates greater recollection or reporting of earlier events by cases than by controls."[1] There is a long-standing recognition in epidemiology that recall bias can produce spurious associations between reported exposures and disease. Weiss states that "recall bias is one of the principal threats to an interview- or questionnaire-based case-control study."[2] Greenland considers that "generally, in the absence of a sound basis for assuming nondifferential misclassification, it would seem prudent not to base inferences on methods that depend on the assumption."[3] Levois and Switzer suggest that "a sound basis for assuming nondifferential recall of exposure would presumably involve both the collection of data to test that assumption, and the absence of any specific reason to suspect that recall bias might be likely."[4]

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1 Abby Lippman & Susan Mackenzie, *What is "Recall Bias" and Does it Exist?, in* Prevention of Physical and Mental Defects (M. Marois ed., 1985).

2 Noel S. Weiss, *Dr. Weiss Replies: Analytic Approaches for Dealing with Possible Recall Bias in Case-Control Studies,* 141 Am. J. Epidemiology 280 (1995).

3 Sander Greenland, *Variance Estimation for Epidemiologic Effect Estimates under Misclassification,* 7 Stat. Med. 745 (1988).

4 Maurice Levois & Paul Switzer, *Differential Exposure Misclassification in Case-Control*

This paper compares the treatments of recall bias, as examined in the epidemiological literature, relating to two different associations. The first association considered is that between female breast cancer and a history of induced abortion. The second association is that between female lung cancer and a history of exposure to spousal smoking.

Brind et al. outline the case for a causal association between induced abortion and breast cancer.[5] They point out that of twenty-three epidemiological studies carried out worldwide since 1957, eighteen have reported a positive association; ten of these studies have demonstrated statistically significant results. In addition, they describe a biological plausibility argument based on the growth promotion properties of estrogen, citing an animal study by Russo and Russo in which "the incidence of breast cancer is dramatically increased in rats whose pregnancies are aborted."[6]

In outlining the case for a causal association between passive smoking and lung cancer, the scientific editors of a 1992 Environmental Protection Agency (EPA) report point to the fact that, of the thirty studies considered, twenty-four "demonstrated an increased risk of lung cancer in the" ever-exposed "group using the crude spousal smoking surrogate; nine of these were statistically significant."[7] They use the dose-related association between active smoking and lung cancer to infer biological plausibility. In addition, they claim that "in lifetime rat studies, intrapulmonary implants of mainstream smoke condensate cause a dose-dependent increase in the incidence of lung carcinoma"[8] and that "sidestream smoke condensate also induces lung carcinomas by intrapulmonary plantation."[9]

Studies of Environmental Tobacco Smoke and Lung Cancer, 51 J. Clinical Epidemiology 37 (1998).

5 *See* Joel Brind et al., *Re: Induced Abortion and Risk for Breast Cancer: Reporting (Recall) Bias in a Dutch Case-Control Study,* 89 J. Nat'l Cancer Inst. 588 (1997).

6 J. Russo & I.H. Russo, *Susceptibility of the Mammary Gland to Carcinogenesis,* 100 Am. J. Pathology 497 (1980).

7 Jennifer Jinot & Steven Bayard, *Respiratory Health Effects of Passive Smoking: EPA's Weight-of-Evidence Analysis,* 47 J. Clinical Epidemiology 339 (1994).

8 M.F. Stanton et al., *Experimental Induction of Epidermoid Carcinoma in the Lungs of Rats by Cigarette Smoke Condensate,* 49 J. Nat'l Cancer Inst. 867 (1972); G.E. Dagle et al., *Pulmonary Carcinogenesis in Rats Given Implants of Cigarette Smoke Condensate in Beeswax Pellets,* 61 J. Nat'l Cancer Inst. 905 (1978).

The outlines in the two preceding paragraphs are very similar. An additional point of similarity is that meta-analyses of epidemiologic studies of both associations produce pooled odds ratios greater than 1.0 but less than 2.0. Nevertheless, as I shall demonstrate, the consensus in the epidemiological community is that the association between lung cancer and environmental tobacco smoke (ETS) exposure reflects a causal relationship whereas the association between breast cancer and induced abortion does not. The purpose of this paper is to explore the validity of this distinction.

Section 2 begins with a brief description of recall bias and of methods for assessing its potential impact. Section 3 deals with the breast cancer/induced abortion association, and Section 4 with the lung cancer/spousal smoking association. The treatment of each association follows the following pattern: (a) a description of a single case-control study, an assessment of the sensitivity to recall bias of that study's findings and a description of the authors' treatment of recall bias, (b) a review of the literature bearing on the validation of questionnaire assessment of the particular exposure, and (c) an examination of the public health consensus concerning the particular association. The treatments in (b) and (c) were based on MEDLINE searches using the keywords "recall bias," "breast (lung) cancer," and "induced abortion (environmental tobacco smoke)."

Section 3 indicates that the potential for recall bias to produce a spurious association of breast cancer with a history of induced abortion has been intensively debated. This debate has, in large part, been responsible for a public health consensus in which observed weak associations between breast cancer and induced abortion have been ascribed to bias. Next, Section 4 indicates that, while many studies have been carried out on the validity of questionnaire assessments of ETS exposure, very few allow comparison between cases and controls in terms of validity and thereby an assessment of the potential for recall bias. There has been little debate concerning the potential for recall bias to produce a spurious association between lung cancer and a history of exposure to spousal ETS. Nevertheless, epidemiological evidence very

9 G. Grimmer et al., *Contribution of Polycyclic Aromatic Compounds to the Carcinogenicity of Sidestream Smoke of Cigarettes Evaluated by Implantation into the Lungs of Rats*, 43 Cancer Letters 173 (1988).

similar to that relating to the association between breast cancer and induced abortion has led to a public health consensus in which observed weak associations between lung cancer and spousal smoking have been adjudged to reflect a causal relationship. In Section 5, I discuss possible explanations for this divergence and make recommendations regarding the treatment of recall bias in the execution of case-control studies.

The Problem of Recall Bias

Consider a case-control study designed to investigate the association between a particular disease and exposure to a putative risk factor. Suppose, for simplicity, that the exposure status of subjects is dichotomous so that subjects are either exposed or unexposed. Given the true exposure status of each subject the following table may be constructed:

	Cases	*Controls*
Exposed	N_{11}	N_{01}
Unexposed	N_{10}	N_{00}

The strength of the association between exposure and disease status is usually measured using the odds ratio:

$$OR = \frac{N_{11}N_{00}}{N_{10}N_{01}}$$

In many studies only assessments of true exposure status are available and these may be error-prone. Let us write the table based on assessed exposure status as:

	Cases	*Controls*
Exposed	$\tilde{N}_{11}$	$\tilde{N}_{01}$
Unexposed	$\tilde{N}_{10}$	$\tilde{N}_{00}$

The odds ratio measuring the strength of the association between assessed exposure and disease status is given by:

$$OR^* = \frac{\tilde{N}_{11}\tilde{N}_{00}}{\tilde{N}_{10}\tilde{N}_{01}}$$

Let $D_1 = \tilde{N}_{11} - N_{11}$ denote the difference between the number of cases assessed as exposed and the number of cases actually exposed. Let $D_0 = \tilde{N}_{00} - N_{00}$ denote the difference between the number of controls assessed as unexposed and the number of controls actually unexposed. Then:

$$OR^* = \frac{\tilde{N}_{11}\tilde{N}_{00}}{\tilde{N}_{10}\tilde{N}_{01}} = \frac{(N_{11}+D_1)(N_{00}+D_0)}{(N_{10}-D_1)(N_{01}-D_0)}$$

Clearly OR* is an increasing function of both D_1 and D_0. Recall bias is said to occur if the values of D_1 and D_0 are such that OR* is not equal to OR.

By way of example, consider a case-control study in which the past exposure of subjects is self-assessed. A tendency for cases to over-report past exposure and for controls to under-report past exposure will imply $D_1 > 0$ and $D_0 > 0$ and therefore OR* > OR.

One way to assess the possible effects of recall bias on the analysis of a particular table is to consider a range of reasonable choices for (D_1, D_0) and, for each choice, to analyze the following 2 X 2 table:

	Cases	*Controls*
Exposed	$\tilde{N}_{11} - D_1$	$\tilde{N}_{01} + D_0$
Unexposed	$\tilde{N}_{10} + D_1$	$\tilde{N}_{00} - D_0$

There are two ways in which values for D_1 and D_0 may be estimated.

Marshall defines the positive predictive value of an exposure assessment procedure as the proportion of subjects assessed as exposed who are actually exposed and the negative predictive value as the proportion of subjects assessed as unexposed who are actually unexposed.[10]

10 *See* Roger J. Marshall, *Validation Study Methods for Estimating Exposure Proportions and Odds Ratios with Misclassified Data*, 43 J. Clinical Epidemiology 941 (1990).

Let $a_0(a_1)$ be the positive predictive value for controls (cases) and let $b_0(b_1)$ be the negative predictive value for controls (cases). Then:

(2.1) $$D_0 = \tilde{N}_{00}(1 - b_0) - \tilde{N}_{01}(1 - a_0)$$

is an increasing function of a_0 and a decreasing function of b_0.

Similarly:

(2.2) $$D_1 = \tilde{N}_{11}(1 - a_1) - \tilde{N}_{10}(1 - b_1)$$

is a decreasing function of a_1 and an increasing function of b_1. The positive predictive value of an exposure assessment procedure may be estimated by taking a random sample of subjects assessed as exposed and determining as accurately as possible the proportion who were actually exposed. The negative predictive value may be estimated in a similar fashion. These validation studies must be carried out separately for cases and controls. Given estimates of the predictive values, estimates of D_1 and D_0 may be found using equations 2.1 and 2.2, respectively.

Barron looks at the problem in a somewhat different way. He defines the sensitivity of an exposure assessment procedure as the proportion of truly exposed subjects who are assessed as exposed and the specificity as the proportion of truly unexposed subjects who are assessed as unexposed.[11] Let $\alpha_0(\alpha_1)$ be the sensitivity among controls (cases) and let $\beta_0(\beta_1)$ be the specificity among controls (cases). Greenland[12] has shown that:

(2.3) $$\begin{aligned} D_0 &= N_{01}(1-\alpha_0) - N_{00}(1-\beta_0) \\ &= \frac{\tilde{N}_{01}(1-\alpha_0) - \tilde{N}_{00}(1-\beta_0)}{\alpha_0 + \beta_0 - 1} \end{aligned}$$

which is a decreasing function of α_0 and an increasing function of β_0. Similarly:

(2.4) $$\begin{aligned} D_1 &= N_{10}(1-\beta_1) - N_{11}(1-\alpha_1) \\ &= \frac{\tilde{N}_{10}(1-\beta_1) - \tilde{N}_{11}(1-\alpha_1)}{\alpha_1 + \beta_1 - 1} \end{aligned}$$

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11 *See* B.A. Barron, *The Effects of Misclassification on the Estimation of Relative Risk*, 33 Biometrics 414 (1977).

12 *See* Sander Greenland, *Basic Methods for Sensitivity Analysis of Biases*, 25 Int'l J. Epidemiology 1107 (1996).

which is an increasing function of α_1 and a decreasing function of β_1. The sensitivity of an exposure assessment procedure may be estimated by taking a random sample of subjects *known* to have been exposed and determining the proportion who were assessed as exposed. The specificity may be estimated in a similar fashion. These validation studies must be carried out separately for cases and controls. Given estimates of the sensitivity and specificity, estimates of D_0 and D_1 may be found using equations 2.3 and 2.4, respectively.

The potential for recall bias should be analyzed as a routine part of the analysis of all case-control data. Whether this analysis should be based on predictive values or on sensitivity/specificity is very much a matter of choice. One disadvantage of the use of predictive values is that they depend, by definition, on the prevalence of exposure in the group in question and may differ between cases and controls when the prevalence of exposure differs in the two groups. However, the analysis that I have outlined based on estimation of D_0 and D_1 automatically adjusts for this prevalence dependence. Often predictive values are easier to estimate than are sensitivity and specificity. Estimation of the latter requires a random sample of subjects known to have been truly exposed and a random sample of subjects known to have been truly unexposed. On the other hand, estimation of the former requires assessment of the true exposure status of a random sample of subjects reported to have been exposed and a random sample of subjects reported to have been unexposed. I will use both ways of assessing recall bias in this paper.

Induced Abortion and Breast Cancer

The Rookus and van Leeuwen Study

Rookus and van Leeuwen describe a case-control study designed to investigate the possibility of an association between a history of induced abortion and the development of breast cancer in Dutch women.[13] The study included 918 women who were diagnosed with invasive breast cancer during the period from 1986 through 1989. Each case was matched to a control woman of the same age living in the same region

13 *See* Matti A. Rookus & Flora E. van Leeuwen, *Induced Abortion and Risk for Breast Cancer: Reporting (Recall) Bias in a Dutch Case-Control Study*, 88 J. Nat'l Cancer Inst. 1759 (1996).

of Holland. All cases and controls were interviewed by the same trained interviewer using a structured questionnaire.

Consider the measure of exposure which defines a subject as having been exposed if the subject ever had an induced abortion. The following table refers to parous women only and is based on exposure status as assessed by questionnaire:

	Cases	*Controls*	*Total*
Exposed	43	26	69
Unexposed	716	775	1,491
Total	759	801	1,560

The table yields a crude odds ratio of OR = 1.79 with 95% confidence interval [1.06, 3.03]. The authors used multivariate conditional logistic regression methods for individually matched case-control studies to produce an odds ratio of 1.9 with 95% confidence interval [1.1, 3.2].

Table 1 shows the values of the adjusted crude odds ratio for various combinations of D_0 (the excess of unexposed among controls) and D_1 (the excess of exposed among cases). It can be seen that the adjusted odds ratio fails to reach significance at the 5% level if $D_0 + D_1 > 6$. Suppose, for example, that all assessments are correct except that 1% of controls who denied having had an induced abortion did, in fact, have one. Then equations 2.1 and 2.2 yield $D_0 = 7.75$ and $D_1 = 0$. Clearly quite low levels of recall bias can produce an adjusted odds ratio that fails to reach significance at the 5% level.

Rookus and van Leeuwen examined the possibility of recall bias by comparing the study results from the predominantly Roman Catholic region of southeastern Holland to those obtained in the supposedly more liberal western region.[14] Among parous women aged forty-five or younger, the adjusted odds ratio for induced abortion was 14.6 in the southeastern region and a nonsignificant 1.3 in the western region. The two odds ratios were significantly different (p = 0.017). No such difference was found between the odds ratios for spontaneous abortion. The authors also collected information on oral contraceptive use from both the women and their current or former prescribers. In comparison

14 *See id.*

with the prescribers, control subjects in the southeastern regions underreported the duration of their oral contraceptive use by 6.3 months more than control subjects in the western regions (p = 0.007). No such difference was apparent among cases (p = 0.735). Controls in the southeastern region underreported the duration of their oral contraceptive use by 4.5 months more than did cases from the same region (p = 0.061). No such difference was apparent in the western region (p = 0.235). Finally, the authors calculated odds ratios comparing women with twelve or more years of oral contraceptive use to women with less than four years of use. When information from study subjects alone was used, the resulting odds ratios were 1.3 for the southeastern region and 0.9 for the western region. When information from study subjects and their prescribers was used, the resulting odds ratios were 0.9 for the southeastern region and 1.1 for the western region. No significant regional difference was found for either pair of odds ratios.

The authors conclude that they had "found evidence that the estimated 90% increased risk for breast cancer after induced abortion was largely attributable to underreporting of abortion by healthy control subjects."[15]

Table 1
Odds Ratios Based on the Rookus and van Leeuwen (1996) Study Adjusted for Various Choices of D_0 (the Excess of Unexposed Among Controls) and D_1 (the Excess of Exposed Among Cases)

	D_0										
D_1	0	1	2	3	4	5	6	7	8	9	10
0	**1.79**	**1.72**	**1.66**	**1.60**	**1.54**	**1.49**	**1.44**	**1.40**	**1.35**	**1.31**	**1.28**
1	**1.75**	**1.68**	**1.62**	**1.56**	**1.51**	**1.45**	**1.41**	**1.36**	**1.32**	**1.28**	**1.24**
2	**1.70**	**1.64**	**1.58**	**1.52**	**1.47**	**1.42**	**1.37**	**1.33**	**1.29**	**1.25**	**1.21**
3	**1.66**	**1.59**	**1.54**	**1.48**	**1.43**	**1.38**	**1.34**	**1.29**	**1.26**	**1.22**	**1.18**
4	**1.61**	**1.55**	**1.50**	**1.44**	**1.39**	**1.35**	**1.30**	**1.26**	**1.22**	**1.19**	**1.15**
5	**1.57**	**1.51**	**1.46**	**1.40**	**1.35**	**1.31**	**1.27**	**1.23**	**1.19**	**1.15**	**1.12**
6	**1.53**	**1.47**	**1.41**	**1.36**	**1.32**	**1.27**	**1.23**	**1.19**	**1.16**	**1.12**	**1.09**
7	**1.48**	**1.43**	**1.37**	**1.33**	**1.28**	**1.24**	**1.20**	**1.16**	**1.12**	**1.09**	**1.06**
8	**1.44**	**1.39**	**1.33**	**1.29**	**1.24**	**1.20**	**1.16**	**1.13**	**1.09**	**1.06**	**1.03**
9	**1.40**	**1.34**	**1.29**	**1.25**	**1.21**	**1.16**	**1.13**	**1.09**	**1.06**	**1.03**	**1.00**
10	**1.35**	**1.30**	**1.25**	**1.21**	**1.17**	**1.13**	**1.09**	**1.06**	**1.03**	**0.99**	**0.97**

Values in Bold are Significant at the 5% Level for a One-Sided Test.

15 *Id.*

Validation of Questionnaire Assessment of Exposure to Induced Abortion

Lindefors-Harris et al. compared information on induced abortion obtained from women in interviews within a Swedish case-control study with data on the same women from a nationwide registry of induced abortions.[16] The following table is based on information given in interviews concerning past exposure to induced abortion:

	Cases	*Controls*	*Total*
Exposed	26	44	70
Unexposed	291	468	759
Total	317	512	829

The table yields a crude odds ratio of OR = 0.95 with 95% confidence interval [0.56, 1.62]. The following table is based on information obtained from the registry:

	Cases	*Controls*	*Total*
Exposed	24	59	83
Unexposed	293	453	746
Total	317	512	829

The table yields a crude odds ratio of OR = 0.63 with 95% confidence interval [0.37, 1.07]. The fact that the odds ratio based on interview data was 1.5 times as large as that based on registry data is cited as evidence of a recall bias which "may explain the tendency toward increased risk of breast cancer which, according to several case-control studies, appears to be associated with induced abortion."[17]

The data given in Lindefors-Harris et al. also allow for estimation of sensitivities and specificities.[18] Among controls, 59 subjects were registered as having had an abortion and this was reported by 43 of them, while 453 subjects did not appear in the registry, and 452 of

16 *See* Britt-Marie Lindefors-Harris et al., *Response Bias in a Case-Control Study: Analysis Utilizing Comparative Data Concerning Legal Abortions from Two Independent Swedish Studies,* 134 Am. J. Epidemiology 1003 (1991).

17 *Id.*

18 *See id.*

these denied having had an abortion. Thus, for controls, the sensitivity is estimated as 43/59 and the specificity as 452/453. Among cases, 24 subjects were registered as having had an abortion, and this was reported by 19 of them, while 293 subjects did not appear in the registry, and 286 of these denied having had an abortion. Thus, for cases, the sensitivity is estimated as 19/24 and the specificity as 286/293. The following corrected table results from using equations 2.3 and 2.4 to apply these estimates of sensitivities and specificities to Rookus and van Leeuwen's estimates of $D_0 = 7$ and $D_1 = 11$:

	Cases	*Controls*	*Total*
Exposed	32	33	65
Unexposed	727	768	1,495
Total	759	801	1,560

The table yields a crude odds ratio of OR = 1.02 with 95% confidence interval [0.61, 1.73] — down from the uncorrected odds ratio of 1.79.

Brind et al. comment at length on the Lindefors-Harris et al. results[19] and agree with Daling et al. who were of the opinion that "it is reasonable to assume that virtually no women who truly did not have an abortion would claim to have had one."[20] They point out that, for the Lindefors-Harris et al. data, the odds ratio associated with all positive reports of induced abortion history (whether from interview or from registry data) is 0.82 and, therefore, the interview based value of 0.95 is inflated by a factor of 16% and not 50% as stated by Lindefors-Harris et al.[21]

The Brind et al. argument is equivalent to setting equal to 1 the specificities for both cases and controls and estimating the sensitivities as before. When equations 2.3 and 2.4 are used to apply these estimates to Rookus and van Leeuwen's estimates of $D_0 = 10$ and $D_1 = -9$, the following corrected table is the result:

19 *See* Brind et al., *supra* note 5.

20 Janet R. Daling et al., *Risk of Breast Cancer among Young Women: Relationship to Induced Abortion*, 86 J. Nat'l Cancer Inst. 1584 (1994).

21 *See id.*

	Cases	*Controls*	*Total*
Exposed	52	36	88
Unexposed	707	765	1,472
Total	759	801	1,560

The table yields a crude odds ratio of OR = 1.56 with 95% confidence interval [0.99, 2.48] — down from the uncorrected odds ratio of 1.79. The downward adjustment is far less severe than before, and the adjusted odds ratio almost attains statistical significance.

The Public Health Consensus

Two papers reviewing the evidence regarding the possible association between induced abortion and breast cancer appeared within one month of each other in 1996. Both reviews examined largely the same collection of studies but came to strikingly different conclusions.

Michels and Willett concluded that "the potential for bias in case-control studies of induced abortions owing to the highly sensitive nature of this experience is so great that case-control studies may be incapable of providing a clear answer."[22] Brind et al. performed a meta-analysis of twenty-one studies leading to a pooled odds ratio of 1.3 (95% confidence interval = [1.2, 1.4]) and concluded that there was "a remarkably consistent, significant positive association between induced abortion and breast cancer incidence."[23] Based on their treatment of the Lindefors-Harris et al. results as described in the previous section, the authors ruled out "any reasonable possibility that the association is the result of bias."[24]

The consensus among editorial commentaries seems to be that any conclusion of an established association between breast cancer and a history of induced abortion is, at best, premature.

Rosenberg states that the odds ratio of 1.50 found in the study by Daling et al. "is small in epidemiologic terms and severely challenges our ability to distinguish if it reflects cause and effect or if it simply

22 Karen B. Michels & Walter C. Willett, *Does Induced or Spontaneous Abortion Affect the Risk of Breast Cancer?*, 7 Epidemiology 521 (1996).

23 Brind et al., *supra* note 5.

24 *Id.*

reflects bias."[25] She offers the opinion that "reassurance that reporting bias does not explain the results will come only when confirmatory findings are provided by case-control studies based on complete records of abortions or by follow-up studies in which abortions are recorded before the occurrence of breast cancer."[26]

Weed and Kramer argue that some credence has been given "to the idea that the modest relationship reported in studies stretching back four decades can be explained, at least in part and perhaps even in large measure, by reporting (recall) bias" and conclude that "there is as yet insufficient evidence to claim that a true association exists between induced abortion and breast cancer."[27]

Gammon et al. offer the opinion that the "slight increase in risk observed in some studies may or may not reflect a real association between induced abortion and breast cancer, given the many limitations of the published investigations."[28] They go on to identify as the most important of these limitations "the difficulty in obtaining, especially from control subjects, accurate recall of an event that was illegal in the United States before 1973, and has gained increasingly violent public attention since that time, casting considerable doubt on whether even recent abortions are accurately reported."[29] Citing the study by Newcomb et al. which reported "an overall modest 23% increase in risk reflecting a 35% increase among women reporting an induced abortion before 1973, but only a 12% increase among those reporting an induced abortion after that date," they claim that "the modest heterogeneity underscores the difficulty in obtaining accurate recall, especially among controls."[30]

In their commentary on the study of Rookus and van Leeuwen, Brind et al. close with the following provocative question: "When there exists reproducible, biologically plausible evidence of a significant

25 Lynn Rosenberg, *Induced Abortion and Breast Cancer: More Scientific Data Are Needed*, 86 J. Nat'l Cancer Inst. 1569 (1994).

26 *Id.*

27 Douglas L. Weed & Barnett S. Kramer, *Induced Abortion, Bias, and Risk for Breast Cancer: Why Epidemiology Hasn't Reached its Limit*, 88 J. Nat'l Cancer Inst. 1698 (1996).

28 Marilie D. Gammon et al., *Abortion and the Risk of Breast Cancer: Is there a Believable Association?*, 275 JAMA 321 (1996).

29 *Id.*

30 *Id.*

positive association, however modest, between a common elective exposure (i.e., induced abortion) and a common life-threatening illness (i.e., breast cancer), how can the public health possibly be well served by policymakers' steadfast adherence to the contrary presumption of harmlessness?"[31] The authors of the original study responded as follows: "

> However much the possible biologic mechanisms underlying the abortion-breast cancer association may appeal to us and how large the public health issues may be in case of a true relationship, our first and foremost concern should be directed at the basic question of whether or not the epidemiologic data are unbiased. Therefore, in reply to the final question raised by Brind et al., we would like to comment that, in our view, public health and epidemiologic research are equally disserved by inferring a causal association when an obvious type of bias has not been ruled out convincingly.[32]

Passive Smoking and Lung Cancer

The Fontham Study

Fontham et al. describe a case-control study designed to investigate the possibility of an association between lifetime exposure to ETS and the development of lung cancer in nonsmoking women.[33] Eligible cases consisted of female nonsmoking residents of five metropolitan areas of the United States with microscopically confirmed primary carcinoma of the lung who were diagnosed between December 1, 1986 and November 30, 1988. A population based control group was selected by random digit dialing and supplemented by random sampling from the Health Care Financing Administration files for women sixty-five years and older. Controls were frequency matched to cases on race and age in a 2:1 ratio of controls to cases and met the same residence and personal tobacco use criteria as cases. A lifetime history of exposure to ETS was obtained via questionnaire. The questionnaire was completed by all 1,253 controls and by 412 of the

31 Brind et al., *supra* note 5.

32 Rookus & van Leeuwen, *supra* note 13.

33 *See* Elizabeth T.H. Fontham et al., *Environmental Tobacco Smoke and Lung Cancer in Nonsmoking Women: A Multicenter Study,* 271 JAMA 1752 (1994).

653 cases; the questionnaires for the remaining 241 cases were completed by the next of kin.

Consider the measure of exposure that defines a subject as having been exposed if the subject ever lived with a spouse who smoked and unexposed otherwise. The following table is based on exposure status as assessed by questionnaire:

	Cases	*Controls*	*Total*
Exposed	433	766	1,199
Unexposed	218	487	705
Total	651	1,253	1,904

The table yields a crude odds ratio of OR = 1.26 with 95% confidence interval [1.04, 1.54]. The odds ratio, when adjusted for the potential confounding variables age, race, study area, education, intake of fruits and vegetables, supplemental vitamin index, dietary cholesterol, family history of lung cancer, and employment in high risk occupations, is OR = 1.29 with 95% confidence interval [1.04, 1.60].

Fontham et al. conclude, "the findings of this study support the conclusion that long-term exposure to ETS increases risk of lung cancer in women who have never personally used tobacco."[34]

Table 2 shows the values of the adjusted odds ratio for various combinations of D_0 (the excess of unexposed among controls) and D_1 (the excess of exposed among cases). It can be seen that the adjusted odds ratio fails to reach significance at the 5% level if $D_0 + 2D_1 = 20$. Suppose, for example, that all assessments are correct except that 1% of controls who denied exposure were, in fact, exposed and that 2% of cases who reported exposure were, in fact, unexposed. Then equations 2.1 and 2.2 yield $D_0 = 4.87$ and $D_1 = 8.66$, and hence $D_0 + 2D_1 = 22.19 > 20$. Clearly quite low levels of recall bias can produce an adjusted odds ratio that fails to reach significance at the 5% level.

The authors of the Fontham study attempted to address the problem of recall bias. In the first three years of the study, two control groups, one with colon cancer and one from the general population, were selected for case-control comparisons. It was hoped that recall bias between cases and colon cancer controls would be minimized since both

34 *Id.*

groups are similarly motivated to recall earlier exposure. This hope may not be entirely justified since there has been widely publicized interest in the ETS/lung cancer relationship but not in the ETS/colon cancer relationship. In Fontham et al. the odds ratio for spousal smoking was 1.37 using population controls and 1.21 using colon cancer controls; when adjusted for potential confounding variables these odds ratios became 1.29 and 1.28, respectively. The authors claim that "the internal consistency of findings with the two control groups suggests that recall bias resulting from having a diagnosis of cancer is not a likely explanation of the observed effect" but do admit that "the possibility remains that nonsmoking lung cancer cases and nonsmoking colon cancer cases are not similarly motivated to remember exposures to the tobacco smoke of others."[35] The use of a colon cancer control group was not extended into the final two years of the study.

Table 2
Odds Ratios Based on the Fontham et al. (1994) Study
Adjusted for Various Choices of D_0 (the Excess of Unexposed Among Controls) and D_1 (the Excess of Exposed Among Cases)

	D_0										
D_1	0	2	4	6	8	10	12	14	16	18	20
0	1.26	1.25	1.25	1.24	1.23	1.22	1.21	1.20	1.20	1.19	1.18
1	1.25	1.25	1.24	1.23	1.22	1.21	1.20	1.20	1.19	1.18	1.17
2	1.25	1.24	1.23	1.22	1.21	1.20	1.20	1.19	1.18	1.17	1.16
3	1.24	1.23	1.22	1.21	1.20	1.20	1.19	1.18	1.17	1.16	1.16
4	1.23	1.22	1.21	1.20	1.20	1.19	1.18	1.17	1.16	1.16	1.15
5	1.22	1.21	1.20	1.20	1.19	1.18	1.17	1.16	1.16	1.15	1.14
6	1.21	1.20	1.20	1.19	1.18	1.17	1.16	1.16	1.15	1.14	1.13
7	1.20	1.20	1.19	1.18	1.17	1.16	1.16	1.15	1.14	1.13	1.12
8	1.20	1.19	1.18	1.17	1.16	1.16	1.15	1.14	1.13	1.12	1.12
9	1.19	1.18	1.17	1.16	1.16	1.15	1.14	1.13	1.13	1.12	1.11
10	1.18	1.17	1.16	1.16	1.15	1.14	1.13	1.13	1.12	1.11	1.10

Values in Bold Are Significant at the 5% Level for a One-Sided Test.

In their discussion of the validity of questionnaire based assessments of ETS exposure, Fontham et al. cite three references: Pron et al., Coultas et al. and Riboli et al. These studies are described below. Pron et al. report a study in which a total of 117 control subjects initially

35 Elizabeth T.H. Fontham et al., *Lung Cancer in Nonsmoking Woman: A Multicenter Case-Control Study,* 1 Cancer Epidemiology Biomarkers & Prevention 35 (1991).

interviewed in a lung cancer case-control study conducted in Toronto, Canada between 1983 and 1984 were re-interviewed on average six months later.[36] One hundred eight or 95% of 114 respondents gave identical responses when questioned as to the smoking status of their spouses.

Coultas et al. assessed the reliability of questionnaire responses on lifetime exposure to tobacco smoke in the home for a sample of 149 adult nonsmokers recruited in New Mexico in 1986.[37] A structured questionnaire on lifetime exposure to ETS was administered by a trained interviewer to each subject on two occasions separated by approximately four to six months. All of the sixty-seven subjects who, at the first interview, reported that their spouse smoked reported the same at the second interview.

Riboli et al. consider a large international study in which 1,369 nonsmoking women were interviewed.[38] The subjects were either control subjects from previous or ongoing case-control studies or were volunteers from stratified population samples. They present the results of the analysis of self-reported recent exposure to ETS from any source in relation to urinary concentrations of cotinine. The authors calculate mean cotinine/creatinine levels for various subgroups of subjects. Of particular relevance is the comparison of the mean cotinine/creatinine levels across the four groups determined by the reported presence or absence of exposure in the home and in the workplace. The mean cotinine level is 2.7 for those who report no exposure at either location, 4.8 for those who report exposure at work but not at home, 9.0 for those who report exposure at home but not at work, and 10.0 for those who report exposure at both locations. No attempt is made to quantify the degree of overlap among the four groups in terms of cotinine levels.

None of the three papers cited bear directly on the question of recall bias in the assessment of lifetime exposure to ETS. The Riboli paper concerns recent exposure rather than lifetime exposure and was carried out on healthy nonsmoking subjects. The two test-retest studies

36 *See* Gaylene E. Pron et al., *The Reliability of Passive Smoking Histories Reported in a Case-Control Study of Lung Cancer*, 127 Am. J. Epidemiology 267 (1988).

37 *See* David B. Coultas et al., *Questionnaire Assessment of Lifetime and Recent Exposure to Environmental Tobacco Smoke*, 130 Am. J. Epidemiology 338 (1989).

38 *See* Elio Riboli et al., *Exposure of Nonsmoking Women to Environmental Tobacco Smoke: A 10-Country Collaborative Study*, 1 Cancer Causes and Control 243 (1990).

show a high degree of reliability in the assessment of ETS exposure but, once again, only for control subjects. None of the cited studies allow comparison of cases and controls in terms of reliability or validity of ETS exposure assessments which is the comparison of interest when considering the potential for recall bias.

Validation of Questionnaire Assessment of Exposure to ETS

Herrmann compared smoking data obtained from cases or controls and their respective next-of-kin as part of a study of colon cancer in the United States and reported that the percentage of complete agreement on whether the subject smoked exceeded 85% for both cases and controls.[39]

Sandler and Shore report a study of long-term effects of transplacental and childhood exposure to cigarette smoke, in which 518 cancer cases and 518 healthy controls were interviewed concerning parents' smoking habits during childhood and prior to birth.[40] Parents or siblings of the study subjects were also interviewed to obtain the same information. There was 95.7% agreement between subjects and mothers as to whether the mother ever smoked cigarettes and 86.4% agreement between subjects and mothers as to whether the father ever smoked cigarettes. The authors report no major differences between cases and controls in overall agreement between mothers and subjects on mothers' or fathers' smoking habits. They do, however, report some differences between cases and controls for conditional agreement. As an example, they quote that when the mothers smoked in the house, cases reported this 98% of the time but controls reported this only 85% of the time. Conversely, if the mothers' answers can be believed, only 80% of cases whose fathers did not smoke reported this fact, while 86% of controls whose fathers did not smoke reported accordingly.

To measure the reliability of passive smoking histories, Brownson et al. conducted re-interviews for 110 subjects (thirty-seven cases and seventy-three controls) as part of a larger study of lung cancer among non-smoking women in Missouri.[41] In identifying the presence or

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39 *See* N. Hermann, *Retrospective Information from Questionnaires: Comparability of Primary Respondents and their Next-of-Kin*, 121 Am. J. Epidemiology 937 (1985).

40 *See* Dale P. Sandler & David L. Shore, *Quality of Data on Parents' Smoking and Drinking Provided by Adult Offspring*, 124 Am. J. Epidemiology 768 (1986).

41 *See* Ross C. Brownson et al., *Reliability of Passive Smoke Exposure Histories in a Case-*

absence of exposure to ETS due to spousal smoking, there was agreement between both interviews for 73% of cases and for 89% of controls. The corresponding percentages for exposure to ETS due to the smoking of all household members were 68% and 86%, respectively. In identifying the presence or absence of exposure to ETS during childhood due to parental smoking, there was agreement between both interviews for 92% of cases and for 95% of controls. The corresponding percentages for exposure to ETS during childhood due to the smoking of all household members were 76% and 86%, respectively. The authors conclude by expressing the hope "that an increasing focus on instrument reliability and validity will result in development of standardized questions on passive smoking."[42]

Tunstall-Pedoe et al. carried out a cross-sectional random population survey involving 2,278 nonsmoking subjects in order to explore the relationship between ETS exposure and coronary heart disease (CHD).[43] Each subject was sent a questionnaire to complete and a clinic appointment. The questionnaire included the standard Rose angina and possible infarction questionnaire, the Medical Research Council cough and phlegm questionnaire, and questions on prior medical diagnoses. In addition, subjects were asked to answer the question, "Have you been exposed to tobacco smoke from someone else in the last three days?" with possible answers of "4 – yes, a lot; 3 – yes, some; 2 – yes, a little; 1 – none at all." Of the 2,278 subjects, 292 or 13% answered "yes, a lot" while 618 or 27% answered "none at all." In analyses comparing the group who answered "yes, a lot" with the group who answered "none at all," significant positive associations were found for CHD (OR = 1.6, 95% CI [1.1, 2.4]), chronic phlegm (OR = 2.3, 95% CI [1.4, 3.9]), and chronic cough (OR = 2.3, 95% CI [1.3, 3.9]). In the course of the clinic visit, subjects were asked to provide a blood sample from which serum cotinine readings were obtained. The subjects whose cotinine value was among the highest 13% of values obtained were deemed to have been "highly exposed" while the subjects

Control Study of Lung Cancer, 22 Int'l J. Epidemiology 804 (1993).

42 *Id.*

43 *See* Hugh Tunstall-Pedoe et al., *Passive Smoking by Self-Report and Serum Cotinine and the Prevalence of Respiratory and Coronary Heart Disease in Scottish Heart Health Study*, 49 J. Epidemiology & Community Health 139 (1995).

whose cotinine value was among the lowest 27% of values obtained were deemed to have been "unexposed." Of the subjects deemed to have been highly exposed, 25% gave answer 4 to the ETS question, 32% gave answer 3, 31% gave answer 2 and 12% gave answer 1. Of the subjects deemed to have been unexposed, 8% gave answer 4 to the ETS question, 18% gave answer 3, 36% gave answer 2 and 38% gave answer 1. Clearly the correlation between the two measures of exposure was poor. In analyses comparing the "highly exposed" group with the "unexposed" group, the significant positive associations noted above disappeared: CHD (OR = 1.2, 95% CI [0.9, 1.7]), chronic phlegm (OR = 1.2, 95% CI [0.7, 2.0]), and chronic cough (OR = 1.1, 95% CI [0.6, 1.9]). The authors conjecture that biased reporting of ETS exposure may account for this discrepancy and conclude that "the validity of different measures of tobacco smoke exposure needs further investigation."[44]

In the context of a case-control study, Nyberg et al. compared reports concerning spousal smoking habits given by lung cancer cases and controls with those given by the next-of-kin.[45] Of the 108 controls, forty-nine reported that the spouse was a regular smoker and fifty-nine that the spouse was not. The disagreements between index and next-of-kin were that, in six instances, a positive report by the index was not confirmed by the next-of-kin. Of the 115 cases, sixty reported that the spouse was a regular smoker and fifty-five that the spouse was not. The disagreements between index and next-of-kin were that, in eight instances, a positive report by the index was not confirmed by the next-of-kin, and in one instance a negative report by the index was not confirmed by the next-of-kin.

The Public Health Consensus

Even though the potential problems of recall bias in case-control studies of lung cancer and ETS was raised some time ago,[46] the 1992 EPA report on the respiratory health effects of passive smoking fails to

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44 *Id.*

45 *See* Fredrik Nyberg et al., *A European Validation Study of Smoking and Environmental Tobacco Smoke Exposure in Nonsmoking Lung Cancer Cases and Controls*, 9 Cancer Causes and Control 173 (1998).

46 *See* S.J. Kilpatrick, *Misclassification of Environmental Tobacco Smoke Exposure: Its Potential Influence on Studies of Environmental Tobacco Smoke and Lung Cancer*, 35 Toxicological Letters 163 (1987).

mention recall bias,[47] as do the review papers of Jinot and Bayard, Axelrad et al., and Hackshaw et al.[48] All four reviews conclude not only that the association between lung cancer and ETS exposure is real, but that it is causal.

Tredaniel et al. identified recall bias as a factor that "must be considered,"[49] but limited their consideration to pointing out that Fontham et al. had found that "the pattern of risk was the same, when cases were compared to colon cancer or population controls."[50]

Reynolds and Fontham recognize that recall bias is "endemic to retrospective research which relies on self-report."[51] They proceed to argue "against recall bias as the explanation for the findings from the case-control studies," citing the general consistency of the evidence from cohort studies and the elevated ETS-associated risks reported from studies which used cancer patients or other hospitalized patients as controls.[52]

Dockery and Trichopoulos, while recognizing that "questionnaire-derived information concerning long-term exposure to ETS is difficult to integrate over time and almost impossible to validate with an appropriate gold standard," nevertheless conclude that long-term exposure to ETS causes lung cancer in non-smokers.[53]

In an editorial commenting on the 1992 EPA report, Heath is of the view that "the collective findings here strongly support a cause-effect association" and asks "how quickly and completely will the report's findings be translated into effective community action?"[54]

47 *See* Office of Research & Development, Environmental Protection Agency (EPA), Pub. No. EPA/600/6-90/006F, Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders (1992).

48 *See* Jinot & Bayard, *supra* note 7; Robert Axelrad et al., *Setting the Record Straight: Secondhand Smoke is a Preventable Health Risk*, 3 Tobacco Control 263 (1994); A.K. Hackshaw et al., *The Accumulated Evidence on Lung Cancer and Environmental Tobacco Smoke*, 315 British Med. J. 980 (1997).

49 Jean Tredaniel et al., *Exposure to Environmental Tobacco Smoke and Risk of Lung Cancer: The Epidemiological Evidence*, 7 European Respiratory J. 1877 (1994).

50 *Id.* (citing Fontham, *supra* note 35).

51 Peggy Reynolds & Elizabeth T.H. Fontham, *Passive Smoking and Lung Cancer*, 27 Annals Med. 633 (1995).

52 *Id.*

53 Douglas W. Dockery & Dimitrios Trichopoulos, *Risk of Lung Cancer from Environmental Exposures to Tobacco Smoke*, 8 Cancer Causes and Control 333 (1997).

54 Clark W. Heath, *Passive Smoking: Environmental Tobacco Smoke and Lung Cancer*,

Davis, in an editorial accompanying the review by Hackshaw et al., congratulates the authors on their careful adjustment for bias and concludes that the accumulated evidence makes it clear "that exposure to environmental tobacco smoke is a cause of lung cancer."[55] He calls for "a total ban on smoking" and urges that "health advocates should pursue all strategies that would help accomplish that goal, including education, legislation, regulation, and litigation."[56] As in the original review, there is no mention of recall bias.

There have been some contrary views. Wynder and Hoffmann comment that "the limited reliability of data obtained by questionnaire, and the relatively limited number of nonsmokers with lung cancer who were not exposed to carcinogens in occupational settings, point to the need for a prospective epidemiological study with exposure assessment by biomarkers to bring about a conclusive evaluation of the question on causality between involuntary smoking and lung cancer."[57] Boyle is of the opinion that "there is still more work to be done in assessing the association between passive smoking and a variety of diseases, including lung cancer."[58] He suggests that "studies should be conducted only with valid methods of assessing exposure, which should certainly include biologic markers such as cotinine or the longer lasting 4-aminobiphenyl hemoglobin adducts" and that "research on new biologic markers is still needed, and ideally, such markers should measure exposure over the longer period relevant to the induction of the disease."[59]

Discussion

Inaccuracies do not necessarily invalidate the conclusions that may be drawn from a case-control study. In a situation where errors occur randomly and in a similar fashion for both cases and controls, the only

341 Lancet 526 (1993).

55 Ronald M. Davis, *Passive Smoking: History Repeats Itself*, 315 British Med. J. 961 (1997).

56 *Id.*

57 E.L. Wynder & D. Hoffmann, *Smoking and Lung Cancer: Scientific Challenges and Opportunities*, 54 Cancer Research 5284 (1993).

58 Peter Boyle, *The Hazards of Passive – and Active – Smoking*, 328 New Eng. J. Med. 1708 (1993).

59 *Id.*

effect of such errors is to reduce the power of the study and to make it more difficult to establish an association between exposure and disease. However, in a situation where the pattern of errors is such that cases tend to over-report exposure relative to controls, there is considerable potential for the errors to produce misleading conclusions. This is the phenomenon known as recall bias.

In a paper addressing the problem of recall bias in case-control studies, Raphael offers the opinion that "it is not the task of one's critics to prove that recall bias exists" and contends that "it is the researcher's task to either present a strong case against the existence of this threat to the study's validity and/or try to statistically control for recall bias in one's analysis."[60]

As indicated in Section 1, the epidemiological evidence relating to the association between lung cancer and exposure to spousal ETS is strikingly similar to that relating to the association between breast cancer and exposure to induced abortion. Section 3 indicates that considerations of recall bias have produced a public health consensus in which the observed weak associations between breast cancer and induced abortion have been adjudged to reflect that bias. Section 4 indicates that, without a careful assessment of the potential for recall bias, epidemiological evidence very similar to that relating to the association between breast cancer and induced abortion has led to a public health consensus in which the observed weak associations between lung cancer and spousal smoking have been adjudged to reflect a causal relationship. Let us consider some possible explanations for this divergence.

First, one might argue that exposure to ETS causes lung cancer based on induction from epidemiologic studies of the association between active smoking and lung cancer. For example, Trichopoulos argues that since "data from large analytic epidemiologic studies of the association between active smoking and lung cancer have consistently demonstrated dose-dependent relationships that extend to minimal exposure levels and have no apparent threshold" and since "sidestream smoke is qualitatively similar to mainstream smoke and is readily absorbed in the body" that therefore "an excess lung cancer risk from

60 Karen Raphael, *Recall Bias: A Proposal for Assessment and Control*, 16 Int'l J. Epidemiology 167 (1987).

exposure to ETS should have been assumed even if there were no conclusive epidemiologic evidence."[61] However, Doll doubts if "extrapolation from the experience of active smokers is justified; not because of doubt about the nature of the dose-response relationship in active smokers, but because the physical and biochemical differences between active and passive smoking are too great" and suggests that "the only way we can assess the effect of passive smoking is by case-control or cohort studies of passive smokers themselves."[62] This view echoes that given by the U.S. Surgeon General in 1979 who argued that "involuntary smoking be evaluated as a separate problem not subject to simple extrapolation of our understanding of dose-response relationships for cigarette smoking."[63]

Second, one might argue that the results of prospective cohort studies cannot be affected by recall bias. Hackshaw et al. cite four cohort studies which examined the relative risk for women due to living with a spouse who smokes.[64] All four relative risks were above 1.0 but only one was significantly different from 1.0. The significant relative risk of 1.45 with a 95% confidence interval of [1.02, 2.08] was reported in Hirayama.[65] While prospective studies may not suffer from recall bias, they are particularly prone to bias due to confounding since it is difficult to collect information on confounders for cohorts consisting of large numbers of subjects. Katzenstein considers that "the evidence is overwhelming that confounding must be controlled for in epidemiological studies of ETS and lung cancer" and finds it "perplexing and indefensible that investigators continue not to control for relevant confounders."[66]

Third, one might argue that the ETS-lung cancer association is supported by positive dose-response data. Jinot and Bayard state that

61 Dimitrios Trichopoulos, *Risk of Lung Cancer and Passive Smoking*, *in* Important Advances in Oncology (1995).

62 Richard Doll, *Assessment of Risk from Low Doses: Contribution of Epidemiology*, 73B Trans IchemE S8 (1995).

63 U.S. Surgeon General, U.S. Public Health Service, Report No. PHS 79/-50066, Smoking and Health: A Report of the Surgeon General (1979).

64 *See* Hackshaw et al., *supra* note 48.

65 *See* T. Hirayama, *Cancer Mortality in Nonsmoking Women with Smoking Husbands Based on Large-Scale Cohort Study in Japan*, 13 Preventive Med. 680 (1984).

66 A.W. Katzenstein, *Environmental Tobacco Smoke and Lung Cancer Risk: Epidemiology in Relation to Confounding Factors*, 18 Env't Int'l 341 (1992).

"all 17 studies with data by exposure level demonstrated an increased risk of lung cancer in the highest exposure group, and 9 of the 17 were statistically significant."[67] However, dose-response type data is even more susceptible to recall bias than is data specifying merely the presence or absence of exposure.[68] Levois and Switzer describe procedures whereby dose-response analyses may be adjusted to account for specified patterns of exposure misclassification.[69] In applying their procedures to data from Fontham et al., they demonstrate how modest differential exposure misclassification can change what appears to be a statistically significant dose response relationship into one that is "decidedly nonsignificant."[70] Similar results are described by Barry.[71]

Fourth, one might argue that recall bias is more likely to arise in reports of abortion history than it is in reports of exposure to spousal ETS. Due to its sensitive nature, errors in reporting of abortion are likely to involve failures to disclose and the tendency for such errors to occur may be stronger among controls than it is among cases who appear motivated to report anything that might account for their cancer. In contrast, exposure to ETS may not be something that is perceived by people to be embarrassing, shameful, or otherwise stigmatizing. Hence, reporting errors in the ETS context may come about as a result of random error due to imperfect recall. The study by Tunstall-Pedoe et al. strongly suggests that recall bias does occur in the reporting of ETS exposure.[72] In that study, associations found to exist between subjective exposure assessments and disease are not found when exposure assessments via cotinine are used instead of subjective assessments. The authors themselves suggest that recall bias may be the sole reason why associations were found when subjective exposure assessments were used.

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67 Jinot & Bayard, *supra* note 7.

68 *See* Daniel Barry, *Differential Recall Bias and Spurious Associations in Case-Control Studies*, 15 Stat. Med. 2603 (1996).

69 *See* Levois & Switzer, *supra* note 4.

70 *Id.*

71 *See* Barry, *supra* note 68.

72 *See* Tunstall-Pedoe et al., *supra* note 43.

A fifth possible explanation may lie in the manner in which personal values affect the interpretation of scientific data. Carlo et al. report an experiment designed "to investigate the extent to which personal values and experiences among scientists might affect their assessment of risks from dioxin, radon, and ETS."[73] The experiment involved a telephone survey of 1,461 epidemiologists, toxicologists, physicians, and general scientists. Each participant was read a vignette designed to reflect the mainstream scientific thinking on one of the three substances. For half of the participants the substance in question was identified while for the other half it was not. The authors report their findings for the subgroup given information concerning ETS as follows: "Participants who knew they were being asked about ETS rather than Substance X were significantly more likely to consider the substance an environmental health hazard (88% vs. 66%, $p < .001$)."[74] Similar, though less pronounced, findings were reported for radon whereas knowing the name of the substance had little effect on the scientists' evaluation of dioxin. The authors conclude that the results "suggest that scientists' interpretations of scientific facts may be influenced by values and experiences" and advise that "scientists should note that such influences could lead to biased estimates of environmental health risks."[75] This bias is closely related to the wish bias identified by Wynder et al. who are of the opinion that "such a bias, by the epidemiologist, or any other scientist, reflects badly on the scientific method."[76] The intrusion of such personal value judgments into the process of scientific evaluation has also created a concern that epidemiology is sometimes used as a tool for the advancement of certain public policy goals rather than for the advancement of scientific knowledge. For instance, Chavkin, while acknowledging that "the study of patterns of disease and health-related behaviors is fundamental to public health," goes on to warn that "caution and rigor are essential to the interpretation and application of such epidemiological data."[77] She claims that "some legislative efforts

73 George L. Carlo et al., *The Interplay of Science, Values, and Experiences Among Scientists Asked to Evaluate the Hazards of Dioxin, Radon, and Environmental Tobacco Smoke*, 12 Risk Analysis 37 (1992).

74 *Id.*

75 *Id.*

76 E.L. Wynder et al., *The Wish Bias*, 43 J. Clinical Epidemiology 619 (1990).

77 Wendy Chavkin, *Topics for Our Times: Public Health on the Line — Abortion and*

to curtail access to abortion have flagrantly violated this principle" and cites, as an example, "the use of preliminary and inconsistent epidemiological data regarding abortion and breast cancer risk to advance a political agenda."[78]

The proper conduct of case-control studies relying on self-reports of past exposure requires strenuous efforts to determine whether recall bias occurs and, if so, to quantify the magnitude of this bias. The methods for assessing sensitivity to recall bias exemplified in this paper should be routinely applied. Validation studies of the assessment instruments used should be carried out for both cases and controls. The conclusions of studies would be greatly strengthened if the extent of the recall bias required to insubstantiate them was considerably greater than that found in these validation studies.

Beyond, 86 Am. J. Pub. Health 1204 (1996).

78 *Id.*