# CONFLICTING RESULTS ON ENVIRONMENTAL TOBACCO SMOKE FROM THE AMERICAN CANCER SOCIETY

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**Abstract**

This commentary has been written to defend our paper in the May 17 *BMJ*, which has been subjected to great deal of misguided criticism due largely to an unprofessional press release issued by the American Cancer Society (ACS) on May 15. We have responded in detail to the misrepresentations and misstatements made by ACS, mainly through Michael J. Thun, M.D. In particular, we show that our analysis of the Cancer Prevention Study (CPS I), based on spousal smoking, produces results regarding environmental tobacco smoke (ETS) that are just as reliable as those from other spousal smoking studies. Furthermore, we show that our CPS I results are quite consistent with the previously published results from CPS I and CPS II. In addition, we have uncovered two examples where MJT clearly exaggerates the impact of ETS. In one case, lung cancer data were combined in an inappropriate way to produce a significant positive dose-response relationship with spousal smoking in CPS II, when a more complete presentation of the data shows no relationship. In a second case, US results on ETS and CHD have been selectively and inconsistently combined in a meta-analysis to produce a summary RR~1.22, when appropriately combined results produce a summary RR~1.05. In conclusion, the available results from CPS I and CPS II, when examined in their totality, show ETS has no consistent relationship with lung cancer or CHD. However, ACS pronouncements about ETS, such as their May 15 press release, conflict with the totality of their own evidence. Because ACS controls such a large portion of the data relevant to ETS and mortality, they have a special obligation to analyze and summarize it fully and objectively.

## Conflicting Results on Environmental Tobacco Smoke from the American Cancer Society

### Introduction

Our paper in the May 17 *BMJ* has generated very strong reactions and a great deal of regrettable confusion (1). The tone was largely set by the press release issued by the American Cancer Society (ACS) on May 15 (2), even before the full version of the paper was accessible on bmj.com. The clear intent of this press release, orchestrated by Michael J. Thun, M.D., was to discredit our study by making a series of charges that are largely false or misleading. Coming from a well-known and authoritative source, these charges were parroted by many other anti-smoking activists and organizations, in most cases without any understanding of the real issues involved. The tactic of trashing our study in the press took the focus off an objective assessment of what is a complex and carefully analyzed study. Owing to the prominence given to MJT's attempts to discredit our study, we will concentrate on responding to specific points made by him, both in the ACS press release (2) and in his May 19 and May 20 rapid responses posted on bmj.com (3, 4). Most other issues regarding the study can be answered by carefully reading the full *BMJ* paper, our January 9 response to reviewer comments, and this commentary.

Our response will focus on four areas: 1) tobacco industry involvement in the study; 2) ACS misrepresentations regarding the results of our paper and CPS I; 3) ACS misrepresentations regarding the results of CPS II; and 4) the failure of ACS to fully and objectively analyze CPS I and CPS II.

### 1) Tobacco industry involvement in the study

The tobacco industry played no role in our paper other than providing the final portion of the funding for the 40-year study, which was initiated by ACS. The tobacco industry never saw any version of our paper before it was published, never attempted to influence the writing of the paper in any way, and did not even know the paper was being published until it became public. We accurately stated our competing interests in the paper. No matter what the sins of the tobacco industry have been in the past, in this instance their funds have been used to support independent, high quality epidemiologic research that would not have otherwise been possible.

The ACS claim that our peer-reviewed study published in a world-renowned journal is "Part of Organized Effort to Confuse Public About Secondhand Smoke" is a contemptible, baseless fabrication. Indeed, one must ask why ACS would chose to attack a peer-reviewed publication of research based on its own CPS I before reading the paper and without presenting a shred of evidence that our results are incorrect. The vehemence of ACS's attack and its choice of venue reveal ACS's desire to exercise total control over which results from CPS I and CPS II are made public and to discredit any dissenting opinion. It is a curious feature of this *ad hominem* attack that no reference is made to the fact that both authors have a substantial record of achievement in conducting epidemiologic studies with direct relevance to the paper published in *BMJ*. In order to paint us as agents of the tobacco industry, this record, dating back to 1974 (5), has to be totally ignored. Until the intemperate attack by MJT neither of us had ever had his professional integrity challenged.

It is particularly surprising that ACS chose to focus its attack on JEE, because during the period 1973-91 ACS provided substantial funding for his epidemiologic research (6-9). The high quality of his ACS-sponsored research impressed Dr. E. Cuyler Hammond and Lawrence Garfinkel, former heads of ACS epidemiology. His relationship with these world-renowned epidemiologists dates back to 1978 and eventually led to his gaining access to the original California (CA) CPS I data. He was given special permission to conduct long-term follow-up on individual subjects, permission that has been granted to no one else outside of ACS. While ACS did not fund the long-term follow-up, it did allow JEE to seek funds from other sources for this purpose.

JEE received funding from the University of California Tobacco-Related Disease Research Program (www.ucop.edu/srphome/trdrp) in 1991 to initiate the CA CPS I follow-up study with the full cooperation of Clark W. Heath, Jr., M.D, who was in charge of ACS epidemiology at that time (10). But this source of funding was not continued in spite of the substantial progress made. The evaluation of the 1997 JEE proposal to TRDRP acknowledged that the CA CPS I follow-up study was being conducted by "very well-qualified investigators . . . who performed exceedingly well", but JEE was told he was "flogging a dead horse" and it was "time to call it quits." JEE, of course, strongly disagreed with this assessment and the follow-up continued in 1998 with funding from the Center for Indoor Air Research (11). GCK joined the effort at this point. The original intent of the CIAR project was to work closely with ACS, to conduct long-term follow-up in six states in addition to California, and to make this the largest and most definitive ETS study. However, cooperation with ACS became strained once MJT was put in charge of epidemiology. Initially, he was pleased that we had obtained funding from CIAR and was willing to work with us on addressing his concerns. Then, he stopped communicating with us and he never granted access to the data from the other states. In spite of these difficulties, we were able to complete the California portion of the CPS I ETS study and *BMJ*, after an unusually thorough review, saw fit to publish our paper.

2) <u>ACS misrepresentations regarding the results of our paper and CPS I</u>

a. MJT claims that CPS I is uninformative for studying ETS because in 1959 "exposure to secondhand smoke was so pervasive that virtually everyone was exposed to ETS, whether or not they were married to a smoker" (2). Contrary to this *ex cathedra* assertion, which is not based on any factual evidence presented by MJT, we have shown in great detail in Tables 4 and 5 of our full paper that 1959 spousal smoking is strongly related to self-reported history of total ETS exposure as of 1999 among females. The relationship among males is positive but weak, which we acknowledge in the paper. Our 1999 questionnaire asked "In your work or daily life, are (were) you regularly exposed to cigarette smoke from others?" Indeed, this questionnaire was designed to address MJT's concerns about ETS exposure in CPS I. To clarify his misleading characterization of the 1999 questionnaire, responses regarding ETS exposure were received from about 8% of the original 1959 subjects. This represented about 20% of the subjects not known to be dead, and about 40% of the subjects who actually received the 1999 questionnaire.

A similar relationship is evident in CPS II based on the most comprehensive analysis available of CPS II, the 1995 doctoral dissertation of Victor M. Cardenas (12). This dissertation is well known to, but never cited by, MJT, who served on dissertation committee. A robust correlation is seen between 1982 spousal smoking and 1982 self-reported current ETS exposure at home among women, based on Table 17 of the Cardenas dissertation (12). The strong correlations between spousal smoking

and self-reported ETS exposure in CA CPS I and CPS II are summarized in Table A. At least for women, spousal smoking and self-reported exposure are both good indicators of relative ETS exposure.

Table A. Spousal smoking status versus self-reported ETS exposure among female never smokers: percentage distribution for CA CPS I (1) and CPS II (12).

CA CPS I results based on Table 4 (1)

| | History of regular exposure to cigarette smoke from others in work or daily life as of 1999(%) | | | |
|---|---|---|---|---|
| 1959 spousal smoking | None | Light | Moderate/ heavy | Total 1999 subjects |
| Never | 61.7 | 24.3 | 14.0 | 645 |
| 1-19 cpd | 25.5 | 28.8 | 45.7 | 208 |
| 20-39 cpd | 19.7 | 20.9 | 59.4 | 426 |
| 40+ cpd | 16.2 | 12.5 | 71.3 | 80 |

CPS II results based on Table 17 (12)

| | Current number of hours per day of ETS at home as of 1982(%) | | | |
|---|---|---|---|---|
| 1982 spousal smoking | 0 | 1-2 | 3+ | Total 1982 subjects |
| Never | 98.0 | 1.3 | 0.7 | 78,853 |
| 1-19 cpd | 48.6 | 18.6 | 32.8 | 8,832 |
| 20-39 cpd | 19.5 | 11.9 | 68.6 | 14,422 |
| 40+ cpd | 11.7 | 6.7 | 81.6 | 6,355 |

Furthermore, 55% of the women in CA CPS I had their occupation coded as “none or housewife” as of 1959, and few of these women ever worked outside the home based on the 1999 questionnaire. Thus, for these women a smoking spouse would be the major source of ETS exposure and exposure in places outside the home would be of secondary importance. The results in Table 8 are essentially unchanged when the analysis is restricted to women who were housewives, indicating that no relationship exists in this less contaminated subgroup.

b. MJT criticizes us for the long 39-year follow-up period, during which changes in exposure status would have taken place. However, these changes in spousal smoking did not change the relative lifetime ETS exposure of subjects, because smoking cessation occurred among all levels of smokers during the course of follow-up (10). Furthermore, MJT fails to acknowledge that we examined follow-up periods of 6, 7 and 13 years (Table 9) and that the CHD results for these shorter periods were no different from those for the total follow-up period (Tables 7-8). During these shorter periods changes in smoking and marital status would be relatively small. Also, our results in Tables 7 and 8 are unchanged when the analysis is restricted to subjects who responded to the 1972 questionnaire and deaths during 1960-72 are omitted.

c. MJT neglects the inconvenient fact that *all* subjects in CPS II were alive during 1950s and 1960s and thus would be expected to have lifetime ETS exposure patterns reasonably similar to those of CPS I subjects, just displaced by 23 years. Indeed, when one looks at the percentage of never smokers married to smokers in CA CPS I and CPS II by years of birth, the patterns of spousal smoking

are strikingly similar. This comparison is shown in Table B using our CA CPS I data and CPS II data from Table 20 of the Cardenas dissertation (12). Lifetime ETS exposure is highly relevant since lung cancer and CHD are long-latency diseases that take decades to develop. Instead of making an *ex cathedra* assertion, MJT can provide actual new evidence on the relationship between spousal smoking and lifetime ETS exposure since the 1950s by reinterviewing currently living CPS II subjects.

Table B. Percentage of never smokers married to ever smokers by years of birth in CA CPS I (as of 1959 and 1972) and in CPS II (as of 1982) from table 20 (12).

| Birth Years | Age at enrollment (1959) | (1972) | (1982) | CA CPS I (1959) (%) | CA CPS I (1972) (%) | CPS II (1982) (%) |
|---|---|---|---|---|---|---|
| Males | | | | | | |
| 1923-27 | 32-36 | 45-49 | 55-59 | 30.9 | 31.8 | 28.1 |
| 1918-22 | 37-41 | 50-54 | 60-64 | 31.0 | 30.9 | 26.1 |
| 1913-17 | 42-46 | 55-59 | 65-69 | 30.6 | 32.3 | 23.4 |
| 1908-12 | 37-41 | 60-64 | 70-74 | 29.1 | 29.1 | 21.4 |
| <1908 | 52+ | 65+ | 75+ | 16.9 | 19.6 | 16.1 |
| Females | | | | | | |
| 1923-27 | 32-36 | 45-49 | 55-59 | 68.0 | 63.8 | 69.4 |
| 1918-22 | 37-41 | 50-54 | 60-64 | 68.5 | 65.6 | 68.3 |
| 1913-17 | 42-46 | 55-59 | 65-69 | 70.0 | 67.1 | 67.4 |
| 1908-12 | 37-41 | 60-64 | 70-74 | 72.8 | 69.1 | 66.6 |
| <1908 | 52+ | 65+ | 75+ | 72.1 | 70.6 | 63.0 |

d. MJT's assertion that our CPS I analysis is useless for the study of ETS is blatantly inconsistent with the fact that he has never objected to Garfinkel's 1981 CPS I analysis of spousal smoking and lung cancer during 1960-72 (13). Garfinkel concluded "Compared to nonsmoking women married to nonsmoking husbands, nonsmokers married to smoking husbands showed very little, if any, increased risk of lung cancer" (13). The results from Garfinkel's CPS I study have been included in the 1992 EPA report (14), the 1997 *BMJ* meta-analysis (15), and the 2003 IARC Monograph 83 (awaiting confirmation) (16). Monograph 83 was written by an IARC Working Group that includes MJT (17).

e. MJT's double standard is on full display in his 1999 ETS-CHD meta-analysis (18), where he provides two reasons for excluding the 1960-72 CPS I results by LeVois and Layard (19). His first reason is that LeVois and Layard did not present RRs for nonsmokers married to current smokers as a whole. However, these RRs can be readily calculated from other RRs in the paper or directly from the CPS I data. Also, he neglects to point out that the paper by Sandler (20), which he saw fit to include, only gives the RR for nonsmokers married to ever smokers. His second reason for excluding the CPS I results is that "the referent group does not and cannot exclude people exposed to ETS outside the home." But neither do the majority of the studies included in his meta-analysis, since they are also limited to spousal smoking! After 'justifying' the exclusion of CPS I results from the 1960s, MJT proceeds without comment to use the results of three other cohorts from the 1960s, Sandler (20), Hirayama (21), and Humble (22). The Humble cohort had 20 years of follow-up with only the baseline questionnaire data to classify exposure (22). It is clear from Table 1 of his meta-analysis below that MJT has no objection to studies of spousal smoking initiated in the 1960s or studies which present only the RR for ever smokers so long as they show the desired result.

**Table 1.** Prospective epidemiologic studies of ischemic heart disease and ETS exposure from a smoking spouse.

| Reference | Population | Years | No. of never smokers | End point | Events in men/women | Age-adjusted RR (95% CI) | Adjusted multivariate RR (95% CI) |
|---|---|---|---|---|---|---|---|
| Hirayama, 1984 (*6*)<br>Hirayama, 1990 (*7*) | Japan | 1966–1981 | 91,540 women | Death | 254 | 1.31 (1.01, 1.69)[a] | 1.40) |
| Garland et al., 1985 (*8*) | Rancho Bernardo, U.S. | 1974–1983 | 695 women | Death | 19 | 2.25[b] | 2.7[c] |
| Svendsen et al., 1987 (*9*) | MRFIT, U.S. | 1973–1982 | 11,245 men | Incidence and death | 69 | 1.48 (0.89–2.47) | 1.61 (0.96, 2.71) |
| Butler, 1988 (*10*) | Spouse pairs | | 9,378 women | | 80 women | 1.40 (0.51–3.84)[d] | |
| | AHSMOG | 1976–1982 | 3,488 women | | 75 men | 0.57 (0.14, 2.32)[e] | |
| | | | 1,489 men | Death | 70 women | 1.42 (0.94, 2.15)[e] | |
| Sandler et al., 1989 (*11*) | Maryland, U.S. | 1963–1975 | 4,162 men<br>14,873 women | Death | 370 men<br>988 women | | Men 1.31 (1.05, 1.64)[f]<br>Women 1.19 (1.04, 1.36) |
| Hole et al., 1989 (*12*) | Scotland | 1972–1985 | 671 men<br>1,784 women | Death | 84 total | 1.75[c] | 2.01 (1.21–3.35)[c] |
| Humble et al., 1990 (*13*) | Georgia, U.S. | 1960–1980 | 513 women | Death | 76 | 1.34 (0.84–2.21)[g] | 1.59 (0.99–2.57)[g] |
| Steenland et al., 1996 (*3*) | American Cancer Society, U.S. | 1982–1989 | 101,227 men<br>208,372 women | Death | 2,494 men<br>1,325 women | | Men 1.22 (1.07–1.40)<br>Women 1.10 (0.96–1.27) |
| Kawachi et al., 1997 (*4*) | Nurses, U.S. | 1982–1992 | 32,046 women | Incidence and death | 152 | | 2.11 (1.03–4.33) |

AHSMOG, Adventist Health Smog; MRFIT, Multiple Risk Factor Intervention Trial. [a]Spouse smokes 20+ cigarettes per day. [b]Based on only 2 deaths in nonsmokers married to current smokers. [c]Combines people whose spouses smoked formerly and current smokers. [d]Based on only 4 deaths in nonsmokers married to current smokers. [e]Calculated by authors. [f]Household exposure, not spousal. [g]Death from all cardiovascular disease.

3) <u>ACS misrepresentations regarding the results of CPS II</u>

a. A further example of the ACS misrepresentations on the ETS issue can be found in the following simple comparison of statements about the findings in CPS II. The statement in the ACS press release by Harmon J. Eyre, MD, ACS's national chief medical officer, says (2): "CPS-II is one of more than 50 studies now published that have shown non-smokers married to smokers have an increased risk of lung cancer". However, the Cardenas dissertation comes to the following conclusion on page viii (11): "This study found no evidence of an association between self-reported ETS and lung cancer risk among nonsmokers. However, using spousal smoking habits to assess exposure, we found ETS is only weakly, and not statistically significantly, related to lung cancer risk among nonsmoking women in seven years of follow-up of the CPS II cohort."

b. Another more serious misrepresentation of CPS II results is evident when one compares the published Cardenas paper (23) with the Cardenas dissertation (12). Table 4 of the Cardenas paper (23) presents exposure to spousal smoking among women by the husband's level of smoking, but is deceptively labeled. Women with the highest level of exposure, labeled "40+ cpd by spouse", have a RR of 1.9 (95% CI 1.0-3.6) and the P for dose-response trend is 0.03. However, Table 38 of the Cardenas dissertation (12) makes clear that the RR for *current* smokers of 40+ cpd is only 0.9 (95% CI 0.2-3.9) and the P for trend is 0.34. If it were not for Table 38 the reader would not know that Table 4 is based on the combination of current and former smokers. This combination of current and former smokers by cpd is highly unorthodox, has not been done in other ETS studies, and is not meaningful for assessing a trend based on current smoking. The Cardenas dissertation makes it very clear that there is no dose-response relationship between spousal smoking and lung cancer in CPS II. Tables 4 and 38 are shown side by side below.

**Table 4**. Number of lung cancer deaths, person-years (PY) at risk, and rate ratios (RR) with 95 percent confidence intervals (CI) among never-smoking women according to various indices of spousal smoking, ACS

| | No. of women | Lung cancers | PY | RR[b] | (CI) |
|---|---|---|---|---|---|
| Cigarettes per day by spouse[a] | | | | | |
| 0 | 46,149 | 30 | 333,946 | 1.0 | — |
| 1-19 | 11,467 | 9 | 83,074 | 1.1 | 0.5-2.2 |
| 20-39 | 24,735 | 22 | 179,751 | 1.2 | 0.7-2.2 |
| 40+ | 9,871 | 13 | 71,618 | 1.9 | 1.0-3.6 |
| | | | | | Trend[b] $P = 0.03$ |

[a] The referent group includes never-smoking women married to husbands who did not smoke during the marriage. The exposed categories are split into approximate tertiles, and are restricted to never-smokers married to cigarette smokers with complete smoking data, married only once, and with valid information on age at marriage.

[b] From a Cox PH model adjusted for age, race, education, dietary consumption of vegetables and total fat, asbestos exposure, blue collar employment, and history of chronic lung disease.

**Table 38. Lung Cancer Adjusted Rate Ratios (95% CI) among nonsmoking spouses according to the amount of cigarette smoked by spouses* if married once and with data on age at marriage, CPS II, 1982-1989.**

| Exposure | Husbands | | Wives | | All Nonsmokers |
|---|---|---|---|---|---|
| Packs of cigarettes: by current smokers | Deaths/PY | multivariate RR (95% CI) | Deaths/PY | multivariate RR (95% CI) | multivariate RR (95% CI) |
| Nonsmokers | 46/314,944 | 1.0 | 30/311,333 | 1.0 | 1.0 |
| < 1 pack | 5/14,310 | 3.0 | 5/32,524 | 1.7 | 2.1 |
| | | (1.1-7.9) | | (0.7-4.4) | (1.1-4.1) |
| 1 - 1.9 packs | 0/15,054 | 0.0 | 10/69,060 | 1.6 | 1.2 |
| | | (0.0-NC) | | (0.8-3.4) | (0.6-2.3) |
| 2+ packs | 0/2,308 | 0.0 | 2/24,900 | 0.9 | 0.8 |
| | | (0.0-NC) | | (0.2-3.9) | (0.2-3.5) |
| p test for trend | | 0.6 | | 0.34 | 0.55 |
| by former smokers | Deaths/PY | multivariate RR (95% CI) | Deaths/PY | multivariate RR (95% CI) | multivariate RR (95% CI) |
| Nonsmokers | 46/314,944 | 1.0 | 30/311,333 | 1.0 | 1.0 |
| < 1 pack | 1/34,042 | 0.2 | 4/61,677 | 0.6 | 0.5 |
| | | (0.0-1.7) | | (0.2-1.8) | (0.2-1.2) |
| 1 - 1.9 packs | 0/15,915 | 0.0 | 12/120,585 | 0.8 | 0.7 |
| | | (0.0-NC) | | (0.4-1.7) | (0.3-1.4) |
| 2+ packs | 1/3,559 | 2.8 | 11/49,304 | 2.0 | 1.9 |
| | | (0.4-21.6) | | (1.0-4.0) | (1.0-3.7) |
| p test for trend | | 0.28 | | 0.29 | 0.6 |

(n=148,204)

* Analyses restricted to nonsmoking spouses married to nonsmoking spouses and those married to cigarette smokers (and not other type of tobacco), with complete smoking data, married once at the time of interview, and with valid data on age at first marriage.

§ Cox regression model stratified for age, gender, 'race', schooling, total intake of foods containing carotenoids, total fat as nutrient index, occupational exposure to asbestos and history of chronic lung disease. NC=not calculable

c. Another analysis which sheds light on the CPS II findings concerning ETS is the initial report which linked data on ambient air pollution from 151 U.S. metropolitan areas with mortality data from CPS II for individuals who resided in those areas (24). The results of this analysis showed that in never smokers there was a statistically significant association of all cause mortality with both sulfate and fine particle concentrations after controlling for covariates, including *hours per day of ETS exposure*. The authors, one of whom was MJT, did not report the specific results for ETS exposure. However, in order to resolve a major dispute over the validity of the results (25), a reanalysis was

conducted by the Health Effects Institute (26). The Cox proportional hazards regression model (PHREG) results included in the appendix of the resulting HEI Reanalysis Report make it clear that the independent variable "passive" (hours per day of ETS exposure) shows no association whatever with mortality from lung cancer, cardiopulmonary disease, or all causes in never smokers (27). For lung cancer, RR(passive) = 1.005 (0.957-1.055) in CPS II agrees well with RR(8 level index) = 0.97 (0.91-1.04) in CA CPS I. A portion of the actual PHREG computer printout for lung cancer is shown below. The PHREG program is the same as that used in our CA CPS I study.

Table3: Adjusted Mortality Risk Ratios (and 95% Confidence Intervals) by Lung Cancer Related Death for the Sulfate Particles
Never-smokers
The PHREG Procedure

Analysis of Maximum Likelihood Estimates

Conditional Risk Ratio and 95% Confidence Limits

| Variable | Risk Ratio | Lower | Upper | Label |
|---|---|---|---|---|
| PASSIVE | 1.005 | 0.957 | 1.055 | Passive Smoking |
| EDULOW | 1.426 | 1.053 | 1.932 | Less than high school education |
| INDUSEXP | 1.434 | 1.018 | 2.019 | Occupational exposure |
| BMI | 0.940 | 0.909 | 0.973 | Body Mass Index |
| ALC | 0.969 | 0.870 | 1.079 | Alcohol Drinking |
| SULFATES | 1.511 | 0.734 | 3.108 | Sulfate Particles |

d. Contrary to the impression MJT tries to create, there is substantial agreement between the results of CA CPS I and CPS II for both lung cancer and CHD, as seen in Tables C and D. For lung cancer, all RRs for CA CPS I are consistent with those for CPS II from both the Cardenas dissertation (12) and the Cardenas paper (23), although the RRs in the paper are inexplicably higher than those in the dissertation. All RRs are consistent with no effect or with a 20% increase in risk. For CHD, all RRs for CA CPS I are consistent with those for CPS II from the Steenland analysis (28), except for the male RR's for current smokers of 1-19 cigarettes per day. This one difference drives the differences for all current smokers and ever smokers. Only the male RR's for current smokers in CPS II are significantly greater than 1.00. All other RRs from CPS II and all RRs from CA CPS I are consistent with 1.00. All RRs from the LeVois and Layard analysis of CHD for the full CPS I (19) are consistent with those for CA CPS I.

Table C. Relative risk (RR with 95% CI) of ETS exposure (spousal smoking) related to deaths from lung cancer among never smokers in CA CPS I and CPS II.

| Spousal smoking | 1960-98 CA CPS I Age-adjusted RR (95% CI) | 1982-89 CPS II Age-adjusted RR (95% CI) | 1982-89 CPS II Age-adjusted RR (95% CI) |
|---|---|---|---|
| Lung cancer | Enstrom (1) Tables 7 & 8 | Cardenas dissertation (12) Table 36 | Cardenas paper (23) Table 3 |
| Males | | | |
| Never | 1.00 | 1.0 | 1.0 |
| Former | 0.92 (0.37-2.30) | 0.9 (0.5 –1.6 ) | 1.1 (0.6 -2.2 ) |
| Current--total | 0.69 (0.34-1.39) | 0.9 (0.3 –1.9 ) | 1.0 (0.5 -2.0 ) |
| Ever | 0.75 (0.42-1.35) | 0.9 (0.5 -1.5 ) | 1.0 (0.6 -1.8 ) |
| Females | | | |
| Never | 1.00 | 1.0 | 1.0 |
| Former | 1.08 (0.73-1.60) | 1.0 (0.7 -1.5 ) | 1.1 (0.8 -1.6 ) |
| Current--total | 0.93 (0.65-1.33) | 1.3 (0.8 -1.9 ) | 1.3 (0.8 -1.8 ) |
| Ever | 0.99 (0.72-1.37) | 1.1 (0.8 -1.5 ) | 1.2 (0.8 -1.6 ) |

Table D. Relative risk (RR with 95% CI) of ETS exposure (spousal smoking) related to deaths from CHD among never smokers in CA CPS I, CPS II, and CPS I. (* = RR was based on combining other RRs)

| Spousal smoking | 1960-98 CA CPS I Age-adjusted RR (95% CI) | | 1982-89 CPS II Fully-adjusted RR (95% CI) | | 1960-72 CPS I Age-adjusted RR (95% CI) | |
|---|---|---|---|---|---|---|
| Coronary heart disease | Enstrom (1) Tables 7 & 8 | | Steenland (28) Table 2 | | LeVois (19) Table 4 | |
| Males | | | | | | |
| Never | 1.00 | | 1.00 | | 1.00 | |
| Former | 0.94 | (0.78-1.12) | 0.96 | (0.83-1.11) | 0.95 | (0.83-1.09) |
| Current | | | | | | |
| 1-19 cigs/day | 0.91 | (0.78-1.06) | 1.33 | (1.09-1.61) | 0.99 | (0.89-1.09) |
| 20 cigs/day | 0.92 | (0.74-1.15) | 1.17 | (0.92-1.48) | | |
| 21+ cigs/day | 1.20 | (0.88-1.64) | 1.09 | (0.77-1.53) | | |
| Current--total | 0.94 | (0.83-1.07) | 1.22 | (1.07-1.40) | 0.98* | (0.90-1.07) |
| Ever | 0.94 | (0.85-1.05) | 1.09* | (0.99-1.21) | 0.97 | (0.90-1.05) |
| Females | | | | | | |
| Never | 1.00 | | 1.00 | | 1.00 | |
| Former | 1.02 | (0.93-1.11) | 1.00 | (0.88-1.13) | 0.99 | (0.93-1.05) |
| Current | | | | | | |
| 1-19 cigs/day | 1.07 | (0.96-1.19) | 1.15 | (0.90-1.48) | 1.04 | (0.97-1.12) |
| 20 cigs/day | 1.04 | (0.92-1.16) | 1.07 | (0.83-1.40) | | |
| 21-39 cigs/day | 0.95 | (0.80-1.12) | 0.99 | (0.67-1.47) | | |
| 40+ cigs/day | 0.83 | (0.65-1.06) | 1.04 | (0.67-1.61) | 0.95 | (0.78-1.15) |
| Current--total | 1.01 | (0.93-1.09) | 1.10 | (0.96-1.27) | 1.04* | (0.98-1.11) |
| Ever | 1.01 | (0.94-1.08) | 1.04* | (0.95-1.15) | 1.03 | (0.98-1.08) |

e. Table E summarizes the RRs for ETS and CHD by exposure status (former/never, current/never, ever/never) from all US cohort studies and compares our meta-analysis with the MJT meta-analysis (18). After excluding the CPS I results from his meta-analysis on dubious grounds, MJT then proceeds to arbitrarily select those relative risks which suit his purpose. It is striking that he did not even give a clear definition of exposure status. This allowed him, in a number of instances, to simply select the higher relative risk from among "current/never" and "ever/never" in the individual studies. For example, from the studies by Svendsen, Butler, and Steenland, MJT uses the RR (current/never), whereas from the studies by Garland and Sandler, he uses the RR (ever/never). This pattern of using selected, unlabeled RRs can be clearly seen by looking back at Table 1 of the MJT meta-analysis (18). If one is consistent in maintaining the distinction between "current/never" and "ever/never," the summary RRs are considerably reduced, particularly in women, even without CPS I results. Inclusion of the CA CPS I results has a major impact on the meta-analysis and yields summary RRs of about 1.05 for the US cohort studies, far less than the RR=1.22 calculated by MJT. The inclusion of the LeVois and Layard CPS I results (19) also yields summary RRs of about 1.05.

Table E. Meta-analysis of relationship between ETS exposure and CHD mortality for US cohort studies in groups. Relative risk (RR & 95% CI) compares never smokers with ETS exposure to never smokers with no ETS exposure. Signs used: # indicates multivariate-adjusted RRs are used (otherwise age-adjusted RRs are used); * indicates RR was approximated by Enstrom from available published data; ^ indicates RR was approximated by MJT; * indicates RR was based on combining other published RRs. JEE & GCK meta-analysis is compared with MJT meta-analysis (18).

| Group & Study | JEE & GCK meta-analysis by ETS exposure category | | | | | | MJT meta-analysis | |
|---|---|---|---|---|---|---|---|---|
| | RR(former/never) | | RR(current/never) | | RR(ever/never) | | RR(exposed/unexposed) | |
| Males | | | | | | | | |
| A Svendsen | | | 2.11 | (0.69-6.46) | | | #1.61 | (0.96-2.71) |
| A Butler-AHSMOG | | | | | 0.55* | (0.31-0.99) | ^0.57 | (0.14-2.32) |
| A Sandler | | | | | #1.31 | (1.05-1.64) | #1.31 | (1.05-1.64) |
| A Steenland | #0.96 | (0.83-1.11) | #1.22 | (1.07-1.40) | #1.09* | (0.99-1.21) | #1.22 | (1.07-1.40) |
| B Enstrom | 0.94 | (0.78-1.12) | 0.94 | (0.83-1.07) | 0.94 | (0.85-1.05) | | |
| C LeVois | 0.95 | (0.83-1.09) | 0.98* | (0.90-1.07) | 0.97 | (0.90-1.05) | | |
| Summary--A | 0.96 | (0.83-1.11) | 1.23 | (1.08-1.41) | 1.11 | (1.01-1.21) | 1.25 | (1.12-1.40) |
| Summary--A & B | 0.95 | (0.85-1.07) | 1.07 | (0.97-1.17) | 1.03 | (0.96-1.11) | | |
| Summary--A & C | 0.95 | (0.86-1.05) | 1.05 | (0.98-1.13) | 1.03 | (0.97-1.09) | | |
| Females | | | | | | | | |
| A Garland | 3.00 | ~(0.8-12.0) | 2.25 | ~(0.5-11.0) | ~2.73 | ~(0.7-11.0) | #2.7 | |
| A Butler-SpPair | 0.96 | (0.55-1.66) | 1.40 | (0.51-3.84) | 1.05* | (0.64-1.70) | 1.40 | (0.51-3.84) |
| A Butler-AHSMOG | | | | | 1.51* | (0.99-2.29) | ^1.42 | (0.94-2.15) |
| A Sandler | | | | | #1.19 | (1.04-1.36) | #1.19 | (1.04-1.36) |
| A Humble | | | 1.29 | (0.79-2.10) | | | #1.59 | (0.99-2.57) |
| A Steenland | #1.00 | (0.88-1.13) | #1.10 | (0.96-1.27) | #1.04* | (0.95-1.15) | #1.10 | (0.96-1.27) |
| A Kawachi | | | 1.87 | (0.56-6.20) | | | #2.11 | (1.03-4.33) |
| B Enstrom | 1.02 | (0.93-1.11) | 1.01 | (0.93-1.09) | 1.01 | (0.94-1.08) | | |
| C LeVois | 0.99 | (0.93-1.05) | 1.04* | (0.98-1.11) | 1.03 | (0.98-1.08) | | |
| Summary--A | 1.01 | (0.89-1.14) | 1.13 | (0.99-1.29) | 1.10 | (1.02-1.19) | 1.19 | (1.09-1.30) |
| Summary--A & B | 1.02 | (0.95-1.09) | 1.04 | (0.97-1.11) | 1.05 | (1.00-1.11) | | |
| Summary--A & C | 0.99 | (0.94-1.05) | 1.06 | (1.00-1.12) | 1.05 | (1.01-1.09) | | |
| Both Sexes | | | | | | | | |
| Summary--A | 0.99 | (0.90-1.08) | 1.18 | (1.07-1.29) | 1.10 | (1.04-1.17) | 1.22 | (1.13-1.30) |
| Summary--A & B | 1.00 | (0.94-1.06) | 1.05 | (0.99-1.11) | 1.05 | (1.00-1.09) | | |
| Summary--A & C | 0.98 | (0.94-1.02) | 1.05 | (1.01-1.10) | 1.04 | (1.01-1.08) | | |

4) Failure of ACS to fully and objectively analyze CPS I and CPS II

MJT has failed to fully and objectively analyze the data in CPS I and CPS II, which, if fully utilized, represent the vast majority (about 90%) of prospective results on ETS in relation to CHD and lung cancer. In addition, if fully utilized, CPS I and CPS II represent about 90% of the total (prospective and case-control) results on ETS and CHD. Specific aspects of this failure are: a) failure to present any ETS analysis of CPS I in response to the 1995 analysis of LeVois & Layard (19); b) failure to present any ETS analysis of CPS II beyond 7-year follow-up, in spite of existence of 12-year follow-up data (29) and 16-year follow-up data (30); c) failure to use the 1992 CPS II Nutrition Cohort, which is a 15% subsample of the CPS II cohort, to refine 1982 CPS II ETS analyses with regard to misclassification and other issues by using repeated measurements of active and/or passive smoking collected during 1992-2001 (31). All CPS I and CPS II questionnaires can be viewed and downloaded from the ACS website (32). Because ACS controls such a large portion of the relevant epidemiologic data on the relationship between ETS and mortality, they have a special obligation to fully and objectively analyze and summarize it.

In view of their demonstrated tendency to select data which will produce the desired association and to suppress other data, we point to MJT's statement (2): "The American Cancer Society welcomes thoughtful, independent peer review of our data." We challenge ACS to have an independent analysis done on CPS II with 16-year follow-up, on full CPS I with 13-year follow-up, and on CA CPS I with 39-year follow-up by an objective group of investigators with input, but not control, by MJT, JEE, & GCK.

Conclusions

Careful consideration of these points makes it abundantly clear that our paper was attacked by MJT not because of specific errors in our analysis, which have yet to be identified, but because of our null results for CHD and lung cancer. In addition, we were attacked for being skeptical that the association of ETS with CHD is as strong as is generally believed. This kind of skepticism has an important role in science, since it can lead to a more critical assessment of the available data, to better studies to illuminate the nature of the association of CHD with ETS exposure, and to the identification of other causal factors. But clearly in the area of passive smoking, one voices skepticism at one's own peril.

The attempt to suppress valid data and divergent opinions does a disservice to science and the public. It is highly unprofessional to engage in *ad hominem* attacks and unfounded insinuations of dishonesty rather than judging research on its merits, as has been eloquently stated by Rothman (32). As made clear by this episode, the self-righteous defenders of public health are far from being free of their own self-interests and biases. Furthermore, their misrepresentations are much more insidious than those of the tobacco industry for the simple reason that they have the public's trust. Rothman has argued that no one is objective – we all have our biases. Objectivity is achieved through the *process* of critically evaluating the work itself. This is the only way to get at the truth and not by indulging in what Rothman refers to as "the new McCarthyism in science" (33).

Reviews of the health effects of ETS often make the argument that conclusions about the health effects of ETS must take into account the totality of the evidence, the "mosaic of evidence," as one reviewer put it (34), including epidemiology, toxicology, and experimental evidence. We agree. We have no problem believing that exposure to ETS is associated with excess risk of lung cancer and CHD and we clearly state that our results "do not rule out a small effect." We also concur that it is possible that existing epidemiologic studies may actually *under-estimate* the effects of ETS due to misclassification of exposure or confounding. However, based on the results presented in our paper and in this commentary, we feel that the association "may be considerably weaker than generally believed."

What we are against is the selective use of data and the exclusion of facts that do not fit with a preconceived conclusion. And this is not because we are tools of the tobacco industry, but because we believe this approach debases science and does a disservice to the public. We are against overstating the certainty of the science for what may be perfectly laudable political/social ends. The demand for a lock-step conformity and for political correctness is antithetical to true science and rational inquiry.

As a final point, we believe the primary reason our CPS I results and the objectively analyzed CPS II results show little or no relationship between ETS and deaths from lung cancer and CHD may be because levels of ETS exposure are lower than is generally stated. We note with interest *The Wall Street Journal* letter from Dr. Melvin W. First, who 28 years ago found that ETS exposures were equivalent to smoking a small fraction (0.004) of one cigarette per hour (35). We wonder how many investigators like Dr. First would be willing to step forward if they did not fear having their reputations trashed by the ACS and other anti-smoking organizations.

THE WALL STREET JOURNAL. OPINION THURSDAY, MAY 29, 2003

## Breathing Others' Smoke: It's Not Going to Kill You

In regard to your May 16 story "Passive Smoke Doesn't Kill—Or Does It?": James Enstrom's finding that exposure to environmental smoke cannot be associated with increased risk of cancer and heart disease comes as no surprise to me as I authored, with a colleague, a study published in the New England Journal of Medicine (292:844-845, 1975) detailing the results of inconspicuous air samplings at restaurants, cocktail lounges, transportation terminals, etc. "to evaluate the health implications for nonsmokers" and found that the concentrations of tobacco smoke were equivalent to smoking about 0.004 cigarettes an hour while in these facilities. It should be recalled that smoking in public places was normal and prevalent a quarter-century ago.

Nor am I surprised at the scurrilous responses of the concerned voluntary health associations. Publication of the paper cited above resulted in many angry voices on the phone wanting to learn the funding source, although it was noted that it had been funded "by the Massachusetts Lung Association and its local affiliates." That is another interesting tale—the Lung Association put our report in a drawer and never released it. It is also curious that none of the surgeon general's reports ever mentioned this study.

Nor am I surprised that an attempt is being made to trash Dr. Enstrom's conclusions because the study was funded in part by money from tobacco interests. Does this mean that all the researchers funded by anti-smoking agencies are biased in the opposite direction? I trust not. Such charges are deeply insulting to academics in good standing.

For the record, I am a non-smoker and as a responsible public heath professional I do not advocate smoking.

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