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Defending Legitimate Epidemiologic Research

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http://www.spiked-online.com/Articles/0000000CAA11.htm

Introduction

This commentary presents a detailed response to the extensive attacks that have been made on my legitimate epidemiologic research in the May 17, 2003 *British Medical Journal* (1) and on my professional reputation and scientific integrity. I have vigorously defended the honesty and scientific integrity of my research and I have identified and addressed several unethical and erroneous attacks by powerful organizations and individuals who have attempted to suppress and discredit findings that do not support their ideological and political agendas. Other attacks on me are not dealt with here and will be addressed separately. Hopefully, my defense will encourage and/or help other honest scientists to defend their research against unwarranted and illegitimate criticism.

This subject is quite complex and is most clearly explained by presenting in chronological order all the relevant details that I have been able to uncover during the past three years. The type of attack to which I have been subjected is not unique to me or my research, but the nature and scope of this attack is unusual. The attack is primarily due to the fact that I published politically incorrect findings based on research that was partially funded by the tobacco industry. In recent years certain papers have come under attack because of the real or alleged conflicts of interest of their authors (2) or because their findings are disliked by special interest groups (3). In most of these cases the authors and/or their research findings have been attacked without any direct evidence or even a strong argument that errors exist in their papers. However, epidemiologic research connected with the tobacco industry is an incendiary and highly emotional subject.

Before proceeding, I want to make a clear distinction between my situation, where scientific misconduct has been alleged or implied but not documented, and other situations where scientific misconduct has actually occurred. Three recent instances of serious scientific misconduct in biomedical sciences involve South Korean cloning researcher, Woo Suk Hwang (4,5), Norwegian oncologist, Jon Sudbo (6), and Canadian nutritional immunologist, Ranjit Kumar Chandra (7). The long-term adverse consequences of scientific misconduct in these and several earlier cases have recently been discussed in detail (8). These cases involve scientists guilty of clearly documented fraud and many scientific papers that are based on this fraud have now been withdrawn by the major journals that published them, including *Science, New England Journal of Medicine,* and *The Lancet*. Indeed, the scientific misconduct by Hwang was so egregious that

he went from being a national hero as a cloning researcher in South Korea in late 2005 to being a dishonest and disgraced scientist who was fired by Seoul National University in early 2006 (5).

Being able to distinguish between real and implied scientific misconduct is very important to the integrity of science in general and to the integrity of individual scientists in particular. Falsely accusing honest scientists of scientific misconduct is just as wrong as real scientific misconduct itself. Implying that an honest scientist has committed scientific misconduct simply because he has received funding from the tobacco industry is wrong and falls under the category of "the new McCarthyism in science" (2). Indeed, none of the actual cases of scientific misconduct described above involve the tobacco industry or tobacco industry funding in any way; they involve scientists who are simply dishonest.

Background on May 17, 2003 *BMJ* Paper

I begin with a presentation of the background necessary to understand the issues involved with the May 17, 2003 *British Medical Journal (BMJ)* paper that I wrote with Dr. Geoffrey C. Kabat (1). This account primarily involves me and thus is written in the first person, but it also refers to Kabat, where appropriate and not otherwise noted. This paper, which found no relationship between environmental tobacco smoke (ETS) and tobacco related mortality in a prospective study of Californians during 1960-1998, represents the largest (in terms of statistical power) and most detailed (in terms of results presented) epidemiologic study on ETS and mortality ever published in a major medical journal. The study is based on the California portion of the original 25-state Cancer Prevention Study (CPS I), which was begun by the American Cancer Society (ACS) in 1959 and which has been conducted at UCLA by me since 1991. Kabat and I are both highly qualified epidemiologists who have had long and successful careers dating back to the 1970s. Our paper was deemed to be scientifically sound and worthy of publication after being peer reviewed by two distinguished epidemiologists, a *BMJ* statistician, and a *BMJ* editorial committee. The details of the entire peer review process and the names of all the individuals involved in the review process are available under the category "Prepublication history" (9). The paper survived the rigorous review process and selection criteria of the *BMJ*, which publishes less than 10% of the total submissions it receives (10).

Instantaneous ACS Attack

As soon as the embargo was lifted on the press coverage of the paper, it was immediately condemned in a May 15, 2003 press release by the ACS (11), "American Cancer Society Condemns Tobacco Industry Study for Inaccurate Use of Data." This press release has subsequently been posted on the ACS web site in a slightly different format (12). As I will demonstrate later, the ACS press release makes a several entirely false statements about the study, such as:

1) "Tobacco Industry Study" was "Part of Organized Effort to Confuse Public About Secondhand Smoke"

2) "Society researchers repeatedly advised Dr. Enstrom that using CPS-I data to study the effects of secondhand smoke would lead to unreliable results"

3) "this study is neither reliable nor independent"

4) "The study suffers from a critical design flaw: the inability to distinguish people who were exposed to secondhand smoke from those who were not"

5) "exposure to secondhand smoke was so pervasive [in 1959] that virtually everyone was exposed to ETS, whether or not they were married to a smoker".

Also, the press release contains a number of out of context quotes from formerly confidential tobacco industry documents (http://tobaccodocuments.org/about.php), that have nothing to do with the conduct, analysis, or publication of *BMJ* paper. My tobacco industry funding and competing interests were clearly and accurately described in more than 200 words in the *BMJ* paper (1). However, in order to raise doubts about my honesty and scientific integrity, the ACS made a great effort to locate and extract selective quotes from the professional correspondence I have had with the tobacco industry over a number of years. This *ad hominem* attack diverted attention from paper itself and obscured its contribution to the body of epidemiologic evidence regarding the lethality of ETS.

Instantaneous *BMJ* Rapid Responses Attack

In May 1998 the *BMJ* began posting electronic letters to the editor, known as "rapid responses" (RRs), stating "our intention is to post all but the libellous, gratuitously rude, trivial, irrelevant, or incomprehensible on the website within 72 hours" (13). These RRs were seen as a way to allow all points of view to be expressed in the electronic version of the *BMJ* (bmj.com) and they were unique to a major medical journal when they started. Beginning on May 15, 2003, dozens of individual readers and prominent anti-smoking activists around the world contributed unedited, highly critical RRs to bmj.com about me and the *BMJ* paper. More than 150 RRs have now been posted on bmj.com and many of them are *ad hominem* attacks on me because of my contacts with and funding from the tobacco industry (14). The overall content and nature of these RRs was summarized by a *BMJ* associate editor in an August 30, 2003 letter (15). Particularly damning are May 19 and 20, 2003 RRs by Michael J. Thun, M.D., the ACS Vice President, Epidemiology and Surveillance Research (16,17), a May 20, 2003 RR by Professor Martin McKee of London (18), a May 30, 2003 RR by Dr. Allan Hackshaw for 14 members of the IARC Working Group (19), and a August 19, 2003 RR by Drs. Phillip S. Gardiner, Charles Gruder, and Francisco Buchting of the University of California Office of the President (20). None of the authors of these and the other critical RRs ever contacted us for a clarification of our contacts with the tobacco industry and any other aspect of our *BMJ* paper before posting their RRs.

Two sociologists, Drs. Sheldon Ungar and Dennis Bray, noticed the RRs and the other media coverage of my paper and described the phenomena that they observed in their own January 2005 paper (21). They described in detail the "efforts to prevent the making of specific scientific claims in any *or* all of the arenas in which these claims are typically reported or circulated" as

they related to my *BMJ* paper. Their "results suggest that the public consensus about the negative effects of passive smoke is so strong that it has become part of a regime of truth that cannot be intelligibly questioned." Given all the controversies in other areas of epidemiology, such as, hormone replacement therapy, number of deaths attributable to obesity, fat and mortality, this state of affairs regarding ETS is quite amazing. Indeed, the evidence regarding the lethality of ETS is not "a regime of truth," but collection of weak results that have turned into a "causal" relationship by carefully chosen committees. As I will discuss later the epidemiologic evidence on this subject has changed in recent years and needs to be completely and objectively reassessed in order to reach a valid conclusion.

In January 2004 *BMJ* Editor Richard Smith defended the free form RRs by explaining that they are consistent with the philosophy of the great English poet John Milton: "Give me the liberty to know, to utter, and to argue freely according to conscience, above all liberties. ..." (22). Then, in July 2004 Richard Smith make a very powerful statement just before resigning as *BMJ* Editor: "If readers once hear that important, relevant, and well argued articles are being suppressed or that articles are being published simply to fulfil hidden political agendas, then the credibility of the publication collapses—and everybody loses." (23). In June 2005 the *BMJ* revised its policy on RRs. RRs are now carefully screened for content and relevance and limited in length before they are accepted: "Responses directed primarily against the messenger rather than the message won't be posted; nor will responses that make reasonable points but are gratuitously offensive." (24). On January 24, 2006 the *BMJ* posted an RR by Kabat and me that updated the defense of our paper in terms of scientific issues (25). However, on January 26, 2006 we submitted a second RR that dealt with some unethical tactics that I recently learned had been used with regard to our *BMJ* paper. Unfortunately, the *BMJ* has declined to post it, and consequentially, I decided to write this commentary and discuss the unethical tactics and other relative issues here.

Authors Defend the *BMJ* Paper

The attack described above was quite startling to me as someone whose honesty and scientific integrity had not been questioned in the 33-year period from July 1970, when I received my Ph.D. (26), until May 2003 (1). It was also startling that the attack was initiated by the ACS, the very organization that had given me the original California Cancer Prevention Study (CPS I) data in 1991 upon which the *BMJ* study was based. Kabat and I initially dealt with some of the initial controversy by responding to specific criticisms in our August 30, 2003 *BMJ* letter (27) and in our January 31, 2004 *Lancet* letter (28). In particular, in these letters we have refuted the five false statements by the ACS with the following response:

1) This was not a "Tobacco Industry Study," but rather a UCLA study conducted by two well qualified epidemiologists. This was not "Part of Organized Effort to Confuse Public About Secondhand Smoke" because only accurate findings were published and because the tobacco industry played no role in the conduct, writing, or publication of the paper and did not even know it was being published until it appeared.

2) It is a contemptible fabrication that "Society researchers repeatedly advised Dr. Enstrom that using CPS-I data to study the effects of secondhand smoke would lead to unreliable results."

Indeed, the ACS Vice President for Epidemiology prior to Thun worked closely with me on the overall CA CPS I follow-up study from 1991 until 2001 because he felt that this was a valuable project. He was a co-author on the first version of the ETS and mortality paper when it was submitted to the New England Journal of Medicine in 2001 and was co-author on my first publication based on the CA CPS I cohort, which dealt with smoking cessation and mortality trends (29). He was not able to remain as co-author on the ETS and mortality paper after 2001 because of his retirement from the ACS and his growing distance from the project.

3) It is absolutely false that "this study is neither reliable nor independent." First, the ACS could not possibly know before it was conducted that the study would produce unreliable results. Indeed, the *BMJ* peer review process found that the results were sound and worthy of publication. Second, the study was conducted independent of influence from both the ACS and the tobacco industry and the ACS has identified no specific errors in the study in three years.

4) It is absolutely false that "The study suffers from a critical design flaw: the inability to distinguish people who were exposed to secondhand smoke from those who were not." This cohort study was done in the same way as the other spousal smoking studies and our 1999 follow-up questionnaire survey results clearly showed that there were subjects who had varying degrees of exposure to ETS as shown in Tables 4 and 5 of the *BMJ* paper.

5) It is absolutely false that "exposure to secondhand smoke was so pervasive [in 1959] that virtually everyone was exposed to ETS, whether or not they were married to a smoker" The results of the 1999 survey shown in Table 4 of the *BMJ* paper clearly shows that among never smokers married to never smokers as of 1959, 43.5% of males and 61.7% of females reported no regular exposure to cigarette smoke from others in work or daily life as of 1999.

Although the ACS disputes the validity of this 1999 survey, they have not conducted their own survey of the approximately 50 million Americans alive as of 1950 in order to obtain actual evidence that all Americans alive during the 1950s and 1960s were equally exposed to ETS. The ACS cannot simply make an unsubstantiated claim that "virtually everyone was exposed to ETS" and expect this claim to negate all the evidence presented in my *BMJ* paper.

In addition to the published letters cited above, we submitted to the *BMJ* on June 30, 2003 Manuscript BMJ/2003/084269, a detailed commentary that vigorously defended specific aspects of the *BMJ* paper. We showed that there was, in fact, substantial agreement between our results regarding ETS and those of the ACS and pointed out inconsistencies in ACS findings that have not been previously noted. Unfortunately, on September 19, 2003 the *BMJ* declined to publish this commentary, possibly because of the controversy that had erupted over the *BMJ* paper. We then spent the next two years attempting to publish various portions of this commentary in other journals and we have finally been successful this year, as described in our January 24, 2006 RR to bmj.com (25). Portions of Manuscript BMJ/2003/084269 are presented later in this paper.

BMJ **Editors Support the** ***BMJ*** **Paper**

In spite of the numerous attacks on me and my research, the *BMJ* has stood behind my May 17, 2003 *BMJ* paper since its publication. For all of the vehemence of the RRs, only about 3%

referred to actual data in the paper and none identified anything approaching scientific fraud (15). Indeed, our paper wound up ranked among the "Top tens on bmj.com" in 2003 (30). *BMJ* Editor Richard Smith strongly defended his decision to publish the paper on both May 18, 2003 (31) and August 30, 2003 (32). To date, no impropriety, bias, or omission has been identified in the review process and no error in the results has been identified in the paper, not even by Thun, who is in a position to check our findings and to publish additional findings.

Press Coverage and Commentary on the *BMJ* Paper

Most of the press coverage of the study was muted or equivocal because of the issues raised by the ACS criticism of the paper, particularly my tobacco industry funding. Typical of this type of newspaper coverage was the May 16, 2003 Wall Street Journal article, printed on page B1 under the title "Passive Smoke Doesn't Kill—Or Does It?" and on the Internet under the title "Does Passive Smoke Kill? Study Sparks Controversy," included the statement "The American Cancer Society's top epidemiologist, Michael Thun, called the paper "critically flawed" and "a bad study in a good journal" (33). The May 16, 2003 Los Angeles Times article on page A26, "Study Downplays the Health Risks From Secondhand Smoke," concludes with the following quote from Dr. Jonathan Samet, Professor and Chair of Epidemiology at the Johns Hopkins University Bloomberg School of Public Health: "We have one very flawed study that does not find an association. It flies in the face of so much evidence and so much scientific understanding that it just doesn't contribute." (34).

Obviously, press coverage such as this is very discouraging. Fortunately, positive support was received from a few independent observers, who provided important insight into the strong reactions against our study and probable explanations for them. The most detailed and perceptive press account was the May 18, 2003 *Sunday Telegraph* newspaper article, "Warning: the health police can seriously addle your brain," by Robert Matthews (35). Among many things, he stated "After studying the health of tens of thousands of people married to smokers, US researchers found that they face no significant extra risk of lung cancer or heart disease. It may sting your eyes, take your breath away and make your clothes smell, but other people's cigarette smoke will not kill you. The demise of a supposed major risk to public health might be expected to prompt celebration among medical experts and campaigners. Instead, they scrambled to condemn the study, its authors, its conclusions, and the journal that published them. The reaction came as no surprise to those who have tried to uncover the facts about passive smoking. More than any other health debate, the question of whether smokers kill others as well as themselves is engulfed in a smog of political correctness and dubious science."

In addition, three particularly supportive commentaries have been written. Michael Fumento, a Senior Fellow at the Hudson Institute, wrote a September 11, 2003 syndicated column , "Second-hand Smoke is Harmful to Science," that concluded "So give the *BMJ* and Enstrom and Kabat an "F" for political correctness. But give them an "A" for honesty and courage." (36). Elizabeth Whelan, D.Sc., President of the American Council on Science and Health (ACSH), in an August 13, 2004 ACSH column entitled "American Cancer Society a Danger to Science?", wrote "I am writing to support the honesty and integrity of Dr. Enstrom, who has served as a Scientific Advisor to the American Council on Science and Health since 1984. His peer-reviewed research

was published in one of the world's best medical journals. Simply because it was partially funded by the tobacco industry does not make the research less credible or less reliable." (37). Michael Fitzpatrick, M.D., a general practice physician in London, wrote a November 15, 2004 Spiked commentary entitled "We have ways of making you stop smoking," which stated "The intense moral fervour and political commitment now driving the campaign against passive smoking has created a climate inimical to serious scientific inquiry. . . . The authors, James Enstrom and Geoffrey Kabat, were subjected to a barrage of personal attacks and unfounded insinuations of dishonesty. In response, they pointed out the selective reporting of the anti-smoking campaigners and their attempts to suppress divergent data." (38). These commentaries put our *BMJ* findings in context and describe the excesses of the anti-smoking critics, such as the ACS and other similar groups.

Comparison with Other Epidemiologic Research

To further document the validity of our *BMJ* findings, we have compared them with the other US epidemiologic evidence on ETS and coronary heart disease (CHD), in a new peer-reviewed meta-analysis of environmental tobacco smoke and coronary heart disease mortality in the United States (39), which is cited in our January 24, 2006 RR to bmj.com (25). This comprehensive meta-analysis focuses on the U.S. cohort studies of ETS and CHD death in never smokers. These cohort studies are all fairly similar in design; ETS exposure was approximated by spousal smoking; CHD death was the endpoint; and they constitute the majority of the world-wide evidence. In contrast to the previous major meta-analyses on this topic, such as the one in 1999 by Thun (40), our analysis includes the results of our 2003 study and the 1995 study by LeVois and Layard based on CPS I data (41). We have applied consistent criteria to the selection of results included in the analysis. The results are summarized in terms of overall relative risks and dose-response relationships. In addition, available data on misclassification of ETS exposure, personal monitoring of actual ETS exposure, and dose-response data for active smoking are discussed in order to characterize the estimates of ETS exposure in epidemiologic studies.

Contrary to the claims of the ACS and other critics, our results do not differ in any material way from those of the other studies, particularly for females. Because females have been exposed to higher levels of ETS from their spouse and have been exposed to less ETS outside of the home, they are more likely than males to show an effect of ETS exposure due to spousal smoking. Furthermore, we specifically refuted the unsubstantiated claim by Thun that our *BMJ* study is "fatally flawed because of misclassification of exposure" (42). Thun implied that virtually everyone in the U.S. during the 1950s and 1960s was equally exposed to ETS because it was so pervasive. Results from four independent surveys, as well as our 1999 CA CPS I survey, show that Americans were not equally exposed to ETS. Additional surveys show that exposure to ETS comes primarily from spousal smoking, not public smoking. Indeed, there was a clear relationship between spousal smoking and self-reported ETS exposure among never smokers who lived a major portion of their life before the introduction of restrictions on public smoking in the 1970s. One of these surveys is contained in the 1995 Cardenas dissertation, "Environmental tobacco smoke and lung cancer mortality in the American Cancer Society's

Cancer Prevention Study II" (43). Although Thun served on the Cardenas dissertation committee, to my knowledge, he has never cited results from this dissertation.

We found that when all relevant studies are included in the meta-analysis and the results of the individual studies are appropriately combined, current or ever exposure to ETS, as approximated by spousal smoking, is associated with roughly a 5% increased risk of death from CHD in never smokers, not the widely cited 25% in the meta-analyses of Thun and others. Furthermore, we found no dose-response relationship and no elevated risk associated with the highest level of ETS exposure in males or females.

ACS Misrepresentations Regarding ETS

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 their major 1982 Cancer Prevention Study (CPS II) cohort. The statement in the May 15, 2003 ACS press release Harmon J. Eyre, MD, ACS's national chief medical officer, says: "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" (12). However, the 1995 Cardenas dissertation found that the CPS II study is inconclusive: "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." (43).

Another more serious misrepresentation of CPS II results is evident when one examines the 1997 Cardenas peer-reviewed paper (44), which was based on the 1995 Cardenas dissertation (43). Table 4 of the Cardenas paper 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 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. Key sections of Tables 4 and 38 are shown side by side in Table A below and they reveal a serious discrepancy in the presentation of the same data. Because Table 38 appears to present the underlying findings and because these findings contradict Eyre's statement above, the ACS should clarify this major discrepancy. However, no clarification has been made and only the positive dose-response relationship in Table 4 is ever cited.

For instance, the Table 4 findings are now cited in the 2004 WHO IARC Monograph 83 "Tobacco Smoke and Involuntary Smoking" (45). This major 1452-page report contains a review of the epidemiologic evidence on ETS and lung cancer on pages 1231-1271 (46) . The section "Exposure-response relationships" on page 1236 contains the statement "The study by

Cardenas *et al*. (1997) also found a significant exposure-response relationship. When the husbands smoked 1-19, 20-39, ≥40 cigarettes/day, the relative risks for women exposed to secondhand smoke were 1.1, 1.2, and 1.9 respectively (p value for trend test, 0.03)". In addition, a January 2004 JNCI summary of IARC Monograph 83 shows results for ≥40 cigarettes/day in Table 3 and it contains the erroneous value RR=1.9 (47). Obviously Thun, a member of the IARC Working Group for Monograph 83, did not notify the IARC Working Group about the 1995 Cardenas dissertation. This type of selective analysis and presentation of results has been termed "publication bias *in situ*" and it is often difficult to detect (48). I was able to detect this irregularity only because I knew of the Cardenas dissertation. In other scientific fields, such as, those where actual scientific fraud has recently occurred (3-7), the type of data manipulation done in Table 4 would most likely be considered as a serious ethical violation.

ACS Violation of *BMJ* Press Embargo

Since our honesty or scientific integrity had not been questioned before May 2003, it seemed quite implausible and indeed incredible that we would be subjected to an immediate large scale *ad hominem* attack because of this one paper in the *BMJ*. In order to better understand this attack, I have gradually pieced together the sequence of events that I believe initiated it. I am presenting this history in order to expose the unethical tactics that were used to libel legitimate epidemiologic research and to disrupt the normal press coverage of this research.

On May 9, 2003 I was notified by Emma Dickinson, BMA Press Officer, that an embargoed *BMJ* press release was to be issued on May 13, 2003 about our paper to be published in the May 17, 2003 *BMJ*. The strict publication/broadcast embargo regarding our paper was to last until 00:01 hours (UK time) on May 16, 2003, or 19:01 (7:01 PM) EDT on May 15, 2003 in Florida and 16:01 (4:01 PM) PDT on May 15, 2003 in California. This notification was given in explicit terms in the following email message to me:

> Subject: Your paper which is appearing in the 17 May 2003 issue of the BMJ
> To: jenstrom@ucla.edu, zetkin@bristol.ac.uk
> From: EDickinson@bma.org.uk
> Date: Fri, 9 May 2003 16:40:45 +0100
>
> We are hoping to press release your contribution which is to appear in next week's BMJ [17 May 2003] and would like you to approve the draft copy below. Please could you reply before 2pm on Tuesday 13 May 2003. I apologise for the short notice. Yours will be one of a selection of papers/editorials/letters that we are planning to include on the press release. The press release will also be posted onto the internet on the BMJ page of EurekAlert, the website of the American Association for the Advancement of Science and Alphagalileo, the media resource centre for European science, engineering and technology. I would be grateful if you could advise your co-authors (if appropriate) that your paper is to feature in our round-up release.
>
> We issue an embargoed press release every Tuesday. The publication/broadcast embargo of this week's press release will be 00.01 hrs (UK time) on Friday 16 May, so if you are contacted by journalists from anywhere in the world they can interview you beforehand but should not broadcast or publish anything before then. If you do get contacted please remind journalists that you are giving an interview on the understanding that they will not break our strict embargo. This is to ensure that

doctors have access to the BMJ at the same time as publicity breaks, in order that they are in a better position to advise patients.

If your own organisation decides to promote your work, please make our embargo clear on any press releases and I'd be grateful if you could let me know.

Please could you check the contact details that we have listed for you. Are these details the best means of contacting you next week? If you will not be available (particularly on Thursday, which is when journalists are most likely to contact you) please could you nominate an alternative point of contact. A mobile or home telephone number, not necessarily for publication, might also be useful. You can reach me on tel: +44 (0)20 7383 xxxx; fax: +44 (0)20 7383 xxxx or email: edickinson@bmj.com

Many thanks
Emma Dickinson
Press Officer

On May 9, 2003 I notified the UCLA Health Sciences Communications office about the above message and a UCLA press release was prepared about this study during the next few days. Since the study used the CA CPS I cohort, UCLA notified the American Cancer Society (ACS) about the forthcoming May 13, 2003 embargoed *BMJ* press release and the May 17, 2003 *BMJ* study. The ACS may have learned of the study from other sources as well. The ACS then prepared its own press release about the *BMJ* study and was bound by the same *BMJ* embargo conditions as everyone else writing about this paper. However, based on what is shown below, the May 14, 2003 version of the ACS press release was given to Stanton A. Glantz, Ph.D., Professor of Medicine at the University of California, San Francisco and inserted into a May 15, 2003 email message that Glantz send to his UCSF listserv before the press embargo ended. His message is reprinted below and can be read in its original format at the following web link: http://www.ucsf.edu/its/listserv/stanglantz-l/0090.html .

MEDIA ALERT -- Study Inaccurately Uses ACS Data to Suggest No Link Between Secondhand Smoke & Lung Cancer
From: Stanton A. Glantz (*glantz@MEDICINE.UCSF.EDU*)
Date: Thu May 15 2003 - 09:22:09 PDT

From the American Cancer Society regarding misuse of their CPS I data in the BMJ tobacco industry paper

Media Alert

DATE: 5/14/03

TO: NHO Staff, Division CEOs, COOs, ACS Communications and Cancer Control Directors, NCIC Cancer Information Specialists, and NGRD DC and Field

FROM: David Sampson -- Director, Media Relations

SUBJECT: Media Alert -- Study Using ACS Data Finds No Link Between Secondhand Smoke & Lung Cancer

CONTACTS: David Sampson, 213-368-8523; Shawn Steward, 404-417-5850, or via Lotus Notes

Study Inaccurately Uses ACS Data to Suggest No Link Between Secondhand Smoke & Lung Cancer

A study being published in the British Medical Journal on Friday, May 16, 2003 concludes the link between secondhand smoke and lung cancer (as well as heart disease) may be considerably weaker than previously believed. The study was performed by Dr. James Enstrom at UCLA, and was funded originally by California Proposition 99 cigarette tax. When continued support from that agency was denied, the researcher sought and received significant funding from the tobacco industry's Center for Indoor Air Research. While the link to tobacco company money can be found with a careful search of the journal article, and is mentioned on UCLA's release, it is not mentioned in the BMJ's press release, so journalists may not know about it.

The study used data from the Society's Cancer Prevention Study I (CPS-I) obtained by special permission from the Society. The Society is mentioned in the study as well as in accompanying press materials from the journal and from UCLA.

Because we anticipate a good deal of media coverage on this study, with calls already received from the Wall Street Journal, Los Angeles Times and the BBC, we wanted to prepare you by giving some guidance and perspective from Michael Thun, MD, the Society's vice president of epidemiology and surveillance research:

"We welcome new studies that add valid information to the scientific understanding of cancer risk. However, the study by Enstrom and Kabat is not reliable or informative for several reasons:

The analysis is based on small subset (10%) of the Society's Cancer Prevention Study 1 (CPS-I)

The critical flaw of this study is its crude assessment of exposure and inability to distinguish people who were exposed to secondhand smoke from those who were not at various points in the follow-up. This is especially problematic in this study, because:

a) Participants were enrolled in 1959, when exposure to secondhand smoke was so pervasive that virtually everyone was exposed to ETS, whether or not they were married to a smoker.

b) No information was collected on other sources of ETS exposure besides spousal smoking.

c) No information on smoking by the spouse after 1972 was included in the analysis, even though the observation period continued another 26 years, through 1998, so any smokers who quit between 1972 and 1998 would still have been counted as smokers.

d) Study participants were on average 52 years old at enrollment. Many spouses who reported smoking in 1959 would have died, quit smoking, or ended the marriage during the 38-year follow-up, yet their surviving partners are still classified as "exposed" to ETS in this analysis.

"ACS scientists repeatedly advised Dr. Enstrom that CPS-I data were unsuitable for studying secondhand smoke because the problems outlined above would cause misclassification of exposure and make the results uninterpretable. Furthermore, much of the follow-up of CPS-I through 1998 pertains to older age groups where the effects of many environmental risk factors become less apparent.

"Meanwhile, far more reliable data exists which clearly show an effect of secondhand smoke.

"The Society's Cancer Prevention Study II (CPS-II):

Enrolled patients in the 1980s, when there was much less exposures to tobacco smoke outside the home, and therefore far less 'background noise'
Is about 10 times as large as Dr. Enstrom's study
Has much better follow up, with over 99 percent of those originally entered into the study having been successfully contacted and followed up
Clearly shows an increased risk of lung cancer and heart disease

"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. A similar number find the same relationship to heart disease. These studies have been reviewed by multiple scientific consensus committees, including the U.S. Surgeon General, who certify their credibility. Most recently, the International Agency for Research on Cancer (under the World Health Organization), reviewed the evidence and concluded 'secondhand or environmental tobacco smoke is carcinogenic to humans.'

"We should not be surprised that the best studies continue to show secondhand smoke raises the risk of lung cancer, considering:

Secondhand smoke contains the same carcinogens and other chemicals found in active smoke
There is extensive evidence that people exposed to ETS excrete the same by-products of smoking as smokers themselves

Below find links to the journal report and accompanying editorial:

Article: http://press.psprings.co.uk/bmj/may/ppr1057.pdf

Editorial: http://press.psprings.co.uk/bmj/may/edit1048.pdf

For further background on this issue, please refer to the Society's Cancer Information Database entry on secondhand smoke: (Document link: Database 'Cancer Information Database', View '1. Published\By Category', Document 'SECONDHAND SMOKE')

For more information, contact the media relations team at the National Home Office

This archive was generated by hypermail 2b29 : Thu May 15 2003 - 09:42:37 PDT

Judging from the line "**Date:** Thu May 15 2003 - 09:22:09 PDT", this "MEDIA ALERT" email message was sent to those on the Glantz listserv about 6:38 hours before the *BMJ* press embargo ended at 16:01 PDT on May 15, 2003. From what I can determine, Glantz's listserv goes to hundreds or thousands of anti-smoking activists, as well as to many individuals at academic institutions and to many in the media.

I consider the fact that the ACS press release was distributed prematurely by Glantz to be a highly unethical violation of the *BMJ* press embargo policy by both the ACS and Glantz. Furthermore, there are numerous false and misleading statements in the early May 14, 2003 version, similar to those in the (11) official May 15, 2003 version of the press release (http://www.sdtobaccofree.org/MediaCenter/Press/bmjstudy_acs.pdf). Several of these

statements have been discussed earlier. While the May 14 version above contains no mention of a press embargo, the official May 15 version begins with the line "EDITORS: EMBARGOED UNTIL 7:00 PM EDT MAY 15, 2003".

In my further examination of the Glantz listserv, I have found the following May 14, 2003 email message: http://www.ucsf.edu/its/listserv/stanglantz-l/0088.html . It announces a May 15, 2003 Miami, Florida press conference involving a panel of "international experts," chaired by Julius Richmond, M.D, and including Glantz, Lisa A. Bero, Ph.D., K. Michael Cummings, Ph.D., and James L. Repace:

> Press conference in Miami by former Surgeon General on tobacco industry funded study in BMJ
> **From:** Stanton A. Glantz (*glantz@MEDICINE.UCSF.EDU*)
> **Date:** Wed May 14 2003 - 22:22:31 PDT
>
> There will be a press conference (described below) at 11 am EDT featuring a series of experts taling about the tobacco industry funded studing in BMJ, led by former Surgeon General Julius Richmond. The statements by the experts attending the press conference outline the serious problems with this study. Please pass this information on to anyone you wish, including media. These statements also provide important information about what is wrong with the paper.
>
> International Experts Slam Tobacco Industry Second Hand Tobacco Smoke Study
> "Marry a Smoker, Get Less Cancer," says Industry sponsored study.
> Former U.S. Surgeon General Julius Richmond, M.D., to Chair Panel of Experts
>
> PRESS ADVISORY For information contact:
> 11:00 AM Hotel Intercontinental
> Thursday May 15, 2003 Beth Kress
> Theater Mezzanine Level
> 305-321-5356
>
> Several of the world's top scientists in Miami attending the Second Annual Symposium of the Flight Attendant Medical Research Institute (FAMRI) will be holding a press conference to debunk an about to be published tobacco industry study that claims that second hand tobacco smoke does not cause heart disease and lung cancer.
>
> Scheduled to be published in Friday's British Medical Journal, the study was paid for by the tobaccos industry's Center for Indoor Air Research. The 46 State Attorneys General closed the Center under allegations of fraud as part of the 1998 Master Settlement Agreement with the tobacco industry. Julius Richmond, M.D., U.S. Surgeon General from 1977-1981 and Chair of FAMRI's Medical Advisory Board, will Chair the press Conference. "This study is just the latest in a long string of studies designed to deny the evidence and confuse the public," said Richmond. "The first study linking second hand tobacco smoke and lung caner was published 22 years ago when I was Surgeon General and the evidence has only become stronger since then."
>
> Another speaker Michael Cummings, Ph.D., Chair of the Department of Cancer Prevention, Epidemiology and Biostatistics at Roswell Park and an expert in the 1959 data set analyzed in the study said, "this data set is simply not appropriate in answering the question of whether

second hand tobacco smoke caused any disease whatsoever. The key to any Epidemiology study is comparing people who are exposed to second hand tobacco smoke to people who are not exposed. Using marriage to a smoker in 1959 as a measure to exposure to second hand tobacco smoke over a 40 year period makes no sense."

James Repace, an expert on measuring exposure to second hand tobacco smoke added, "it was simply impossible to find people not exposed to second hand tobacco smoke in 1959. The lack of an unexposed control group assured a negative conclusion in this study regardless of the true effect of second hand tobacco smoke on cancer and heart disease.'

Lisa Bero, Ph.D., Professor of Clinical Pharmacology and Health Policy at the University of California, San Francisco, and an expert on the influence of financial ties on research outcomes observed, "this may be another example of where the financial disclosure at the end of the paper does not fully describe the extent of involvement of the tobacco industry in the study." Bero's earlier research on the Center for Indoor Air Research showed that most of the studies they funded on second hand tobacco smoke were not selected by scientists but rather selected and controlled by its executives and lawyers. In contrast to research funded by non-tobacco sources the research the Center funded almost always concluded that second hand tobacco smoke was not harmful."

Stanton Glantz, Ph.D., and Professor of Medicine at the University of California, San Francisco reiterated that every independent organized scientific body in the world that has considered the effects of second hand tobacco smoke has concluded that it causes cancer, heart disease, sudden infant death and variety of other diseases in non smokers. "The fact that it is possible to see negative effects on the heart, blood and blood vessels with just thirty minutes of exposure to second hand tobacco smoke proves that these effects are both real and immediate."

Patricia Young, a flight attendant and Trustees of FAMRI will relate the real life effects of second hand tobacco smoke in human terms on herself and friends and colleagues.

This archive was generated by hypermail 2b29 : Wed May 14 2003 - 22:17:29 PDT

Both the email message itself and the Miami press conference at 11 AM EDT on May 15, 2003 were in clear violation of the *BMJ* press embargo, which lasted until 8 hours after the start of the press conference. Furthermore, the listserv message mocks our peer-reviewed UCLA study by categorizing it as a "tobacco industry study" which says "Marry a Smoker, Get Less Cancer."

In addition, keep in mind that neither the ACS, Glantz, or the other Miami "experts" had access to the full ten-page version of our paper at the time of the ACS press release or the Miami press conference. The full version of our paper was not posted on bmj.com until the press embargo lifted at 7:01 PM EDT on May 15, 2003. The abridged five-page paper printed in the *BMJ* was the only version available when the embargoed *BMJ* press release was issued on May 13, 2003. Obviously, these "experts" chose to hastily write a press release and hold a press conference based on limited information. They did not have the integrity or objectivity to even read the full ten-page paper before condemning it.

An additional Glantz listserv message entitled "Fwd: Re: BMJ Study & Editorial Undermining the Case Against SHS Risk" is also important: http://www.ucsf.edu/its/listserv/stanglantz-l/0091.html. Within it is contained an email message from *"Stan Shatenstein"* which was sent to another listserv, *"General Messages"* <*tob-mail@globalink.org*>, on "Thu, 15 May 2003 10:38:44 -0400". The Shatenstein message, which was sent before the press embargo deadline, begins with the sentence "It's helpful to see that the BMA and ACS have already posted their reactions to the BMJ paper by Enstrom and Kabat." This indicates that early on May 15, 2003 there was already widespread knowledge of both the BMA and ACS positions regarding our paper. GLOBALink (http://www.globalink.org/) is a world-wide anti-smoking organization and a number of their members contributed defamatory RRs to bmj.com regarding my *BMJ* paper.

Furthermore, this message states "Stan Glantz noted, in a posting to the US list, that there will be a press conference at 11AM Eastern (16h00GMT), at which he and Lisa Bero will join former US Surgeon General Julius Richmond, as well as Jim Repace and Michael Cummings, to counter some of what the industry will have to say in anticipation and in the wake of this study's publication." and "the paper, under embargo until 7PM Eastern time in North America, or 24h00GMT (midnight in the UK), has already generated great media interest . . . ." These statements indicate that early on May 15, 2003 there was widespread knowledge of the Miami press conference and widespread knowledge that it was to be held before the press embargo ended. Another announcement of this press conference appears on the Action on Smoking and Health web site (http://www.no-smoking.org/may03/05-15-03-4.html). These postings are the ones I have been able to uncover thus far and their may be other actions that were taken by ACS and others that are not publicly available on the Internet.

The early ACS "media alert," the listserv messages from Glantz and Shatenstein, and the Miami press conference poisoned the media coverage of our study well before the *BMJ* press embargo was lifted. These unethical actions undoubtedly help stimulate the avalanche of RRs that further tainted our paper and helped create an atmosphere in which it was virtually impossible for the paper to be judged on its content and its merits. Furthermore, these actions gave currency to the claims that our study results were influenced by the tobacco industry and were at variance with the results of other comparable studies. Both of these claims are utterly false, but they have not stopped the innuendo about us and our research.

ACS Change in Funding Policy

Instead of engaging in a professional dialogue with me regarding my findings on ETS, the ACS has chosen to make it virtually impossible to conduct that type of epidemiologic research that I previously conducted with their cooperation and funding. The ACS decided in February 2004 that scientists who receive financial support from the tobacco industry will be barred from receiving grants from the ACS as of July 1, 2005 and they used our *BMJ* paper as partial justification for their policy change (49). Those who follow issues of research and grant making said the decision of a major supporter of scientific research to adopt a litmus test in deciding who gets grants could have ramifications that extend far beyond the debate over the ethics of accepting research sponsorship from the tobacco industry. I have gone from being an investigator who was once entirely supported by ACS grants to an investigator who cannot even apply for an ACS grant. Although I have done nothing wrong in the conduct and publication of

my *BMJ* study, I have been unable to directly present to ACS officials my response to their inaccurate claims and misrepresentations. The ACS has never contacted me directly to discuss my BMJ study, and the attempt by Elizabeth Whelan to establish contact with the ACS Chairman of the Board in 2004 has gone unanswered (37).

ACS Campaign to Discredit *BMJ* Study

Although I have refuted numerous statements in their May 15, 2003 press release, the ACS has shown no interest in correcting the record with regard to me and my research. Their defamatory press release is now posted at about 1,000 locations on the Internet, based on a current Google search of the title "American Cancer Society Condemns Tobacco Industry Study". Our *BMJ* and *Lancet* letters and our new meta-analysis defending the validity of our *BMJ* paper are being ignored by the ACS. Instead, the ACS and other activist organizations continue to post defamatory information about us and our research.

Our new meta-analysis shows that the relationship between ETS and CHD in US never smokers is very weak (estimated relative risk of 1.05), yet the ACS still continues to state in their 2006 "Cancer Facts and Figures" that "ETS causes an estimated 35,000 deaths from heart disease in persons who are not current smokers" (http://www.cancer.org/downloads/STT/CAFF2006PWSecured.pdf, page 38) (50). The source the ACS uses for this CHD death estimate is a 1992 *JAMA* paper (51), even though over 90% of the US epidemiologic evidence has been published since 1995. Our new meta-analysis shows that most of the US evidence originates from the ACS CPS I and CPS II cohorts, yet the ACS simply ignores or condemns most of this evidence. The CPS I and CPS II evidence is summarized in Table B, as taken from Table 6 of our meta-analysis paper. This evidence shows a very weak overall relationship between ETS and CHD deaths and absolutely no dose-response relationship. Evolution of the ACS's annual "Cancer Facts and Figures" indicates the change in priorities of the organization away from research toward advocacy, which the 2006 version listing advocacy as the top priority (50).

Glantz Campaign to Discredit Enstrom

Ever since the publication of our *BMJ* paper, Glantz has conducted an ongoing campaign attacking me and my research, in spite of the fact that we are both established, long-term faculty members at the University of California. Glantz is well-known as a long-time anti-smoking activist (52,53), whose ultimate goal is "Achieving a smokefree society" (54). However, as a UC faculty member, he is supposed to adhere to the UCSF Campus Code of Conduct (55) and the UC Standards of Ethical Conduct (56). For instance, the Code of Conduct states "Misconduct or Misconduct in Science means fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research." The UC Standards of Ethical Conduct states "Members of the University community are expected to conduct themselves ethically, honestly, and with integrity in all dealings."

However, based on his clearly documented written and verbal attack on me, I do not believe he has adhered to these codes. Thus, I find it necessary to respond to his false and misleading statements and to defend my honesty and scientific integrity. The full details of his campaign are too extensive to present here, but the selected examples below demonstrate the unprofessional tactics that he has used to defame me and to impede the type of legitimate epidemiologic research that I have been conducting at UCLA.

On July 25, 2003 Glantz co-wrote an eight-page letter to the UC Vice Provost for Research in which attempts to make the case that acceptance of tobacco industry funding for research violates current Regents and University policy and should be ended (http://www.ucsf.edu/senate/townhallmeeting/TobIndFundingColeman7-25-03.pdf). On pages 3 and 4 of this letter he claims: "The most recent example of how the tobacco industry uses funding of university research as part of its for propaganda campaign is a May 17, 2003 study from UCLA on the health effects of secondhand smoke published in the *British Medical Journal*. . . . this paper would go down as one bit of poor research done at a university with a reputation for high quality scholarship that slipped into a good journal because of the foibles of the peer review process."

However, Glantz's arguments for banning tobacco industry funding of research at UC, such as, the funding I have received, have been rejected in favor of academic freedom. The matter of tobacco industry funding at UC is discussed in a February 2005 *Nature Medicine* article, where UC Vice Provost for Research Lawrence Coleman stated "Academic freedom must be absolute or no one has it." (57). On May 11, 2005 the UC Academic Senate adopted a strong Academic Senate Resolution on Research Funding Sources which clearly supports the right of individual UC faculty members to accept research support from any source that adheres to University policy, including the tobacco industry (58).

On March 8, 2005 Glantz participated with other UC faculty members in a San Francisco based KQED radio program entitled "**Funders and Academic Research: *Forum*** assesses the controversy surrounding the relationship between funders and academic research," which can be listened to on the Internet (http://www.kqed.org/epArchive/R503080900). This program clearly demonstrates the tactics used by Glantz to defame highly qualified scientists and their peer-reviewed research publications by linking them in some way to the tobacco industry. The "scandal" about me and my *BMJ* study was discussed during minutes 17-19 of this 52 minute program. Glantz made several clearly false and inflammatory statements about me that I need to refute.

First, Glantz claimed that the *BMJ* study "was not funded by the American Cancer Society," but was "done with Philip Morris's money." Actually, the ACS provided all the funding for the CA CPS I study from 1959 to 1991, while I provided all the funding from 1991 to 2003. After adjusting for inflation, about 90% of the total funding came from the ACS, about 5% came from the UC Tobacco-Related Disease Research Program, and about 5% came from a tobacco industry source (Center for Indoor Air Research). These funding sources were clearly disclosed in my *BMJ* paper funding statement. Philip Morris funding was not used for the *BMJ* study.

Then, Glantz said I am "a damn fool" who was told by ACS that I "made inappropriate use of the data." Actually, I have made entirely appropriate use of the ACS data I was given in 1991 after convincing the two ACS Vice Presidents for Epidemiology who preceded Thun of the value of

long-term follow-up of CPS I subjects. Indeed, I am the only outside investigator who has ever been allowed to do follow-up on ACS subjects, and I have now successfully followed most of these subjects for more than 40 years. The ACS and Thun did not complain about my use of their data until I published results that they did not like.

Then, Glantz implied that I am "advocating a pro-tobacco position." Actually, I am a lifelong nonsmoker and I have never advocated a pro-tobacco position in my entire life. Indeed, I have spent much of my epidemiologic career documenting the health benefits of being a nonsmoker, from my first publication on Mormons in 1975 (59) to my major 25-year follow-up study on active California Mormons in 2006 (60). Furthermore, in 1999 I published two papers indicating active smoking may be more dangerous than generally believed because its impact on mortality was less reversible by smoking cessation than generally believed (29,61). My findings regarding lung cancer and smoking cessation were largely confirmed in a 2003 study of Iowa women (62).

Finally, Glantz states "the science that the UCLA study did was crap." Actually, this study is the largest and most detailed epidemiologic study on ETS and mortality ever published in a major medical journal. No errors have been identified in the results in three years and the *BMJ* has stood firmly behind the study in spite of substantial criticism by persons such as Glantz. An objective assessment should convince the reader that this is a very sound and important study.

One additional example of Glantz's unprofessional treatment of my research is contained in his May 24, 2005 *Circulation* report, where he attempts to make the case that passive smoking has nearly as same impact as active smoking on cardiovascular effects (63). In his meta-analysis of the relation between ETS and CHD, he found "The pooled relative risk computed with a random-effects model (computed with Stata Version 7) was 1.31 (95% CI, 1.21 to 1.41), similar to the estimates of earlier meta-analyses." To achieve this result, he omitted the two largest studies, which represent a major portion of the available evidence. Our *BMJ* study, which began in 1960 (1), was omitted based on his unsubstantiated claim that it had "serious misclassification bias" and the 1995 study by LeVois and Layard, which also began in 1960 (41), was omitted without comment and was not even cited. However, Glantz included the other cohort studies which began in the 1960s and 1970s without any comment about their misclassification bias. Kabat and I addressed all these studies and the issue of misclassification bias in our 2006 meta-analysis (39). A good way to access the quality and objectivity of Glantz's scholarship on the relation of ETS and CHD is to compare his 2-page 2005 meta-analysis (63) with our 12-page 2006 meta-analysis (39).

Jonathan M. Samet, M.D., and 2006 Surgeon General's Report

Next, I want to address the false and misleading statements made about my research by Jonathan M. Samet, M.D, M.S., who has played a prominent role in reviews of the epidemiologic evidence on ETS for the past 15 years. Because my study makes a major contribution to the body of epidemiologic evidence and because there is not evidence after three years that it is incorrect, Samet made a false statement to the May 16, 2003 Los Angeles Times, when he said that it was "one very flawed study" that "just doesn't contribute" (34). In addition, in his role as Chairman of the Working Group for IARC Monograph 83 (45) he is listed as one of 14 authors of the May

30, 2003 *BMJ* rapid response (19) and the August 30, 2003 *BMJ* letter (64), which criticized my study. The concluding sentence of these two submissions is: "Enstrom and Kabat's conclusions are not supported by the weak evidence that they offer, and although the accompanying editorial alluded to 'debate' and 'controversy', we judge the issue to be resolved scientifically, even though the 'debate' is cynically continued by the tobacco industry." This is an entirely inaccurate characterization. Our conclusions are fully supported by the extensive evidence presented in our paper, in the "Prepublication History," and in our subsequent letters. I believe that we have supported our conclusions to greater extent than any other published paper dealing with ETS and mortality. Furthermore, we have now shown in our 2006 meta-analysis that our evidence and conclusions are consistent with the entire body of US evidence (39).

Samet was first introduced to my epidemiologic research when he participated in the August 23-25, 1978 NCI Workshop Held in Snowbird, UT August 23-25, 1978 (65). The proceedings of the workshop were published in JNCI in November 1980 and Samet is listed as a participant on page 1195 (last page). I presented three talks at this Workshop and two of them described the reduced cancer death rates among nonsmokers, one dealing with Mormons (66) and another dealing with a representative sample of US nonsmokers (67). If Samet had any interest in fairly portraying my epidemiologic research, which he has been aware of since 1978, then he would not have made false statements about my May 17, 2003 *BMJ* paper when it first appeared.

The most recent and most direct indication of lack of objectivity on the part of Samet became obvious with the June 27, 2006 release and publication of the 727-page Surgeon General's Report on "*The Health Consequences of Involuntary Exposure to Tobacco Smoke"* (68). Samet is the Senior Scientific Editor of this report and the most influential epidemiologist involved with the report. In addition, Glantz is a Contributing Editor and Thun is a Reviewer. Although Samet, Thun, and Glantz are fully aware of the importance of the *BMJ* paper, as evidenced by their extensive efforts to discredit it, the paper is simply omitted from the Surgeon General's Report without comment. A search for "enstrom j" of the entire PDF version of the report (http://surgeongeneral.gov/library/secondhandsmoke/report/fullreport.pdf) (68), reveals that the only mention of the *BMJ* paper is in the Appendix on page 673, where it is listed as one of the papers not included in the report. In addition, a search of the database for the Report prepared (http://apps.nccd.cdc.gov/sgri/) reveals that the *BMJ* paper has been omitted without explanation. This database was prepared by Johns Hopkins University and the Centers for Disease Control and Prevention's Office on Smoking and Health. It includes "approximately 900 key articles regarding involuntary smoking and disease outcomes" and supposedly "reflects the most recent findings in the scientific literature."

In order to illustrate the selective and unscientific nature of this omission, I examined the references used in Chapters 1-10 of the Surgeon General's Report and the references in the Appendix that were not used. Of 38 total references from 2003, 33 were used in Chapters 1-10 and only 5 references, including the *BMJ* paper, were not used. Of 71 references from 2004, 53 were used and 18 were not used; of 39 references from 2005, 26 were used and 13 were not used; of 22 references from 2006, 7 were used and 15 were not used. In summary, the report used 119 references from 2003-2006, but omitted without comment the 2003 *BMJ* paper. Because of this omission, the Surgeon General's Report does not accurately reflect all the peer-reviewed

epidemiologic evidence on the relation of ETS to lung cancer and coronary heart disease mortality in the US.

Furthermore, consider the four misleading or inaccurate statements from report. Chapter 7 contains this misleading statement on page 423: "This chapter considers the full body of evidence on secondhand smoke exposure and lung cancer published through 2002, the ending date for the systematic review of the epidemiologic studies." This is a highly misleading and disingenuous statement because Samet knows that the 2003 *BMJ* results substantially weaken the US evidence (1,27). Our own meta-analysis of all US spousal smoking studies, including all the doctoral dissertations, yields an RR(ever/never) = 1.10 (1.00-1.21).

Chapter 7 contains this inaccurate statement on page 435: "There were no significant differences in the RR estimates by geographic area; the point estimate was 1.15 (95 percent CI, 1.04–1.26) for studies conducted in the United States and Canada, 1.16 (95 percent CI, 1.03–1.30) for studies conducted in Europe, and 1.43 (95 percent CI, 1.24–1.66) for studies conducted in Asia." Obviously, the RR=1.43 for studies in Asia is substantially greater than the RR=1.15 for studies in US and Canada and the RR=1.16 for studies in Europe. Indeed, there is substantial variation around the world and all these results cannot be accurately represented by a single RR~1.25. This variation should have been acknowledged in the Report.

Chapter 8 contains on page 521 selective criticism and dismissal of the analysis by LeVois and Layard of ETS and CHD deaths in the ACS CPS I and CPS II studies (41). This paper is important because of its size and statistical power, as discussed in our 2006 meta-analysis of ETS and CHD deaths in the US (39). One basis for the dismissal is the inaccurate statement "The investigators did not distinguish between current exposures from spousal secondhand smoke and former exposures, nor did they separately report the effect of current spousal smoking on the risk of CHD." Table 4 of the LeVois and Layard paper clearly shows results for three levels of current ETS exposure for both males and females. Furthermore, Table B below summarizes the dose-response relationship between ETS and CHD deaths based on the results from the three largest US studies (1,41,69). There is no difference in the results for these studies and no dose-response relationship in any of them.

Furthermore, note that the meta-analysis of ETS and CHD is summarized in Figure 8.1 on page 524. Since this figure only shows studies through 2001 it obviously omits the 2003 *BMJ* study. The *BMJ* study has a major impact on the meta-analysis, as pointed out in our 2003 *BMJ* letter (27) and our 2006 meta-analysis (39). Note that inclusion of *BMJ* results, yields a relationship between ETS and CHD deaths in the US of RR(current/never)=1.05 (0.99-1.11). This is much less than the summary RR(exposed/unexposed)=1.27 (1.19-1.36) contained in Figure 8.1. The Surgeon General's Report should have pointed out that the ETS and CHD relationship is much larger outside of the US than it is within the US. We estimated that the relationship outside the US is approximately RR~1.5 (39) and the 1999 Thun meta-analysis found RR=1.41 (1.21-1.65) (40). This large RR difference within and outside the US is a subject worthy of further investigation, in order to determine if it is real or due to differences in methodology.

Given the fact that the two largest epidemiologic studies on ETS and tobacco-related mortality (1,41) have been omitted from the Surgeon General's Report and the fact that these two studies substantially weaken the ETS and mortality relationship in the US, the Forward of the Surgeon General's Report makes the inaccurate statement that "In 2005, it is estimated that exposure to secondhand smoke kills more than 3,000 adult nonsmokers from lung cancer, approximately 46,000 from coronary heart disease, ..." Based on a complete and objective evaluation of all the peer-

reviewed US epidemiologic evidence, a more appropriate statement is that ETS exposure is associated with a small fraction of lung cancer and CHD deaths in US never smokers.

An August 23, 2006 "research news and perspective" in JAMA questioned various aspects of the Surgeon General's Report, particularly findings regarding the acute effects of small amounts of ETS exposure and the claim by the Surgeon General that "There is no safe level of exposure to secondhand smoke" (70). This JAMA report is particularly valuable because it quotes two experts who have extensive experience regarding the ETS issue. Michael Siegel, MD, MPH, a professor of social and behavioral sciences at Boston University School of Public Health and a prominent tobacco control researcher, told JAMA "We're really risking our credibility [as public health professionals or officials] by putting out rather absurd claims that you can be exposed briefly to secondhand smoke and you are going to come down with heart disease or cancer. People are going to look at that and say that's ridiculous." In addition to his JAMA comments, Siegel is has posted on his personal website numerous insightful analyses regarding the ETS issue and tobacco control, such as, "Surgeon General's Communications Misrepresent Findings of Report; Tobacco Control Practitioners Appear Unable to Accurately Portray the Science" (http://tobaccoanalysis.blogspot.com/).

John C. Bailar III, MD, PhD, an prominent epidemiologist and biostatistician, who is Professor Emertitus at the University of Chicago, told JAMA "It doesn't make sense for the cardiovascular risk of secondhand smoke to be as high as one third of the risk from direct smoking. . . . That's a far bigger ratio than risk for lung cancer and it's hard for me to believe that it's real." These comments are similar to those in his March 25, 1999 NEJM editorial on ETS and coronary heart disease, in which he stated "I regretfully conclude that we still do not know, with accuracy, how much or even whether exposure to environmental tobacco smoke increases the risk of coronary heart disease" (71).

Jonathan M. Samet, M.D., and Conflict of Interest

A careful examination of the Surgeon General's Report reveals that it contains no conflict of interest disclosures for any of its editors or reviewers. In particular, Senior Scientific Editor Samet did not disclose a serious financial conflict of interest which appears to have compromised his objectivity on ETS. In 2003 Samet received a three-year $600,000 "Dr. William Cahan Distinguished Professor" award from the Flight Attendants Medical Research Institute (FAMRI), which was "made in recognition of the recipients' ongoing work in combating the diseases caused by exposure to second hand tobacco smoke" (http://www.famri.org/awards_history/index.php). In addition, Samet has a prominent role in the multi-million dollar Johns Hopkins FAMRI Center of Excellence (http://www.hopkins-famri.org/about.php). This Center was established in 2005 and currently has 30 FAMRI-funded research projects on "diseases and medical conditions caused from exposure to tobacco smoke," including one by Samet on "Reducing the Risks of Secondhand Tobacco Smoke Globally" (http://www.hopkins-famri.org/investigators.php).

FAMRI is a foundation established as a result of an October 1991 Class Action suit filed in Miami's Dade County Circuit Court in Florida, known as *Broin v. Philip Morris*

(http://www.kinsella.com/broin/). This suit was filed against the tobacco industry on behalf of flight attendants who sought damages for diseases and deaths allegedly caused by their exposure to second hand tobacco smoke in airline cabins (http://www.famri.org/history/index.php). A settlement was reached in October 1997 between the plaintiffs and four tobacco companies. The Settlement Agreement included the establishment of a not-for-profit medical research foundation with funding by the tobacco industry of $300 million. The Foundation was to have no tobacco company involvement, other than funding. The purpose of the foundation was "to sponsor scientific research with respect to the early detection and cure of diseases associated with cigarette smoking" (http://www.kinsella.com/broin/settagree.shtml).

FAMRI, as it was actually established, has a distinctly different mission, which is "to sponsor scientific and medical research for the early detection, prevention, treatment and cure of diseases and medical conditions caused from exposure to tobacco smoke." Since FAMRI's mission statement assumes that diseases like lung cancer and CHD are caused by secondhand smoke, this funding source may have influenced Samet's decision to selectively omit our null study from the Report. In any case, the complete lack of conflict of interest disclosure in the Report is entirely unacceptable and reinforces the importance of the August 23, 2006 JAMA editorial which emphasized that in published articles it is important "that readers are aware of the authors' financial relationships and potential conflicts of interest so that these readers can interpret the article in light of that information" (72).

Jonathan M. Samet, M.D., and the 1992 EPA Report

One might wonder how omissions, distortions, and exaggerations like those pointed out above could occur in a document as important as a Surgeon General's Report on ETS. To better understand this phenomena one must realize that Samet has dealt with the ETS issue like this for many years. In particular, he played a major epidemiological role in the December 1992 report on ETS entitled *"Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders: The Report of the United States Environmental Protection Agency* (73). This EPA report classified ETS as a Group A human carcinogen, which causes about 3,000 lung cancer deaths per year in the US. The findings from this report were used in the *Broin v. Philip Morris* litigation.

However, the epidemiologic methodology and conclusions of the report have been severely criticized. One of the harshest critiques is the 92-page Decision issued by Federal Judge William L. Osteen on July 17, 1998, which overturned the report in the US District Court (74). For instance, in his conclusion Judge Osteen wrote: "In conducting the Assessment, EPA deemed it biologically plausible that ETS was a carcinogen. EPA's theory was premised on the similarities between MS, SS, and ETS. In other chapters, the Agency used MS and ETS dissimilarities to justify methodology. Recognizing problems, EPA attempted to confirm the theory with epidemiologic studies. After choosing a portion of the studies, EPA did not find a statistically significant association. EPA then claimed the bioplausibility theory, renominated the a priori hypothesis, justified a more lenient methodology. With a new methodology, EPA demonstrated from the 88 selected studies a very low relative risk for lung cancer based on ETS exposure. Based on its original theory and the weak evidence of association, EPA concluded the evidence showed a causal relationship between cancer and ETS. The administrative record contains glaring deficiencies. . . ."
In order to more fully understand the EPA report and its inherent flaws, one must read the complete Osteen decision (74), as well as the books "*Passive Smoke: The EPA's Betrayal of*

Science and Policy" by Drs. Gio B. Gori and John C. Luik (75), "*Ashes to Ashes*" by Richard Kluger (76), and *"For Your Own Good: The Anti-Smoking Crusade and the Tyranny of Public Health* by Jacob Sullum (77), and the magazine article "Warning: Secondhand Smoke May NOT Kill You" by Nicholas Varchaver (78). Finally, one must read the January 28, 1993 *Investors' Business Daily* article "Is EPA Blowing Its Own Smoke? How Much Science Is Behind Its Tobacco Finding?" by Michael Fumento, who stimulated my interest in the ETS issue (79).

The House of Lords and Professor Sir Richard Peto

On June 7, 2006, just 20 days before the release of the Surgeon General's Report, the Select Committee on Economic Affairs of the House of Lords in London issued a important report on the management of risk (80), which deals with the issue of passive smoking in England in a quite different manner than the Surgeon General. This report contains the statement "Given the evidence about the impact of passive smoking, we are concerned that the decision to ban smoking in public places may represent a disproportionate response to a relatively minor health concern. It may be that the unstated objective of policy is to encourage a reduction in active smoking by indirect means. This may well be a desireable policy objective, but if it is the objective, it should have been clearly stated."

In the preparation of this report, the committee obtained testimony from Professor Sir Richard Peto of the University of Oxford on February 14, 2006 (81,82). Questions Q381-Q404 are on the subject of the health risks of passive smoking and Sir Richard's complete responses can be found on pages 15-27 of the minutes of evidence (83).

Q381 was "Sir Richard, I wanted to start by asking if you could give us your assessment of the health risks associated with passive smoking in the home or at work and in other public places. It would be helpful if you could give us an indication of both absolute and relative magnitudes of the health risks and also the degree of uncertainty attached to the available statistical evidence."

The beginning of his response was "I am sorry, I know that is what you would like to be given, but the point is that these risks are small and difficult to measure directly. What is clear is that cigarette smoke itself is far and away the most important cause of human cancer in the world – that is, cigarette smoke taken in by the smoker – and passive smoking, exposure to other people's smoke, must cause some risk of death from the same diseases. Measuring that risk reliably and directly is difficult."

Part of his response to Q389 was "The trouble is that because these risks are small they are difficult to measure, for obvious reasons. In many populations the main way cigarette smoke kills smokers is by causing death from heart disease rather than causing death from lung cancer. Studies have been done, as you suggested, on lung cancer patients, asking what they smoke, how they lived – and those studies indicate in aggregate, roughly the sort of risk that you might expect from extrapolation of the risks among smokers. On heart disease, similar studies indicate risks from passive exposure that are a lot bigger than would be expected from extrapolation downwards from the effects of smoking on the smoker. Nobody has really argued the studies away, yet everybody feels uncomfortable with the conclusion, unless it could be better

understood."

Sir Richard's testimony clearly states the substantial doubt that a preeminent epidemiologist has about the quantitative health risks of passive smoking. The very fact that two major reports published in the same month, June 2006, come to substantially different conclusions about the health risks of ETS indicates that these risks are still uncertain and difficult to measure accurately.

Challenge to ACS and Michael J. Thun, M.D.

The precise nature of the relation of ETS and tobacco-related mortality in the US based on observational epidemiologic studies can be largely settled if Thun fully, fairly, and transparently analyses the CPS I and CPS II cohort data that the ACS currently possesses. Because of their size and length of mortality follow-up, these two cohorts contain the vast majority of the potentially available US evidence on this subject. Given the epidemiologic expertise of Thun and the availability of the appropriate CPS I and CPS II data, such an analysis could be conducted in a matter of weeks. In the interest of better understanding cancer etiology, the ACS should fully analyze these important data. I have provided sample Tables C1-C5 so that Thun can present results that are directly comparable to those presented in my *BMJ* paper (1).

In addition, Thun should analyze the CPS II cohort as a "natural experiment" of smoking cessation and mortality trends in a manner similar to what I have done. Such an analysis would test the hypothesis, based on analysis of the CA CPS I and three other US cohorts, that the long-term mortality effects of active smoking are more dangerous than generally believed because they are less reversible by cessation than generally believed (29,61,62). The ACS owes it to the over 2 million Americans who are subjects in the CPS I and CPS II cohorts, as well as to those Americans who support the ACS, to produce epidemiologic findings that accurately and completely describe the mortality risks of active and passive smoking in the United States. If Thun will not conduct such analyses there may be other ways in which these analyses can be done, so that the full truth on this matter can come out.

Conclusion

It is very disturbing that a major health organization like the ACS made false and misleading statements in a press release about our study before even reading our full paper and then cooperated with Glantz in distributing these defamatory statements on a wide scale basis in violation the strict *BMJ* press embargo policy. It is very disturbing that our study continues to be condemned, even though we have presented extensive evidence to refute the unsubstantiated claim that our paper is "fatally flawed." In addition, it is reprehensible that the ACS and Glantz have continued their campaigns to discredit us and "silence" honest research when this research is entirely valid. These actions must be kept in mind when evaluating the honesty and integrity of the ACS and Glantz. The fact that the *BMJ* paper was omitted without comment from the recent Surgeon General's Report must be kept in mind when evaluating the honesty and integrity of Samet.

I want to express my utmost respect for former *BMJ* Editor Richard Smith for publishing our May 17, 2003 paper and for then defending his decision to publish it in spite of massive criticism. Two important factors making this paper was possible were the *BMJ* editorial policy allowing publication of research funded by the tobacco industry (84) and the fact that I had an impeccable professional reputation before the trashing began in May 2003. To counter the trashing, I have presented this vigorous defense of my honesty and scientific integrity.

Hopefully, epidemiology can continue as a field in which all legitimate research findings can be published and objectively evaluated, including those findings considered to be controversial. However, this will happen only if advocacy organizations like the ACS and activists like Glantz refrain from unethically smearing honest scientists and putting out false and misleading statements about their research. In addition, powerful and influential epidemiologists like Samet, who edit a major document such as the Surgeon General's Report, must not omit important and accurate research findings and then proceed as if these findings do not exist. Such omissions and actions seriously distort the evidence on the actual health effects of ETS exposure, particularly within the US.

Hopefully, exposure of this entire sordid episode will help prevent similar episodes in the future. This episode will be particularly valuable if it forces the ACS to fully and objectively analyze and publish the important data that it possesses on both active and passive smoking. In the mean time, epidemiologists and others interested in an independent assessment of the health effects of ETS should carefully read and study this document and the numerous references that are cited, including the Osteen decision, the House of Lords report, the testimony of Sir Richard Peto, the comments of Drs. John C. Bailar III and Michael Siegel.

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Comparison of the CPS II Dose-Response Results of Table 38 in Cardenas dissertation (1995) and Table 4 in Cardenas paper (1997)

Table A. Relative risk (RR & 95% CI) of lung cancer death by ETS exposure (spousal smoking) among female never smokers in CPS II

1995 Cardenas dissertation (43): '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 a time of interview, and with valid data on age at first marriage.'

1997 Cardenas paper (44): '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 once, and with valid information on age at marriage.'

1995 Cardenas dissertation (43)					1997 Cardenas paper (44)		
Spousal smoking (cigarettes per day)	Deaths/ Person-years	1982-89 CPS II Fully-adjusted RR (95% CI)	Deaths/ Person-years	1982-89 CPS II Fully-adjusted RR (95% CI)	Cigarettes per day by spouse	Deaths/ Person-years	1982-89 CPS II Fully-adjusted RR (95% CI)
	Table 38 as shown on page 117		Proper summary of Table 38 data		Table 4: improper summary of Table 38 data		
Never	30/311,333	1.0	30/311,333	1.0	0 (never)	30/333,946	1.0
Former (1-19)	4/61,677	0.6 (0.2-1.8)					
Former (20-39)	12/120,585	0.8 (0.4–1.7)					
Former (40+)	11/49,304	2.0 (1.0–4.0)					
Former--total			27/231,566	1.13 (0.72-1.78)			
Current (1-19)	5/32,524	1.7 (0.7-4.4)	5/32,524	1.7 (0.7-4.4)	1-19 (current or former)	9/83,074*	1.1 (0.5-2.2)
Current (20-39)	10/69,060	1.6 (0.8–3.4)	10/69,060	1.6 (0.8–3.4)	20-39 (current or former)	22/179,751*	1.2 (0.7–2.2)
Current (40+)	2/24,900	0.9 (0.2–3.9)	2/24,900	0.9 (0.2–3.9)	40+ (current or former)	13/71,618*	1.9 (1.0–3.6)
P test for trend for 'former'		P = 0.29					
P test for trend for 'current'		P = 0.34			P test for 'current or former'		P = 0.03

* Current and Former Combined

Table B. Dose-response relationship between ETS exposure and CHD mortality. Relative risk of spousal smoking related to CHD deaths among never smokers in CA CPS I (1), CPS II (69), and CPS I (41) and in the summary RR of the three studies.

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)	Summmary 'Age-adjusted' RR (95% CI)
	Enstrom (1) (extracted from Tables 7 & 8)	Steenland (69) (extracted from Table 2)	LeVois (41) (extracted from Table 4)	Enstrom + Steenland + LeVois
Males				
Never	1.00	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)	0.95 (0.87-1.04)
Current				
1-19 cigs/day	0.91* (0.78-1.06)	1.33 (1.09-1.61)	0.99 (0.89-1.09)	1.02 (0.94-1.10)
20 cigs/day	0.92 (0.74-1.15)	1.17 (0.92-1.48)		
20+ cigs/day			0.96* (0.83-1.11)	1.02 (0.92-1.12)
21+ cigs/day	1.20* (0.88-1.64)	1.09 (0.77-1.53)		
Females				
Never	1.00	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)	1.00 (0.95-1.05)
Current				
1-19 cigs/day	1.07* (0.96-1.19)	1.15 (0.90-1.48)	1.04 (0.97-1.12)	1.05 (0.99-1.12)
20 cigs/day	1.04 (0.92-1.16)	1.07 (0.83-1.40)		
20-39 cigs/day			1.06 (0.98-1.15)	1.04 (0.98-1.10)
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)	0.92 (0.79-1.06)

* indicates RR was based on combining other RRs

Environmental Tobacco Smoke and Lung Cancer and Coronary Heart Disease Mortality in CPS I and CPS II

The five Tables C1-C5 shown below should be completed by Michael J. Thun, M.D., of the ACS to fully present results on ETS and lung cancer and coronary heart disease mortality in the CPS I cohort during 1960-1972 and in the CPS II cohort during 1982-1998 in a format that is the same as that used for the 1960-1998 CA CPS I results in the 2003 *BMJ* paper (1), some of which are shown in Table C1.

Table C1. Level of spousal smoking related to deaths from lung cancer and coronary heart disease among never smokers in California CPS I cohort as of 1959. Relative risk (RR with 95% CI) comparing persons with each level of exposure to those without exposure. Proportional hazards linear model (PHREG) is used and RR is adjusted for age at entry. Results shown are from Tables 7 and 8 of 2003 *BMJ* paper (1).

Spousal smoking (ETS index level) as of 1959	Subjects	Lung cancer (ICD7=162-3,ICD8&9=162) 1Jan60-30Sep72 Deaths	Age-adjusted RR (95% CI)	1Jan60-31Dec98 Deaths	Age-adjusted RR (95% CI)	Coronary heart disease(ICD7=420,ICD8&9=410-4) 1Jan60-30Dec72 Deaths	Age-adjusted RR (95% CI)	1Jan60-31Dec98 Deaths	Age-adjusted RR (95% CI)
	nn,nnn	nnn	x.xx (x.xx-x.xx)	nnn	x.xx (x.xx-x.xx)	nnn	x.xx (x.xx-x.xx)	nnn	x.xx (x.xx-x.xx)
Males									
Never (1)	7,458		1.00	65	1.00			1,860	1.00
Former (2)	624			5	0.92 (0.37-2.30)			126	0.94 (0.78-1.12)
Current									
1-9 cpd (3)	392							81	0.97 (0.78-1.21)
10-19 cpd(4)	513							99	0.86 (0.70-1.05)
20 cpd (5)	458							81	0.92 (0.74-1.15)
21-39 cpd (6)	129							27	1.16 (0.79-1.69)
40+ cpd (7)	45							13	1.29 (0.75-2.22)
Current—total	1,537			9	0.69 (0.34-1.39)			301	0.94 (0.83-1.07)
Ever	2,161			14	0.75 (0.42-1.35)			427	0.94 (0.85-1.05)
Females									
Never (1)	7,399		1.00	51	1.00		1.00	1,053	1.00
Former (2)	6,858			51	1.08 (0.73-1.60)			1,059	1.02 (0.93-1.11)
Current									
Pipe/cigar (3)	2,691							389	0.99 (0.88-1.11)
1-9 cpd (4)	1,102							183	1.13 (0.97-1.33)
10-19 cpd (5)	2,117							310	1.03 (0.91-1.17)
20 cpd (6)	3,288							412	1.04 (0.92-1.16)
21-39 cpd (7)	1,646							167	0.95 (0.80-1.12)
40+ cpd (8)	841							72	0.83 (0.65-1.06)
Current—total	11,685			75	0.93 (0.65-1.33)			1,533	1.01 (0.93-1.09)
Ever	18,543			126	0.99 (0.72-1.37)			2,592	1.01 (0.94-1.08)

Table C2. Level of spousal smoking related to deaths from lung cancer and coronary heart disease among never smokers in 25-state CPS I cohort as of 1959. Relative risk (RR with 95% CI) comparing persons with each level of exposure to those without exposure. Proportional hazards linear model (PHREG) is used and RR is adjusted for age at entry.

Spousal smoking (ETS index level) as of 1959	Subjects	Lung cancer (ICD7=162-3,ICD8=162) 1Jan60-31Dec65 Deaths	Age-adjusted RR (95% CI)	1Jan60-30Sep72 Deaths	Age-adjusted RR (95% CI)	Coronary heart disease (ICD7=420,ICD8=410-4). 1Jan60-31Dec65 Deaths	Age-adjusted RR (95% CI)	1Jan60-30Sep72 Deaths	Age-adjusted RR (95% CI)
	nn,nnn	nnn	x.xx (x.xx-x.xx)	nnn	x.xx (x.xx-x.xx)	nnn	x.xx (x.xx-x.xx)	nnn	x.xx (x.xx-x.xx)
Males									
Never (1)			1.00		1.00		1.00		1.00
Former (2)									
Current									
1-9 cpd (3)									
10-19 cpd(4)									
20 cpd (5)									
21-39 cpd (6)									
40+ cpd (7)									
Current—total									
Ever									
Females									
Never (1)			1.00		1.00		1.00		1.00
Former (2)									
Current									
Pipe/cigar (3)									
1-9 cpd (4)									
10-19 cpd (5)									
20 cpd (6)									
21-39 cpd (7)									
40+ cpd (8)									
Current--total									
Ever									

Table C3. Level of spousal smoking related to deaths from lung cancer and coronary heart disease among never smokers in CPS II cohort as of 1982. Relative risk (RR with 95% CI) comparing persons with each level of exposure to those without exposure. Proportional hazards linear model (PHREG) is used and RR is adjusted for age at entry.

Spousal smoking (ETS index level) as of 1982	Subjects	Lung cancer (ICD9=162) 1Sep82-31Dec89 Age-adjusted			Lung cancer (ICD9=162) 1Sep82-31Dec98 Age-adjusted			Coronary heart disease (ICD9=410-4) 1Sep82-31Dec89 Age-adjusted			Coronary heart disease (ICD9=410-4) 1Sep82-31Dec98 Age-adjusted		
	nn,nnn	Deaths nnn	RR x.xx	(95% CI) (x.xx-x.xx)	Deaths nnn	RR x.xx	(95% CI) (x.xx-x.xx)	Deaths nnn	RR x.xx	(95% CI) (x.xx-x.xx)	Deaths nnn	RR x.xx	(95% CI) (x.xx-x.xx)
Males													
Never (1)			1.00			1.00			1.00			1.00	
Former (2)													
Current													
1-9 cpd (3)													
10-19 cpd(4)													
20 cpd (5)													
21-39 cpd (6)													
40+ cpd (7)													
Current—total													
Ever													
Females													
Never (1)			1.00			1.00			1.00			1.00	
Former (2)													
Current													
Pipe/cigar (3)													
1-9 cpd (4)													
10-19 cpd (5)													
20 cpd (6)													
21-39 cpd (7)													
40+ cpd (8)													
Current--total													
Ever													

Table C4. Total self-reported hours of ETS exposure per day related to deaths from lung cancer and coronary heart disease among all never smokers in CPS II cohort with data on self-reported ETS exposure as of 1982. Relative risk (RR with 95% CI) comparing persons with each level of exposure to those without exposure. Proportional hazards linear model (PHREG) is used and adjusted for age at entry.

Total daily hours of ETS exposure as of 1982	Subjects	Lung cancer (ICD9=162) 1Sep82-31Dec89 Deaths	Lung cancer (ICD9=162) 1Sep82-31Dec89 Age-adjusted RR (95% CI)	Lung cancer (ICD9=162) 1Sep82-31Dec98 Deaths	Lung cancer (ICD9=162) 1Sep82-31Dec98 Age-adjusted RR (95% CI)	Coronary heart disease (ICD9=410-4) 1Sep82-31Dec89 Deaths	Coronary heart disease (ICD9=410-4) 1Sep82-31Dec89 Age-adjusted RR (95% CI)	Coronary heart disease (ICD9=410-4) 1Sep82-31Dec98 Deaths	Coronary heart disease (ICD9=410-4) 1Sep82-31Dec98 Age-adjusted RR (95% CI)
	nn,nnn	nnn	x.xx (x.xx-x.xx)	nnn	x.xx (x.xx-x.xx)	nnn	x.xx (x.xx-x.xx)	nnn	x.xx (x.xx-x.xx)
Males									
0 hours			1.00		1.00		1.00		1.00
1									
2									
3									
4									
5									
6									
7									
8+									
Current total (1+)									
Females									
0 hours			1.00		1.00		1.00		1.00
1									
2									
3									
4									
5									
6									
7									
8+									
Current total (1+)									

Table C5. 1982 level of spousal smoking related to total self-reported ETS exposure among never smokers in 1982 CPS II cohort and 1992 CPS II Nutrition cohort.

Spousal smoking as of 1982	1982 subjects	Percent distribution of 1982 total daily hours of ETS exposure					1992 subjects	Percent distribution of 1992 total weekly hours of ETS exposure				
		0	1	2	3-7	8+		0	1-7	8-14	15-49	50+ .
Males												
Never (1)												
Former (2)												
Current												
1-9 cpd (3)												
10-19 cpd(4)												
20 cpd (5)												
21-39 cpd (6)												
40+ cpd (7)												
Current—total												
Ever												
Females												
Never (1)												
Former (2)												
Current												
Pipe/cigar (3)												
1-9 cpd (4)												
10-19 cpd (5)												
20 cpd (6)												
21-39 cpd (7)												
40+ cpd (8)												
Current—total												
Ever												