specific exposure estimates used in the paper under consid-
eration here.

With regard to the criticism that the half-life for 2.3,7,8-
TCDD (6.9 years) used in the estimation was derived from
a subset of the cohort (n = 48), it is important to note that
the estimate is in agreement with results from other cohorts
(5-7).

Dr. Swaan’s second criticism concerns the appropriateness
of the comparison group. Because the validity of all
comparisons from epidemiologic data depend on the compa-
rability of groups compared, we adopted two comparison
strategies in the current paper and a third in a previous paper
— a standardized mortality ratio (SMR) analysis with mortal-
ity of the German population as reference (8)). One com-
parison involved a cohort of gas workers, and the other used
an internal comparison within the cohort of chemical work-
ers. The two lowest exposure quintiles served as the refer-
ence group. We outlined the advantages and disadvantages
of each comparison in detail in the paper. Our conclusions
were not based on one comparison alone, as Dr. Swaan
suggests.

With respect to the gas worker comparison, Dr. Swaan
mentions the different minimum duration of employment
between the chemical worker cohort (3 months) and the gas
worker cohort (10 years). Because of this difference, we
adjusted the Cox regression models for duration of employ-
ment. In addition, our first SMR analysis (6) had shown that
the elevated cancer risk in the chemical workers cohort is
mainly due to an elevation in the subgroup with long dura-
tion of exposure (≥20 years). Thus, restricting the chemical
worker cohort to workers with duration of employment of
≥10 years increased, rather than decreases, the relative risks
in the comparison with the gas worker cohort. Finally, the
explanation for the selection process in the gas worker
cohort is that in the Cox regression analysis only gas work-
ers actively employed on January 1, 1952 (the start of the
follow-up for the chemical worker cohorts) were included,
leaving 2,528 out of 3,120 male workers.

The last issue that Dr. Swaan raises is that of the statis-
tical analysis. He mentions that the relative risks presented
in Table 3 for total mortality are very high compared with the
SMR in relation to the Federal Republic of Germany (FRG)
population reported in 1991 (8). However, one should com-
pare the relative risks in Table 3—derived from a propor-
tional hazard model including the cohort of gas workers as
unexposed controls—with the SMR for the gas worker
cohort in the 1991 paper, not with the SMR in relation to
the FRG population mortality. For the lower exposure
categories, the magnitude of the gas worker-related esti-
mates increased in 1991 and in the current paper are very
similar. With regard to the estimate in the highest exposure
category, it is important to stress that no comparable expo-
csure category was identified in the earlier paper. Further-
more, the relative risk for total mortality was significant
and substantial not only in comparison with the gas workers,
but also in the internal comparison (relative risk = 1.55, 95%
percent confidence interval 1.06—2.26, Table 5 (5)).

In summary, within the constraints which are inherent to
retrospective mortality studies in an occupational setting, we
see strong indirect evidence against a serious bias in the
exposure estimates. Furthermore, the results derived from
comparisons with different groups using statistical tech-
niques that adjust for basic differences between groups
corroboration each other. Thus, we stand by our conclusion
that these data are evidence of a dose-response relationship
between estimated dioxin levels and risk of all-cause, can-
cer, and cardiovascular mortality. Our findings support the
hypothesis that TCDD is a human carcinogen.

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RE: "A NEW PERSPECTIVE ON JOHN SNOW’S COMMUNICABLE DISEASE THEORY"

Dr. Winkelstein (1) has been commended for describing
again in great detail how John Snow’s investigations on
the spread of cholera were based on strong a priori reasoning.
Snow’s ideas derived from his insight into the etiology of
infectious diseases. As an historical example, it remains
important to remember that Snow’s theory on the commu-
nication of cholera was not derived from his epidemiologic
observations, but preceded them.

Previously, I had called attention to this often neglected
aspect of the history of Snow and cholera, and I had based
my argument on the first edition of Snow’s book, On the
Mode of Communication of Cholera (2), which was written
before he made his observation on water companies and the
Broad Street pump (3, 4). Others in the recent literature

Letters to the Editor 363
had already called attention to this interpretation of his work (5). The first persons who clearly stated that Snow had specified his hypothesis before collecting the facts were his contemporary friend and co-worker, Sir Benjamin Ward Richardson (6), and also Wade Hampton Frost, who wrote the introduction to the 1936 reprint of the second edition of Snow's work (7). Both described how Snow already had his theory "in mind" when he looked for suitable observations to test it.

The historical part of Dr. Winkelstein's paper is beautifully researched. It will remain a cornerstone in the literature about John Snow. However, his perspective is less new than the title of his contribution implies. This perspective is simply repeatedly forgotten, and equally often rediscovered.

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Editor's note: In accordance with journal policy, Dr. Winkelstein was given the opportunity to reply to the above letter, but he chose not to do so.

RE: "FAMILY HISTORY OF CANCER AND RISK OF LUNG CANCER AMONG LIFETIME NONSMOKING WOMEN IN THE UNITED STATES"

We read with interest the report of a deficit of digestive tract cancers in the first-degree relatives of nonsmoking female lung cancer patients (1). We have noted a similar deficit in the first-degree relatives of patients with squamous cell carcinoma of the head and neck (SCCHN) in two separate case-control studies. In the first study of 754 cases of SCCHN and 1,507 age-and-sex-matched hospital controls carried out in southern Brazil (2), we found a reduced risk for colorectal cancer in association with a family history of SCCHN (adjusted relative risk (RR) = 0.60, 95 percent confidence interval (CI) 0.20-1.77). In a second study (3), we found a deficit of colorectal cancer in 1,429 first-degree relatives of 242 cases of SCCHN compared with 934 relatives of 156 spouse controls ascertained at one hospital in Montreal (adjusted RR = 0.49, 95 percent CI 0.18-1.21).

We et al. (1) note the deficit of lung cancer in hereditary nonpolyposis colorectal cancer families. Several population-based studies have shown significant (4, 5) or nonsignificant deficits (6, 7) of second cancers of the colon and rectum after lung cancer (and vice versa).

It appears that there may be an inverse relation between colorectal cancer and both SCCHN and lung cancer. Environmental and genetic aspects of this phenomenon deserve to be explored further.

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Editor's note: In accordance with journal policy, Dr. Wu and her coauthors were given the opportunity to reply to the above letter, but they chose not to do so.