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CASE-CONTROL STUDY METHODS:
RESPONSE RATES, RESPONDENT CHARACTERISTICS AND NONRESPONSE BIAS

Thesis for the degree of

Master of Sciences

Department of Epidemiology and Biostatistics

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Montreal

ABSTRACT

Between 1979 and 1985 a large interview-based case-control study was conducted in Metropolitan Montreal. Eligible cases were males aged 35-70 newly diagnosed with one of 13 sites of cancer in any of the 19 largest hospitals in Montreal. The purpose of this study was to generate hypotheses about possible occupational carcinogens and, to this end, an in-depth interview was sought with each patient concerning occupational history and potential confounding factors. This study provided the context in which to address two methodological issues: 1) whether the response rates or data quality are affected by the length of the interval between the case's diagnosis and the attempt to interview him; and 2) whether non-respondents differ from respondents on variables likely to create non-response bias.

Although it was intended to contact patients within weeks of diagnosis, problems with the case-ascertainment system in some hospitals led to a "natural experiment" whereby some patients were contacted early but others were contacted months or even years after diagnosis. The response rate was about 20% higher for patients contacted within three months of diagnosis than for those for whom the delay was longer. As expected, among those for whom the delay was longer, there were more proxy respondents. An evaluation by chemists and hygienists confirmed that the quality of responses about occupational exposures was lower among proxy respondents than among self-respondents. These results held for most sites of cancer in our study. We conclude that to maximise data quality it is best to interview subjects as soon as possible after their cancer diagnosis has been made.

From the medical records we obtained information on six socio-demographic variables for all eligible subjects (age, income, marital status, ethnic group, smoking habits and alcohol consumption). Respondents and non-respondents were compared on these variables. There were few differences. We were also able to compute an estimate of non-response bias by comparing two odds ratios for each site/socio-demographic factor association: that derived from all eligible subjects and that derived from respondents only. At least as far as these variables were concerned there was no evidence that non-response bias would distort odds ratios by more than 30%. We conclude, therefore, that in this study where the response rates for different sites were in the range 75% to 85%, there was no detectable non-response bias.

RÉSUMÉ

De 1979 à 1985, une vaste étude cas-témoins, basée sur des interviews, a été menée dans la région métropolitaine de Montréal. Les cas éligibles étaient des hommes âgés entre 35 et 70 ans, ayant été diagnostiqués une première fois pour l'un des 13 sites de cancer sélectionnés dans l'un des 19 hôpitaux les plus importants de Montréal. Le but de cette étude était de générer des hypothèses concernant les cancers possiblement causés par le milieu de travail, et, à cet effet, nous avons procédé à une interview détaillée auprès de chaque patient relativement à leur histoire professionnelle et aux variables concomitantes possibles. Le contexte particulier de cette étude nous a permis d'aborder deux questions méthodologiques à la fois, à savoir: 1) si les taux de réponse ou la qualité des données étaient affectés par le laps de temps écoulé entre le moment du diagnostic et celui de l'interview du patient; et, 2) si les personnes n'ayant pas répondu différaient de celles ayant répondu quant à certaines variables susceptibles de créer un bias de non-réponse.

Bien que nous ayons prévu contacter les patients quelques semaines seulement après le diagnostic, nous avons dû faire face à certains problèmes au niveau du système d'identification des cas dans certains hôpitaux, ce qui a eu "tout bonnement" pour effet que certains patients ont été contactés tôt après le diagnostic alors que d'autres l'ont été des mois et même, dans certains cas, des années plus tard. Le taux de réponse, pour les patients contactés en moins de trois mois après le diagnostic, était de 20% plus élevé que pour ceux dont le délai avait été plus long. Pour ces derniers, tel que nous l'avions prévu, une tierce personne avait répondu. Une évaluation effectuée par les chimistes et les hygiénistes a confirmé que la qualité des réponses concernant les expositions en milieu de travail était plus faible lorsque l'interview était effectuée

auprès d'une tierce personne qu'auprès de la personne concernée. Ces résultats s'appliquent pour la plupart des sites de cancer faisant partie de notre étude. Nous avons donc conclu que pour maximiser la qualité de nos données, il est préférable d'interviewer les sujets le plus tôt possible après que le diagnostic de cancer ait été prononcé.

Nous avons extrait des registres médicaux six variables socio-démographiques (âge, revenu, statut social, ethnie, tabagisme et consommation d'alcool) pour tous les sujets éligibles. Les personnes ayant répondu et celles n'ayant pas répondu ont toutes été comparées selon ces variables. Quelques différences sont apparues. Nous avons également été capables d'obtenir une estimation du biais de non-réponse en comparant deux taux de risque pour l'association de chaque site à chacune des six variables socio-démographiques: l'un provenant de l'ensemble des sujets éligibles et l'autre des personnes ayant répondu seulement. A tout le moins, en autant que ces variables sont concernées, il n'y a eu aucune preuve à l'effet que le biais de non-réponse ait affecté les taux de risque de plus de 30%. Par conséquent, nous concluons que pour cette étude où les taux de réponse pour les différents sites variaient entre 75 et 85%, aucun biais de non-réponse possible n'a été détecté.

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INTRODUCTION

The modern case-control study dates from the 1920s with papers by Broders (1920) and Lane-Claypon (1926). However, the method was rarely used until Cornfield (1951) demonstrated that a relative risk can be estimated from either a case-control or a cohort design (Schlesselman, 1982). Landmark work by Cornfield (1954) and Mantel and Haenszel (1959) subsequently provided a solid basis for the analysis of case-control data, and since the 1960s the case-control method has gained rapidly in popularity, particularly for the study of rare diseases such as cancer.

Usually, the purpose of a case-control study is to estimate the strength of an association between a disease and a risk factor. However, there are many potential flaws in design, fieldwork or analysis that may lead to biased estimates of this association. As the method has become more widely used, many of the methodological problems inherent in the case-control approach, especially design and statistical analysis issues, have been addressed by the research community. For instance, there has been considerable work on the question of matching in design and analysis and also some work on the issue of defining an appropriate control group for a given case series (Schlesselman, 1982; Breslow and Day, 1981). Fieldwork issues, however, have been rather neglected. For our purposes, the term "fieldwork" in an interview-based case-control study refers to the implementation of the study design and comprises the following activities: defining a list of subjects who will constitute the target population, ascertaining certain information (mainly medical) from medical records, soliciting interviews from study subjects, interviewing subjects, and managing and processing the data for statistical analysis.

Once the study design has been elaborated, there are potential pitfalls in each component of fieldwork which may lead to bias in study results. Examples of these would include differences in quality of response between cases and controls, perhaps due to differential recall or because of different mixes of self- and proxy respondents in the two groups, or different mixes in the type of instrument used (interviewer or self-administered questionnaire). For a review of these and other potential sources of bias see Sackett (1979).

The focus of this report is on the fieldwork stage in which a subject's participation in an interview-based case-control study of cancer is solicited. One of the key fieldwork problems in such a study, as in many epidemiologic studies, is nonresponse and the bias it may create. In an interview-based case-control investigation, some target population is identified and its members are asked to participate in the research. If the percentage of non-respondents is high, there is some chance that parameter estimates based on respondents will not faithfully represent the corresponding parameters among the entire target population. Two types of questions may be addressed in relation to this issue: What can be done to increase response rates? How much nonresponse bias is there in a case-control study?

This pair of methodologic questions was addressed in the context of an ongoing case-control study in Montreal: a multi-hospital, interview-based study of cancer conducted between 1979 and 1985 to generate hypotheses concerning hitherto undetected carcinogens in the workplace. We will refer to this as the Montreal study. Table 1 reiterates this definition and presents several others which will be used in this thesis and whose meaning may not be self-evident.

Table 1

DEFINITIONS

1. The Montreal study

   A case-control study of 13 sites of cancer carried out in Montreal between September 1979 and June 1985 under the direction of Dr. Jack Siemiatycki of the Institut Armand-Frappier.

2. Target population

   All subjects who fulfill the eligibility criteria for the Montreal case-control study: males, aged 35-70, resident in the Montreal Metropolitan area, newly diagnosed with one of 13 sites of cancer in any of the 19 major hospitals in Montreal.

3. Respondent population

   All members of the target population for whom completed questionnaires are obtained.

4. Case-ascertainment system

   The source and means by which the target population of cases is assembled for the case-control study.

5. Lag time

   The time taken from date of diagnosis to date of first attempt to contact the subject for an interview.

6. Response outcomes

Response rate: the proportion of the target population who participate in the study, or whose family responds on their behalf.

Nonresponse rate: the proportion of the target population who refuse to participate in the study, or who are lost to follow-up through death or are untraceable.

7. Type of respondent

In the Montreal study proxy response was accepted as a last resort from a family member or close friend when the subject was unable to participate. We thus distinguish between self-respondents and proxy respondents.

8. Nonresponse bias

The extent to which estimates of disease-exposure odds ratios in the respondent population deviate from the corresponding parameters in the target population.

The Montreal study provided a unique opportunity to examine selected issues related to participation of subjects in a case-control study of several sites of cancer. For this thesis, it was possible to obtain certain information concerning all or most of the eligible subjects even before they were contacted to participate in the cancer study. It was thus possible to study the relationship between these factors, known at the outset, and the likelihood of response. There were two basic types of factors available - one concerning fieldwork and another concerning the patients' characteristics - and they have formed the bases for two distinct sets of analyses.

The first type of information available arose from a characteristic of study procedure - namely the interval between the time a person's cancer was diagnosed and the time an attempt was made to interview him (referred to as the lag time). In any prospective case-control study of cancer (i.e. one in which newly diagnosed subjects are ascertained in an ongoing fashion after the study has begun), an important decision has to be taken by the investigator as to how long to wait before contacting the subject. It may be rationalized that the earlier one makes contact the better, since cancer patients may die or be difficult to trace after leaving hospital. On the other hand, it may be argued that the patient may be depressed and despondent soon after being told he has cancer and that his willingness to participate in a study would be greater if he were contacted somewhat later. Because of the need to get detailed job histories from the cancer patients in the Montreal study, and because of the short survival time for some types of cancer, we instituted a rapid prospective case-ascertainment system to facilitate interviewing of cases as soon as possible after diagnosis. Although most subjects were approached soon after diagnosis, many, for reasons to be outlined below, were not approached until months or years after diagnosis. Thus, there occurred a kind of "natural experiment" which allowed us to

assess the effect of interval between diagnosis and first contact with the patient on response rates.

While the theoretical possibility that nonresponse from some eligible study subjects may bias the results of a study is well known, there is very little empiric evidence to indicate its actual extent in case-control studies and, under usual study circumstances, where little or nothing is known about nonrespondents, it is often impossible to obtain this information. The second set of data to which we had access provided the material necessary to examine this issue. The hospitals participating in the Montreal study accorded access to the medical dossiers of all eligible subjects so that diagnoses could be verified and certain socio-demographic information abstracted. Because this information was collected for subjects who ultimately responded as well as those who did not, it enabled us to assess whether estimates of odds ratios obtained from respondents differed from those obtained from the entire target population.

OBJECTIVES

GENERAL

1. To determine whether response rates and quality of response are affected by the lag period between a case's diagnosis with cancer and the investigator's attempt to enlist the case's participation.

2. To determine whether differences in socio-demographic characteristics between respondents and nonrespondents in an actual case-control study do lead to bias in estimates of disease-exposure associations.

SPECIFIC

1. To compare response rates and quality of response among three sets of cases - those approached within three months of diagnosis, those approached from four to 12 months after diagnosis, and those approached more than 12 months after diagnosis. As well as examining response rates, we examined reasons for nonresponse in the three lag groups.

   Quality of response was measured by two indices: the proportion of responses from self- as opposed to proxy respondents, and an evaluation of the quality of job descriptions by a chemist/hygienist who had to work with the job descriptions.

   These evaluations were carried out among all males diagnosed with one of thirteen sites of cancer. They were assessed for the entire group of eligible subjects as well as for subsets of the cancer sites.

2. To assess response rates as a function of six characteristics of cancer cases: age, ethnic group, socio-economic status, cigarette smoking and alcohol consumption.

Further, a series of analyses was carried out to examine odds ratios between several risk factors (sub-categories of the above six variables) and several sites of cancer among all eligible subjects. The same analyses were repeated among respondents only and the two sets of odds ratios were compared to provide a portrait of the range of bias due to nonresponse.

ORGANIZATION OF THIS REPORT AND RESPONSIBILITY FOR THIS WORK

This report is organized in three parts. Part A contains background material describing the methods used in the Montreal study, the context in which the methodological investigations were carried out. Parts B and C answer objectives 1 and 2 respectively, and stand on their own as research reports, with distinct reviews of the literature, methods and results. Thus, the results of each section are discussed separately and distinct conclusions presented for each.

In general, the methods described as part of the Montreal study (Part A) constitute work done by this author as the fieldwork supervisor of the Montreal study under the direction of Dr. J. Siemiatycki before this thesis was conceived. The methods described in Parts B and C and, obviously, all statistical analyses and literature reviews in this report, constitute work done by this author for the purpose of this thesis, with normal consultation and direction from my thesis supervisor and other faculty.

PART A

THE MONTREAL STUDY

A.1 GENERAL DESIGN OF THE MONTREAL STUDY

Since 1979, a multi-hospital case-control study to investigate possible associations between occupational exposures and cancer has been in progress in Montreal (Siemiatycki et al., 1982). An active system was established in the 19 main hospitals of Montreal for rapid ascertainment of all histologically confirmed incident cases of 13 sites of cancer amongst males aged 35-70, resident in the Metropolitan Montreal region.

The study protocol requires that detailed information for each patient be obtained on job history and potential confounding factors. Insofar as possible, this information is obtained directly from the patient by means of a probing semi-structured interview. Interviews are carried out by a team of specially trained interviewers.

The crux of the interview is a detailed history of each job ever held by the patient. Each job history is then translated by a team of chemist/hygienists into a chemical exposure history for the individual patient. The methodology has been described in detail by Gérin and Siemiatycki (1984). In brief, each job description is reviewed to determine the nature of the processes used and the consequent exposures. The possible presence of any of the 275 exposures on a checklist is then determined. In the analyses, patients with cancer at a particular site comprise a case series and patients with cancers at all other sites (or subsets thereof) serve as controls. In this way it is possible to estimate, for each site fo cancer, the risk of exposure to 275 specific substances.

A.1.1 The rapid case-ascertainment system in the Montreal study

For some cancers, the mean survival time is less than six months. Therefore, to maximise our ability to get job history information from the person himself (usually a better source than his relatives), a rapid case-ascertainment system was established for the Montreal study.

In this system, the secretaries in the pathology department of each participating hospital were requested to call the study secretary whenever a new cancer case was diagnosed. The hospital secretaries were paid for each case reported to the study. As an additional incentive for rapid reporting, fees differed according to whether the case was still in hospital ($4.50) or not ($3.00) at the time of notification. Members of the study staff periodically visited each hospital to review the pathology reports and medical records to ensure that no cases had been missed and to verify that the diagnosis of each ascertained case was an incident primary cancer. Only incident cases (i.e. cancers diagnosed for the first time) were eligible for the study. Each patient is classified according to the site of his primary tumour.

If the pathology department notified us rapidly of a newly diagnosed case, we were usually able to arrange an interview with the patient before he was discharged from hospital. If the patient had been discharged by the time we were notified or was diagnosed on an outpatient basis, we attempted to initiate contact with him at home within one month of diagnosis.

A.1.2 Follow-up and interviewing in the Montreal study

Every effort was made to obtain a face-to-face interview with each patient. If it became clear that a face-to-face interview would not be possible but that a

telephone interview could be arranged, then the interviewer would administer the questionnaire on the telephone.

As a last resort, when a face-to-face or telephone interview was impossible because of difficulty contacting the patient or his family, we had prepared a self-administered version of the questionnaire that could be sent to the patient for completion and return by mail. Up to three such questionnaires may have been mailed, with at least one sent by registered mail, before attempts to obtain a response were abandoned. Among self- and proxy respondents combined, 80% completed a face-to-face interview, and 9.4% were interviewed by telephone. Only 10.6% of respondents completed a self-administered questionnaire. Among self-respondnets only, 87.3% responded to a face-to-face interview, 7.8% to a telephone interview, and 5.0% to a self-administered questionnaire.

No firm rules were laid down regarding the number of times each strategy was attempted. A weekly meeting was held with the interviewers and decisions were made in conjunction with the fieldwork supervisor (L. Richardson) on a case by case basis. Only the order in which the strategies were attempted was pre-determined (face-to-face, followed by telephone and finally self-administered questionnaire) with a few exceptions. For example, if a patient responded initially with a "soft" refusal we might have waited several months and then attempted a mail strategy.

While considerable resources, both human and financial were allocated to the case-ascertainment system and to attempts to contact patients for an interview, there were not sufficient resources to engage in extensive tracing procedures to locate either patients who moved from the address recorded in the medical record or the families of cases who died with no next-of-kin noted in the medical record. That is to

say, we were unable to use sources other than the medical record (such as government registration records of different kinds) to trace such subjects or their families. Our final response rates should be seen in this context.

PART B

THE EFFECT OF LAG ON RESPONSE RATES

B.1 INTRODUCTION

Many aspects of a case-control study of cancer may influence the response rates. Some of these concern the very research question being addressed; for example, the type of cancer, geographic or socio-cultural characteristics of the population in which the study is carried out, and age and sex characteristics of the particular population of cases. Other aspects may concern the design and/or fieldwork methods employed once the research question has been fixed and the study population selected. Among the latter, are: a) whether cases are ascertained as they are diagnosed or entered into a Registry (prospective ascertainment) or whether the list of eligible subjects is made up of cases diagnosed in the past and assembled into the sampling frame before interviewing begins (retrospective ascertainment); b) what the rules are concerning self- and proxy response; and c) whether the lag time between diagnosis and interview attempt is short or long.

These three features are sometimes determined by the problem under investigation and they are certainly interrelated. For instance, an investigator wishing to conduct a study of a very rare tumour may have no practical alternative but to use retrospective ascertainment and to go back several years in order to amass a sufficient number of cases. Even for a common tumour, the investigator may be constrained because of readier access to cases diagnosed in the past than to cases diagnosed concurrently. If ascertainment is retrospective, this virtually excludes the possibility of a short lag between diagnosis and interview. If, in addition, patients with the tumour being studied have a short survival, it will become necessary to rely largely or perhaps exclusively on proxy response.

Sometimes, however, the choice between retrospective or prospective ascertainment is under the investigator's control and s(he) must weigh the relative merits of each. Whereas the former often has the advantage of larger numbers and greater simplicity of the case-ascertainment strategy, the latter may provide the opportunity to gather interview information of higher quality.

It is self-evident that information obtained from a subject about his lifetime exposures will be at least as valid, and probably more so, than that obtained about him from a relative some months or years after the subject died. Yet even in a study in which most subjects are still alive when ascertained, the investigator has the option of accepting only self-response or of accepting proxy response in cases where self-response is difficult or unobtainable. All other things being equal, a strategy which includes proxy response as a last resort will provide higher response rates than one which does not admit proxy response. However, while the overall response rate will be increased by using proxies it is possible that the data quality from the proxy respondents is inferior. The investigator would have to evaluate each such situation on its own merits. S(he) would need to guess what the differences may be in response rate and in response quality, and determine the relative importance of quantity (overall response rate) vis-à-vis quality (precision of response), if the two are indeed opposed.

For a study using prospective ascertainment, the investigator can often determine whether to institute a short or a long lag period. The objective of this study was to determine whether response rates and quality of response were affected by the lag period between a case's diagnosis with cancer and the investigator's attempt to enlist the participation of the case.

B.2 LITERATURE REVIEW

A thorough search of the literature failed to turn up a single methodological investigation of the relationship between lag time and response rates. Indeed, only a very few published case-control studies even mentioned in their methods sections what the lag period was or the methods and extent of follow-up employed to interview cases. For this reason, we enlarged the scope of this literature review to reflect on possible reasons for variation in response rates between case-control studies, and this constitutes the first part of this section.

The second part of this review examines the literature on self- vs proxy response. Because we have used proxy response as one of the tools to evaluate the relationship between response quality and lag, our assumptions that self-response is superior to proxy response in providing better data (occupational histories) should be examined.

B.2.1 Fieldwork methods and response rates in case-control studies of cancer

Ideally this section should encompass a critical evaluation of studies which have evaluated fieldwork methodology and response rates in case-control studies. Unfortunately, there are none! In the absence of any formal literature on the subject, we felt that if we could examine the fieldwork methods used in different case-control studies of cancer and the response rates achieved, some light might be shed on the relationship between the two. To this end, a Medline search was carried out for case-control studies of any of the thirteen sites of cancer included in the Montreal study. Because the problems of obtaining responses may be quite different for diseases other than cancer, for females as opposed to males, for rural as opposed to urban populations and for non-North American as opposed to North American societies, it was decided to

restrict attention to studies of male cancer patients in urban North America. We included all such studies that were published in the past 15 years and, of course, which reported response rates. The Medline search yielded only 13 studies which met our criteria. The complete list of the 13 studies along with a summary of some fieldwork characteristics is presented in Table B1. Few of the authors presented more than minimal information on fieldwork methods. The method of assembling the cases was usually reported but very little was included concerning interviewing, follow-up and tracing procedures. Therefore, our ability to draw inferences concerning the relationship between fieldwork methods and response rate was extremely limited from the outset.

The studies listes in Table B1 encompass several different sites of cancer. Before addressing the issue of fieldwork and response rates, it is appropriate to make a slight digression to see if response rates differ according to the site of cancer under study. Two of the obvious characteristics of a cancer site which may influence response rates would be the expected survival of patients with the tumour, and varying degrees of difficulty in communicating due to the effects of the tumour or treatment. The latter characteristic is unlikely to be a factor in determining response rates for the sites in this literature review, namely those included in the Montreal study. The choice of sites to be included in the Montreal study was predicated in part on excluding sites likely to pose difficulty in communication (for example head, neck and brain tumours). From the limited number of studies shown in Table B1, there is no clearcut evidence that the site of cancer determines what level of response rate will be achieved. Nevertheless, although studies of cancer with long survival manifested a range of response rates, those with short survival tended to have lower response rates. Bladder cancer, for example, is not usually rapidly fatal, and the response rates in bladder cancer studies range from the low of 64% in San Francisco (Hartge et al.,

Table B1

LIST OF INTERVIEW-BASED CASE-CONTROL STUDIES CONDUCTED IN URBAN NORTH AMERICA INVOLVING MALES, DIAGNOSED WITH ANY OF THE THIRTEEN SITES OF CANCER INCLUDED IN THE MONTREAL STUDY

Author and year	Place	Site(s) of cancer studied	Source of cases	Case characteristics	Case ascertainment*	Proxy response accepted	N of cases	Response rate %
Cole, 1971	Boston	Bladder	Pathology logs	All incident cases aged 20-89 Jan. 1967-June 1968	Retrospective	No	531	83.5
Howe, 1977	Nfld. British Columbia Nova Scotia	Bladder	Provincial Tumour Registries	All incident cases, April 1974 - June 1976	Prospective	No	821	77.0
Hartge, 1984	Atlanta Connecticut Detroit Iowa New Jersey New Mexico New Orleans San Francisco Seattle Utah	Bladder	Tumour Registries	All incident cases, resident in area, aged 20-89	Prospective	No	152 562 540 430 1,258 87 99 561 248 149	70.0 69.0 70.0 82.0 75.0 78.0 83.0 64.0 72.0 79.0
Blot, 1980	Tidewater Virginia	Lung	Death certificates	All male deaths in 1976	Retrospective	Only	405	83.0
Blot, 1982	Jacksonville, Florida	Lung	1) 13 hospitals 2) death certificates	1) all incident cases, 2) all male deaths, 1976	1) Prospective 2) Retrospective	1) yes 2) only	1) 181 2) 217	1) 83.4 2) 77.9
Vernick, 1982	Pittsburgh	Colon	15 hospitals	White patients, aged 45-85, 1975-1978	Retrospective	Not stated	300	78.7
Herrman, 1985	Philadelphia	Colon	Hospitals	All cases aged 45-65 with next-of-kin available 1976-1978	Retrospective	Yes	385	52.5
MacMahon, 1981	Boston and Rhode Island	Pancreas	?	Male and female cases between 1974-1979	Prospective?	?	558	66.0
Gold, 1985	Baltimore	Pancreas	16 hospitals, pathology dept.	All incident cases, 1978-1980	Prospective	Yes	392	70.0
McLaughlin, 1983	Minnesota	Renal pelvis	Tumour Registry	White males, aged 30-79, 1974-1979	Retrospective	Yes	78	95.0
Stemhagen, 1983	New Jersey	Liver	N.J. Tumour Registry and death certificates	All incident cases, 1975-1979	Retrospective	Yes	335	79.0
Williams, 1977 (T.N.C.S.)	Atlanta Birmingham Colorado Dallas Detroit St. Paul (Minn.) Pittsburgh Oakland	All sites except skin	Hospitals Doctors offices pathology and X-ray labs, death certificates	10% sample of all incident cases	Prospective	Yes if interview within 6 months of subject's death	538 655 1,621 1,152 3,330 1,443 1,329 3,111	53.0 54.0 44.0 60.0 58.0 55.0 37.0 73.0
Swanson, 1985	Detroit	Oesoph. colon lung bladder	Metropolitan Detroit Cancer Surveillance System	Incident cases diagnosed in early 1984	Prospective with lag 4-11 months	yes yes yes yes	30 97 147 36	60.0 80.4 85.0 77.8

* Prospective: the ascertainment of cases as they are diagnosed or entered into a registry.
Retrospective: assembly of cases which have been diagnosed in the past into a sampling frame before interviewing begins.

1984) through 77% in three Canadian provinces (Howe et al., 1977) to a high of 88% in Boston (Cole et al., 1971). In contrast three of the four studies of pancreas, liver and oesophageal cancer, all of which are short survival cancers, achieved relatively low response rates (MacMahon et al., 1981 - 66%; Gold et al., 1985 - 70%; Swanson et al., 1985 - 60%), and only one had a response rate generally considered to be reasonably high (Stemhagen et al., 1983 - 79%).

Perhaps the best available guide to the relationship between site of cancer and response rates is the Third National Cancer Study (TNCS) (Williams et al., 1977) in which all sites of cancer were included using a common fieldwork protocol. In Table B1 we presented the TNCS response rates by geographic area. In their publication Williams et al. (1977) also reported response rates by site. For the thirteen sites included in the Montreal study, and collapsing across geographic areas, the response rates vary from 46% (liver) to 63% (Hodgkin's lymphoma). In fact there was a slight relationship between the aggressiveness of the tumour and the response rate achieved. For instance the response rates were 47%, 46% and 48% respectively for three short survival tumours - oesophagus, liver and pancreas; whereas the response rates were 54%, 53% and 56% respectively for three long survival tumours - colon, prostate and bladder.

The above observations pertain to the overall response rates as defined by the investigators themselves. In some studies only self-response was accepted, in some instances both self- and proxy responses were accepted, and in others only proxy response could be accepted. For some of the studies it was possible to calculate the self-response rate (i.e. the percent of the target population answering for themselves). These are shown in Table B2. As might be expected there was a trend for higher self-response rates among cancer sites with long survival (bladder and colon) than among

Table B2

SELF-RESPONSE RATE IN THOSE STUDIES IN TABLE B1 FOR WHICH IT WAS POSSIBLE TO CALCULATE SELF-RESPONSE RATE

Author + year	Site of cancer	N of cases	Self-response rate %
Swanson, 1985	oesophagus	30	30.3*
	colon	97	58.8*
	lung	147	36.1*
	bladder	36	61.1*
Blot, 1982	lung	181	48.6*
Cole, 1971	bladder	531	88.5
Howe, 1977	bladder	821	77.0
Hartge, 1984	bladder	4,086	73.0

* The overall response rate was considerably higher than this because proxy response was accepted.

those with short survival (lung and oesophagus). In fact the self-response rates were highest in the three studies in which the proxy response was not accepted. This may be due to the fact that all three were studies of bladder cancer, a long survival tumour. Alternatively, the investigators may have put more effort into obtaining responses from subjects themselves when they impose a self-response rule from the start. Unfortunately, there is no way of knowing whether the extent of follow-up and effort to obtain self-response was comparable across the five studies.

Turning to fieldwork issues, there was no correlation between response rates achieved and type of case-ascertainment in the studies listed in Table B1. Blot et al. (1980; 1982) using retrospective ascertainment of cases via death certificates, obtained response rates around 80% in two separate studies of lung cancer. However, both were carried out in small cities and the surrounding counties, areas likely to have relatively stable populations which would facilitate tracing the relatives of dead cases. Many of the cases in the Minneapolis-St. Paul study of cancer of the renal pelvis (McLaughlin et al., 1983) were deceased at the time of case-ascertainment. The overall response rate was a very impressive 95%, but it should be noted that 50% of the respondents were proxies. Moreover, the number of cases in the target population was small (98) and it may be much easier to organize successful procedures when tracing such a small sample. Only 11 of the 335 liver cancer patients in the New Jersey study population were still alive when the interviewing started but with the use of extensive tracing procedures they were able to track down and interview family members of 79% of the sample (Stemhagen et al., 1983). These four studies all depended heavily on proxy respondents. Thus, despite retrospective ascertainment, all of these studies wound up with reasonably high response rates.

Cole et al. (1971) ascertained cases retrospectively, searching pathology logs for all patients diagnosed in the 18 month period prior to the start of the study. The published report did not describe the range of lags. However, it seems reasonable to estimate that the lags ranged from six to 24 months, since cases occurring from January 1967 to June 1968 were enrolled, interviewing started in July 1968 and the results of the study were published in 1971. Although the lag time from diagnosis to attempt to interview was, it seems, over 12 months in most cases, and the study was conducted in a large metropolitan area, only 4.3% of the cases were reportedly lost to follow-up. This relatively low rate of loss may have been due to the combination of the longer survival for bladder cancer than for most sites of cancer and the fact that most patients may have been treated and followed-up clinically in the same hospitals from which they were ascertained. The latter aspect would have facilitated tracing.

Both the National Baldder Cancer Study (Hartge et al., 1984) and the Canadian Bladder Cancer Study (Howe et al., 1977) used several sources for case-ascertainment, including tumour registries. In each study cases were reported to the investigator as soon as they were notified to the local registry. It must be noted that all of the Registries participating in these studies engaged in active searching for cases in the reporting hospitals, rather than passively waiting for the hospitals to send reports of cancer diagnoses. Interviews in both studies were said to have been completed within six months of diagnosis.

On balance, therefore, it would seem that there is no simple relationship between retrospective and prospective case-ascertainment and the response rates achieved, especially if proxy response was accepted in the design of the study.

It is interesting that the response rates in the studies involving more than one geographical area (Williams et al., 1977; Howe et al., 1977; Hartge et al., 1984) seem to be lower, in general, than single geographic area studies. It is easy to imagine the multitude of problems that would be involved in setting up, training and motivating staff in a large multi-centre study and the consequent difficulties in ensuring high response rates across centres. Williams et al. (1977) commented that the higher response rates achieved in California than in the other centres participating in the Third National Cancer Survey might have been attributable to a more experienced staff available at the start of the study.

Eight of the studies listed in Table B1 published the reasons for nonresponse. These results are presented in Table B3. The consistency of the patient refusal rate across seven of the eight studies is remarkable and suggests that there may be a "hard core" group of refusers (3% to 8%) that is quite stable in male urban North America. The much higher 18% refusal rate in the Baltimore study (Gold et al., 1985) is the only exception in these studies. Unfortunately, the authors did not provide any information which would allow us to speculate on possible reasons for this high rate of refusal.

Since it may be beyond a researcher's control to reduce this hard core refusal rate, should it exist, in most case-control studies of cancer, it is most important to attempt to find ways to reduce the losses incurred for other reasons such as death or residential mobility. In each study reported, the percentage lost because of death or inability to trace the patient or patient's family is not negligible (between 10% and 20%). In fact, the numbers lost due to death were greater than the numbers lost to mobility in four of the six informative studies in Table B2 (one study was based on death certificates, and the other did not distinguish between the two reasons for nonresponse). As expected, the studies which did not accept proxy response under any

Table B3

CASE-CONTROL STUDIES WHICH REPORTED

REASONS FOR NONRESPONSE AMONG CASES

Study	Proxy accepted	Total N	Physician refusal %	Subject or family refusal %	Patient died or too sick %	Subject or family lost to follow-up %
Cole, 1971	no	531	4.0	3.3	unstated	4.3
Williams, 1977	yes	13,179	14.2	7.3	6.9	14.6
Howe, 1977	no	821	4.1	7.9	9.9	1.0
Blot, 1980	only	405	n.a.*	4.5	n.a.	11.0
MacMahon, 1981	no	558	unstated	7.8	17.6	8.9
Hartge, 1984	no	4,086	3.1	6.2	13.9	3.7
Gold, 1985	yes	392	9.0	18.0	2.6	—
Swanson, 1985	yes	310	3.5	2.6	11.6**	

* n.a.: not applicable. This study was based on proxy interviews with families of deceased cases.

** Data presented does not permit distinction to be made between subjects who died and subjects lost to follow-up.

circumstances, had relatively high proportions of nonresponse due to patients dying before they could be interviewed.

In addition to the fieldwork components mentioned above, there are others which may influence response rates and for which the published studies do not provide even the limited information shown for the factors that we presented in Table B1. Examples of this would include: the accuracy of patients' names, addresses and next-of-kin information as recorded in the hospital or registry, and the skill of interviewers. Partly because of the small number of studies available, the idiosyncratic nature of each and the paucity of information on fieldwork procedures in published studies, it is impossible to draw any general conclusions about the relationship between fieldwork methods and response rates.

The only published study that has discussed lag explicitly,, even though it was not formally evaluated, was the small pilot study involving four sites of cancer reported by Swanson et al. (1985). Most of their cases were approached between four and 11 months after diagnosis and they speculated that had the lag been shorter the self-response rate would have been higher. As a result of the pilot study they decided to institute a rapid case-ascertainment system: "It will be particularly interesting to observe the extent to which rapid reporting improves the proportion of interviews completed with patients, as well as whether there is any improvement in the overall response rate" (Swanson, 1985).

There is clearly a need for research into fieldwork methods to identify those that may maximise response rates in case-control studies, and our study was directed to provide some of the observations requested by Swanson.

B.2.2 Self-response as an index of quality

As described below, part of the evaluation of the effect of lag on response was based on the proportion of interviews obtained by self- as opposed to proxy response. In order to justify the appropriateness of this as an index of quality, it is relevant to review evidence on the quality of proxy versus self-response in studies based on occupational histories. Since the research question of this thesis does not concern the quality of proxy as opposed to self-response per se, there is no attempt in what follows to present an exhaustive review of that topic; rather we present the major findings distilled from this literature, with particular attention to those concerning the quality of occupational history reports.

Several authors have examined the issue of proxy response to various types of questions. There has been some work on the quality of dietary and medical history information obtained from proxy respondents (Enterline and Capt, 1959; Humble et al., 1984; Kolonel et al., 1977; Marshall et al., 1980). More recent reports have examined proxy reporting of occupation and occupational exposures (Pershagen and Axelson, 1982; Rogot and Reid, 1975; Selevan, 1980; Pickle et al., 1983).

An early study by Enterline and Capt (1959) using a design which randomised respondents to a self- or proxy rule in a household health survey compared the reported prevalence of certain medical conditions, dietary fat intake, height and weight and MD visits obtained from the subjects allocated to each respondent rule. They found no statistical difference in levels of reporting between the two types of respondents. Later methodological studies by Kolonel et al. (1977), Marshall et al. (1980) and Humble et al. (1984) compared responses of pairs of spouses for self- and spouse to various questions about diet. While agreement tended to be good overall in all three studies, the wives' proxy reports were in much closer agreement with their

husbands' self-reports than the husbands' proxy reports with their wives' self-reports. That is, wives appeared to be better proxy respondents than husbands on dietary questions.

Rogot and Reid (1973) compared the responses given by a group of British and Norwegian migrants to the US with next-of-kin reports obtained on the same questions after the subject's death. The interval between subject and proxy response varied from two to six years. Subjects and proxies were asked what the subject's main occupation was. However, the variable compared was not the occupation per se, but rather the social class as inferred from the occupation and scored according to the U.K. Registrar General's Classification of social classes. Thus, the occupational spectrum was compressed into seven social class categories. The degree of perfect agreement in attributing social class between the subject and his relative was 77%. The authors noted that there was little tendency on the part of proxy respondents to "upgrade" the occupation of the subject; that is the errors in the proxies' reports were as likely to be in one direction as the other. The subjects and proxies were also asked some questions about smoking habits of the subject. The authors analysed concordance according to two ways of classifying smoking habits, one general and one more specific. The general question was whether the person had ever been a regular smoker, and there were two possible answers: yes or no. The more specific question concerned amount smoked and had five categories: never, occasional, less than one pack per day, one pack per day, more than one pack per day. The investigators found a markedly lower level of agreement between responses to the more detailed question than to the broader question about smoking. Thus the dichotomised smoker/nonsmoker question yielded 92% agreement, while there was only 71% perfect agreement on the five-point semi-quantitative scale.

Pershagen and Axelson (1982) obtained occupational exposure information by questionnaire from the relatives of men who had resided in the neighborhood of a smelter in Sweden before death. They compared this information with data obtained from the employee registers of the smelter company. For the question concerning employment history in the smelter, the sensitivity was 98% (that is, the percent of those truly employed in the smelter for whom the proxy report stated that they had been employed there) and the specificity 99% (that is, the percent of those never employed in the smelter for whom the proxy report stated that they had never been employed there). However, assessment of arsenic exposure from the questionnaire had a sensitivity of 40% with specificity of 90%. This is not surprising. It certainly appeals to common sense to assume that proxy respondents would be much more able to answer a general question concerning the plant where a man worked than to identify the chemicals he was exposed to. The very high sensitivity and specificity in this Swedish study may significantly overestimate the validity of such reports in urban North America where job and residential mobility are probably much higher than in a small town in Sweden.

In her doctoral thesis, Selevan (1980) compared the responses of spouse pairs for self- and spouse to questions about the presence or absence in the individual's employment history of a checklist of 12 occupation categories and 32 chemical exposures. As reproduced in Table B4, these were very specific items. While the overall agreement was 73% for all 44 categories combined, agreement for some of the individual categories was as low as 13%. These findings recall those of Pershagen and Axelson (1982) and indicate the poor quality of proxy reports for specific occupational exposures.

Table B4

LIST OF THE JOB CATEGORIES AND EXPOSURES ASKED OF 133 SPOUSE PAIRS*

Job categories

Worked:
1) with dyes, textiles, or in a clothing industry;
2) in a plastic industry;
3) in a beauty salon as a hairdresser or beautician;
4) as an electronic worker with small metal parts;
5) in an operating room;
6) in any other job with anesthetic gases;
7) a job with radiation exposure - fluoroscopy, microwaves, radio-isotopes, or X-rays;
8) any (other) kind of job in a hospital or nursing home;
9) in a laboratory;
10) in a dry cleaning shop with dry cleaning agents or solutions;
11) any (other) kind of job in a dry cleaning shop or in a laundry;
12) in any kind of job where you work with or around mercury.

List of 32 specific exposures

Aluminium	Vinyl chloride
Cadmium	Nitrogen oxides
Carbon disulfide	Acetone
Chromium	Benzene
Carbon monoxyde	Carbon tetrachloride
Copper	Chloroform
Cyanide	Formaldehyde
Dimethylformaldehyde	Metal chloride
Estrogens	Perchloroethylene
Fluorine	Toluene
Gasoline	Trichloroethylene
Lead	Xylene
Nickel	Degreasers
Antibiotics	Weed killers
Polychlorinated biphenyl (PCB's)	Rat killers
Selenium	Insect killers

* Selevan, S (1980). Evaluation of data sources for occupation pregnancy outcome studies. Ph.D. thesis, University of Cincinnati. University Microfilms Int., Ann Arbor.

Pickle et al. (1983) compared different types of proxy respondents (spouses, sibs, offspring, friends) by examining the proportions of questions unanswered by each type of respondent. The questions concerned exposure to asbestos and work in shipbuilding. They noted that the ability of a proxy respondent (irrespective of type of proxy) to answer such questions was related to the probability of exposure. That is, proxy respondents had less difficulty providing a response for female subjects, who were less likely to be exposed to either asbestos or shipbuilding than males, than for male subjects.

While research on dietary and medical history indicates that proxy respondents can give good information concerning male subjects, there is undoubtedly some loss of information. However, the relevance of findings on validity of proxy information in these areas for validity of proxy information concerning occupational histories is doubtful. The very meagre evidence available indicates that proxy information on specific chemical exposures or even specific occupations is of dubious quality. In the absence of evidence to the contrary, it seems reasonable to assume that proxy information on job histories is not as accurate as the information that might be obtained from the subject himself. It would thus be preferable to obtain self-response than proxy response for occupational histories.

B.3 METHODS

B.3.1 Definition of lag groups

In section A.1.2 we described the rapid case-ascertainment system that was established for the Montreal study. For a variety of reasons, the intention to contact subjects soon after their diagnosis with cancer was occasionally frustrated. Establishing the basic case-ascertainment system throughout the Montreal area took a considerable amount of time and effort. Some of the hospitals did not agree to participate until several months after the official starting date of the study (September 1979). For these hospitals we had retrospectively to ascertain all eligible cases diagnosed between September 1979 and the time of entry. Furthermore, once the rapid case-ascertainment system was implemented, it took some time before it functioned smoothly. Initially, the pathology secretaries missed a number of cases and these were only picked up later by the study staff in the course of our routine periodic verification of pathology department records. (Such verifications were only undertaken at the end of the first year of the study when we realized the nature of the problem.) Finally, hospital staff turnover, illness and vacations all created other problems, which led to the identification of many cases several months after they had been diagnosed. Thus, despite the attempt to ascertain patients soon after diagnosis, various unavoidable fieldwork problems meant that many cases were only ascertained and contacted several months after diagnosis.

Both the date of diagnosis and date on which we first attempted to contact the patient were recorded for all cases. This made it possible to calculate the interval between them - which we will refer to as "lag time" - and to determine whether lag time was associated with the response rate. To do this, we divided the subjects into three groups that corresponded to the lags which might be expected with three

different modes of case ascertainment. The first, 0-3 months, would be found in an optimal, active case-ascertainment system using a source such as pathology logs to identify patients. The second, 4-11 months, might be typical of a passive ascertainment system dependent on, for example, tumour registration procedures. The third, 12-60 months, might occur if the cases were selected retrospectively for a specific time period in a given geographical area using, for example, data entered into a tumour registry.

B.3.2 Outcome measures: response rate, type of respondent and quality of job history

The response rate is defined as the proportion of the total target population for which a completed questionnaire was obtained, whether the respondent was the subject himself or a proxy.

Nonrespondents are classified into three groups: 1) the case or his family refused to participate - referred to as "refusals"; 2) the patient died before we were able to complete an interview and there is no next-of-kin recorded in the medical record or found at his address (which does not necessarily mean that there was no next-of-kin) - referred to as "died without next-of-kin"; 3) the address and next-of-kin information provided by the hospital was inaccurate or out of date and we were unable to trace the patient or his family - referred to as "lost to follow-up".

The speed with which a patient is contacted after diagnosis may determine whether the patient himself or a proxy provides the response. Thus, we investigated the relationship between the lag time and the type of respondent (self- or proxy), grouping all proxies together regardless of relationship to the case.

Since the crux of the cancer study lies not in the structured part of the questionnaire, but in the open-ended section concerned with the patient's job history, we decided to base our evaluation of quality on the amount of detail provided in the job description obtained in the semi-structured probing interview. The chemists' ability to code exposures was in large measure dependent on the level of detail provided for each job in a man's history. From the information provided by the patients, the chemists determined a list of possible exposures for each job in the man's lifetime. This was done for each job separately, and codes were assigned for the industry, the occupation and each chemical exposure in that job. For the purposes of this investigation the chemists were asked to evaluate the quality of the information for a subset of 1,775 interviews (all interviews conducted between 1981 and 1983) by assigning a 3-level code reflecting the level of detail provided for each job. The range is from good (1) through doubtful (2) to bad (3). When the respondent was able to furnish reasonably precise dates (within a year), the name of the company, the occupation title and some measure of detail as to the tasks involved in a given job, then that job was classified as good.

Obviously the number of jobs in the histories of different subjects is variable. For the purpose of analysis, we considered a good job history to be one in which all of the subject's jobs were given a rating of "good" by the chemists.

B.3.3 Analysis and presentation

Having grouped the subjects into three lag times the analysis focused on two sets of outcome measures shown in Table B5: 1) response outcomes as a function of lag time and 2) type of respondent and quality of work histories as a function of lag time.

Table B5

OUTCOME MEASURES USED TO COMPARE THE THREE LAG TIMES*

a) For all eligible subjects ascertained

Response outcomes

- % response
- % refuse
- % died without next-of-kin
- % lost to follow-up

b) Among respondents only

Self or proxy response

- % self-respondents

Quality of work history as judged by chemists

- % judged to be "good"

* 0 - 3 months

4 -11 months

12-60 months

Although the distribution of subjects into the three lag groups was essentially haphazard, this does not guarantee that there were no systematic differences between subjects in each of the three groups. If there were, then the comparison of response outcomes in the three lag groups might be confounded by these differences. Thus, we compared the subjects in the three groups on the four variables that were available for all subjects in the Montreal study: site of cancer, year of the study in which the case was diagnosed, age and mean census tract income. For each of the outcome measures (type of response outcome, frequency of self-respondents, frequency of "good" quality job histories) we carried out a series of analyses adjusting for various combinations of the potential confounders. In the final analysis of each outcome variable, only those confounders identified as potentially important in the preliminary analysis were adjusted for.

The statistical analysis consisted of estimating the various outcomes of interest - each of which was expressed as a percentage - in each of the three lag groups, but adjusting for those factors identified in the searching procedure for confounders. The confounder variables themselves were expressed as categorical variables. The method used for this was based on the classical additive analysis of variance model:

$$Y_{ijkl} = m + a_i + b_j + c_k + e_{ijkl}$$

where

Y_{ijkl} = the outcome of interest for individual I in lag i with confounders b and c set at values j and k respectively;

= 0 or 1;

m = overall mean;

a_i = deviation in lag i;

b_j, c_k = deviations according to subgroups of the confounding variables;

e_{ijkl} = sampling error term.

Then the value of $m + a_i$ represents the mean outcome of interest (e.g. response rate) in lag i, adjusted for confounders b and c. The fact that the Y's take the values 0 or 1 implies that the various parameters in the model are between 0 and 1. Multiplying by 100 provided percentages. To estimate the values a_i for the three lags, we in fact used an option in the Statistical Package for the Social Sciences Analysis of Variance program entitled Multiple Classification Analysis (Nie et al., 1975). From a theoretical viewpoint the use of this procedure is debatable because the ANOVA model is predicated on a continuous normally distributed outcome variable with constant variance across groups. This is clearly violated when we have a binary outcome. Nevertheless, as Siemiatycki (1976) argued in a similar context, several authors have shown that analysis of variance and multiple linear regression are very robust to departures from the model assumptions, and in particular to binary dependent variables (Cochrane, 1950; Seeger and Gabrielsson, 1968; Neter and Wasserman, 1974). The reason for this robustness is that when percentages in different sub-groups are between 5% and 95%, the variances of the various subgroup estimates do not vary widely. In the data at hand, percentages of respondents in different groups were in the range 60% to 90% and percentages for different reasons for nonresponse were mainly in the range 5% to 30%.

Furthermore, it must be noted that we used the procedure not to make statements about p-values for differences, but rather to make parameter estimates. Siemiatycki (personal communication) has shown in another data set that the parameter estimates obtained from the SPSS Multiple Classification Analysis procedure are almost identical to those obtained from the procedure described by Feldstein (1966). Feldstein's procedure is also based on an additive model but assumed the

outcome variable to be binary. Our reason for using the SPSS approach, which is admittedly an approximation, rather than the Feldstein procedure, was simplicity and availability of the software. While adjustment by another method such as logistic regression based on a multiplicative model is feasible, the preferred model in survey research has been the additive model (e.g. Eaton and Kessler, 1981; Comstock and Helsing, 1973; Siemiatycki et al., 1984).

Issues of statistical inference (whether patterns observed could have been due to chance rather than a systematic effect) are addressed informally by reference to the size of the groups concerned and to estimated standard errors of response outcomes. These standard errors were derived from the crude response rates based on the assumption of a binomial distribution.

B.4 RESULTS

B.4.1 Comparability of subjects in the three lags

Tables B6 to B8 show the distribution of subjects in each of three lag times for site of cancer, year of the study in which the subject was diagnosed, age and mean census tract income. In Table B6 we see that the cases were not equally distributed across the three lag groups in each year of the study. In fact, it is particularly noticeable that 45% of all of the cases who fell into the long lag group during the entire course of the study were diagnosed in the first year. In each successive year as the case-ascertainment system functioned more smoothly the relative proportion of cases ascertained in the long lag diminished. There were small differences in the site distribution by lag, but none were remarkable (Table B7). The longest lag group had proportionately more elderly patients and proportionately more poor patients (Table B8). Chi-square tests of significance showed each variable portrayed in Tables B6 to B8 to be unequally distributed across the three lag groups. Thus it was important to adjust the estimates of outcome measures for imbalances in the distribution of these potential confounders in the three lag groups.

Table B9 shows the crude response rates in each lag and the response rates adjusted for each variable separately and in combination. While the adjusted response rates do not differ markedly from the crude, we felt that it would be appropriate to include age, census tract income and year of diagnosis in all analyses of response rates. Inclusion of site of cancer did not in any way alter the estimates.

Table B10 shows the proportion of self-respondents and the proportion of good quality work histories obtained in each lag adjusted for the same four variables separately. The proportion of self-respondents in each lag was unaffected by

Table B6

DISTRIBUTION OF SUBJECTS ACROSS FIVE YEARS OF CASE ASCERTAINMENT IN EACH OF THREE LAG* TIMES

Year of ascertainment	Overall % of all years	Lag time: 0 - 3 months N	0 - 3 months % of all years	4 - 11 months N	4 - 11 months % of all years	12 - 60 months N	12 - 60 months % of all years
1	25.9	683	22.3	79	18.6	332	45.3
2	13.2	365	11.9	53	12.5	138	18.8
3	13.1	385	12.6	39	9.2	127	17.3
4	22.5	764	25.0	112	26.4	74	10.1
5	25.3	862	28.2	142	33.4	62	8.5
TOTAL	100.0	3,059	100.0	425	100.0	733	100.0

* Lag: time from date of diagnosis to first attempt to interview subjects.

Table B7

DISTRIBUTION OF SUBJECTS BY SITE IN EACH OF THREE LAG* TIMES

Site	Overall % of all sites	Lag time: 0 - 3 months N	0 - 3 months % of all sites	4 - 11 months N	4 - 11 months % of all sites	12 - 60 months N	12 - 60 months % of all sites
Upper GI	9.4	310	10.1	35	8.2	53	7.2
Colorectal	19.4	623	20.4	67	15.8	128	17.5
Liver + pancreas	6.5	148	4.8	30	7.1	94	12.8
Lung	25.3	764	25.0	136	32.0	166	22.6
Bladder + prostate	24.5	790	25.8	94	22.1	151	20.6
Melanoma	4.3	127	4.2	24	5.6	31	4.2
All lymphomas	5.9	162	5.3	25	5.9	60	8.2
Kidney	4.7	135	4.4	14	3.3	50	6.8
TOTAL	100.0	3,059	100.0	425	100.0	733	100.0

* Lag: time from date of diagnosis to first attempt to interview subjects.

Table B8

DISTRIBUTION OF SUBJECTS BY AGE AND INCOME IN EACH OF THREE LAG* TIMES

Socio-demographic characteristic	Overall % of all	Lag time: 0 - 3 months N	0 - 3 months % of all	4 - 11 months N	4 - 11 months % of all	12 - 60 months N	12 - 60 months % of all
Age:							
Under 60	40.7	1,306	42.7	189	44.5	223	30.4
Over 60	59.2	1,751	57.2	235	55.3	510	69.6
Income:							
Low	29.8	584	19.1	132	31.1	542	73.9
Medium	49.9	1,767	57.8	205	48.2	131	17.9
High	20.3	708	23.1	88	20.7	60	8.2

* Lag: time from date of diagnosis to first attempt to interview subjects.

Table B9

RESPONSE RATES* IN EACH OF THREE LAG** TIMES ADJUSTED FOR DIFFERENT COMBINATIONS OF POTENTIAL CONFOUNDING FACTORS

Factor adjusted for+	Lag time		
	0 - 3 months response %	4 - 11 months response %	12 - 60 months response %
None	86.6	83.4	59.4
Site	86.4	83.5	59.8
Year of diagnosis	86.1	82.9	61.5
Age	86.5	85.5	59.7
Census tract income	85.9	83.5	62.0
Age + income + year of diagnosis	85.4	83.0	64.1
Age + income + year of diagnosis + site	85.1	83.0	65.7

* Percentage of all eligible cases for whom responses were obtained.
** Lag: time from date of diagnosis to first attempt to interview subjects.
\+ As described in section B.3.3.

Table B10

TWO INDICES OF QUALITY OF QUESTIONNAIRE DATA - PERCENT SELF-RESPONDENTS* AND PERCENT OF WORK HISTORIES EVALUATED AS GOOD** - IN EACH OF THREE LAG+ TIMES ADJUSTED FOR DIFFERENT POTENTIAL CONFOUNDING FACTORS

Index of quality of questionnaire data	Lag time		
	0 - 3 months %	4 - 11 months %	12 - 60 months %
a) % self-respondents adjusted for++:			
None	82.6	68.1	40.9
Site	82.4	69.3	41.5
Age	82.6	68.0	41.1
Income	82.4	68.2	42.0
Year of diagnosis	82.6	68.1	41.1
b) % work histories evaluated as good adjusted for++:			
None	70.7	67.7	67.6
Site	70.6	68.4	68.0
Age	70.7	67.7	67.6
Income	70.7	67.9	67.5
Year of diagnosis	71.1	67.4	59.7

* Percent of all respondents whose response was obtained directly from the case himself.

** The chemists evaluated the subset of all work histories obtained between 1981 and 1983.

\+ Lag: time from date of diagnosis to first attempt to interview subjects.

++ As described in section B.3.3.

adjustment for any of the four variables. The proportion of good quality work histories was altered only by the year of diagnosis and therefore this was included in all analyses of quality of work histories.

B.4.2 Overall response rates

Between September 1979 and April 1985, 4,070 eligible cases were ascertained for the Montreal cancer study. This constitutes the target population. The overall response rates and patterns of nonresponse for the target population are shown in Table B11. 3,322 (81.6%) of subjects or their families responded, 330 (8.2%) refused, 262 (6.4%) died without next-of-kin available for interview and 156 (3.8%) were lost to follow-up.

B.4.3 The effect of lag on response rates

The lag time from date of diagnosis to first attempt to interview the subject was categorised into three groups: 0 - 3 months, 4 - 11 months, and 12 - 60 months. There were 2,971 eligible subjects in the first group, 429 in the second and 670 in the third. Table B12 shows the response rates and nonresponse patterns in each lag adjusted for age, census tract income and year of diagnosis. There was very little difference in response rates between the first lag (85.4%) and the second (83.0%). However, the response rate decreased dramatically to 64.1% in the third lag where the delay was 12 months or longer. The same is true for the patterns of nonresponse. There was very little difference between the proportion of subjects who refused or died without next-of-kin or were lost to follow-up in the first and second lags. However, the proportion of those who died without next-of-kin or were lost to follow-up increased considerably in the third lag, corresponding to the marked drop in response rates. Only the proportion who refused remained fairly stable across the three lags with a slight decrease in the third lag.

Table B11

RESPONSE OUTCOMES FOR ENTIRE STUDY POPULATION

Response outcome			
Total sample eligible:		N*	4,070
		%	100.0
Responded:		n	3,322
		%	81.6
		S.E.	0.6
Nonresponse:	Refused:	n	330
		%	8.2
		S.E.	0.4
	Died without next-of-kin	n	262
		%	6.4
		S.E.	0.4
	Lost to follow-up	n	156
		%	3.8
		S.E.	0.3

* N: denominator
n: numerator
S.E.: standard error of percentage based on binomial distribution.

Table B12

RESPONSE OUTCOMES BY LAG*

Response outcome		Lag time 0 - 3 months	4 - 11 months	12 - 60 months
Total sample eligible:	N**	2,971	429	670
	%	100.0	100.0	100.0
Responded:	n	2,540	356	430
	%	85.4	83.0	64.1
	S.E.	0.7	1.8	1.9
Nonresponse:				
Refused:	n	250	40	44
	%	8.4	9.2	6.6
	S.E.	0.5	1.4	1.0
Died without next-of-kin	n	95	20	144
	%	3.2	4.7	21.5
	S.E.	0.3	1.0	1.6
Lost to follow-up	n	86	13	52
	%	2.9	3.1	7.8
	S.E.	0.3	0.8	1.0

* Lag: time from date of diagnosis to first attempt to interview subjects.

** N: denominator for all percentages in this column.
n: numerator.
%: adjusted for differences between lag groups in age, mean census tract income and year of diagnosis.
S.E.: standard error based on binomial distribution.

B.4.4 The relationship between lag, response rates and median expected survival for each site of cancer

The rationale for the rapid case-ascertainment system is the desire to interview patients themselves before death, severe illness or residential mobility can intervene. Table B13 shows the median survival time as estimated by the US SEER program (1976), and response rates for each of the sites of cancer studied. As might be expected the response rates were generally higher for sites with relatively longer median survival.

We divided the sites into three larger groups according to the expected median survival: 1) sites with six months survival or less (oesophagus, stomach, liver, pancreas, lung); 2) sites with between six months and two years expected median survival (colon, rectum, kidney); and 3) those with more than two years expected survival (prostate, bladder, melanoma, Hodgkin's and non-Hodgkin's lymphoma). We will refer to these three groups as having short, medium or long survival. This allowed us to examine more precisely the relationship between lag, site of cancer and response outcome.

Table B14 presents the response outcomes by lag for the short survival group. There is hardly any difference in response from the first lag (83.7%) to the second (81.0%), with a marked decrease in response occurring when the lag was 12 months or more (56.9%). The proportion of nonrespondents classified as "refusals" and "lost to follow-up" were stable across the three lags. The main reason for fall off in response after 12 months lag was, as expected, the larger number who "died without next-of-kin".

Table B13

RESPONSE RATES FOR THE SITES OF CANCER INCLUDED IN THE CANCER STUDY, ORDERED BY APPROXIMATE MEDIAN SURVIVAL TIME

Site	Median survival time in years*	N**	Response rate %
Liver	0.2	77	61.0
Pancreas	0.3	152	68.4
Oesophagus	0.4	123	78.9
Stomach	0.5	273	79.9
Lung	0.5	1,038	80.7
Kidney	1.9	199	78.4
Colon	2.2	626	82.6
Rectum	2.2	186	90.3
Prostate	3.4	459	81.7
Bladder	4.0	517	84.5
Non-Hodgkin's lymphoma	4.8	216	83.3
Hodgkin's lymphoma	5.0	56	92.9
Melanoma of skin	9.2	126	82.5

* Median survival time for white males in the U.S.A. - Cancer Patient Survival, Report No. 5: A report from cancer surveillance, epidemiology and end results (SEER) program.

** N: number of eligible subjects with this(ese) site(s) (ie. denominator for the corresponding response rate).

Table B14

RESPONSE OUTCOMES BY LAG* FOR SITES WITH LESS THAN SIX MONTHS MEDIAN SURVIVAL**

Response outcome		Lag time 0 - 3 months	4 - 11 months	12 - 60 months
Total sample eligible:	N+	1,180	201	289
	%	100.0	100.0	100.0
Responded:	n	989	163	164
	%	83.7	81.0	56.9
	S.E.	1.1	2.8	2.9
Nonresponse:				
Refused:	n	85	14	19
	%	7.2	6.9	6.5
	S.E.	0.8	1.8	1.5
Died without next-of-kin	n	71	15	89
	%	6.0	7.5	30.9
	S.E.	0.7	1.9	2.7
Lost to follow-up	n	35	9	17
	%	3.0	4.6	5.7
	S.E.	0.5	1.5	1.4

* Lag: time from date of diagnosis to first attempt to interview subjects.
** Sites included: oesophagus, stomach, liver, pancreas, lung.
\+ N: denominator for all percentages in this column.
n: numerator.
%: adjusted for differences between lag groups in age, mean census tract income and year of diagnosis.
S.E.: standard error based on binomial distribution.

Response outcomes for sites with medium survival are shown in Table B15. The response rates decreased steadily as the lag increased. The larger proportion of nonrespondents in the 12-60 months lag group was due to larger proportions who "died without next-of-kin" and were "lost to follow-up". The relatively high proportion of refusals (14.5%) among those in the 4-11 months lag group must be interpreted cautiously because the numbers of subjects was small and sampling variation large.

For those sites with the longest expected survival there was again, as with short survival, no decrease in response rates from the first lag (85.6%) to the second 86.9%) as shown in Table B16. However, here, too, the response rate decreased substantially after a 12 month lag, due to "died without next-of-kin" and "lost to follow-up".

Figure B1 summarizes the response rates observed in Tables B14, B15 and B16. The six response rates generated in lag 0-3 and lag 4-11 were all between 80.8% and 87.7%. Although there was some evidence of an overall higher response rate in the short lag as compared with the medium lag, this difference was small. Even among the medium survival sites, where the evidence seems to be strongest, the small denominator of cases in the 4-11 months lag group precludes any definitive conclusions. In all three survival groupings there was a fall off in response rates among those contacted after 12 months. The fall off was most dramatic among subjects with short survival cancers.

Figure B2 summarizes the reasons for nonresponse observed in Tables B14, B15 and B16. Refusal rates did not vary greatly among the nine groups, with a low of 5.5% and a high of 14.5%. The latter occurred in a small group and had a large sampling variability. With the exclusion of this outlier, the range was only from 5.5% to 9.8%.

Table B15

RESPONSE OUTCOMES BY LAG* FOR SITES WITH MEDIAN SURVIVAL BETWEEN SIX MONTHS AND TWO YEARS**

Response outcome		Lag time 0 - 3 months	4 - 11 months	12 - 60 months
Total sample eligible:	N+	622	70	125
	%	100.0	100.0	100.0
Responded:	n	546	57	88
	%	87.7	80.8	70.5
	S.E.	1.3	4.7	4.1
Nonresponse:				
Refused:	n	50	10	12
	%	8.0	14.5	9.7
	S.E.	1.1	4.2	2.7
Died without next-of-kin	n	12	2	12
	%	1.9	2.8	9.8
	S.E.	0.5	2.0	2.7
Lost to follow-up	n	14	1	13
	%	2.3	1.5	10.2
	S.E.	0.6	1.5	2.7

* Lag: time from date of diagnosis to first attempt to interview subjects.
** Sites included: colon, rectum, kidney.
+ N: denominator for all percentages in this column.
n: numerator.
%: adjusted for differences between lag groups in age, mean census tract income and year of diagnosis.
S.E.: standard error based on binomial distribution.

Table B16

RESPONSE OUTCOMES BY LAG* FOR SITES WITH MEDIAN SURVIVAL GREATER THAN TWO YEARS**

Response outcome		Lag time 0 - 3 months	4 - 11 months	12 - 60 months
Total sample eligible:	N+	1,169	158	256
	%	100.0	100.0	100.0
Responded:	n	1,002	137	178
	%	85.6	86.9	69.4
	S.E.	1.0	2.7	2.9
Nonresponse:				
Refused:	n	115	15	14
	%	9.8	9.5	5.5
	S.E.	0.9	2.3	1.4
Died without next-of-kin	n	15	3	40
	%	1.3	1.8	15.8
	S.E.	0.3	1.1	2.3
Lost to follow-up	n	37	3	24
	%	3.2	1.6	9.3
	S.E.	0.5	1.0	1.8

* Lag: time from date of diagnosis to first attempt to interview subjects.
** Sites included: prostate, bladder, melanoma, all lymphomas.
+ N: denominator for all percentages in this column.
n: numerator.
%: adjusted for differences between lag groups in age, mean census tract income and year of diagnosis.
S.E.: standard error based on binomial distribution.

FIGURE B1

RESPONSE RATES IN EACH OF THREE LAG TIMES FOR SITES OF CANCER WITH SHORT, MEDIUM AND LONG SURVIVAL

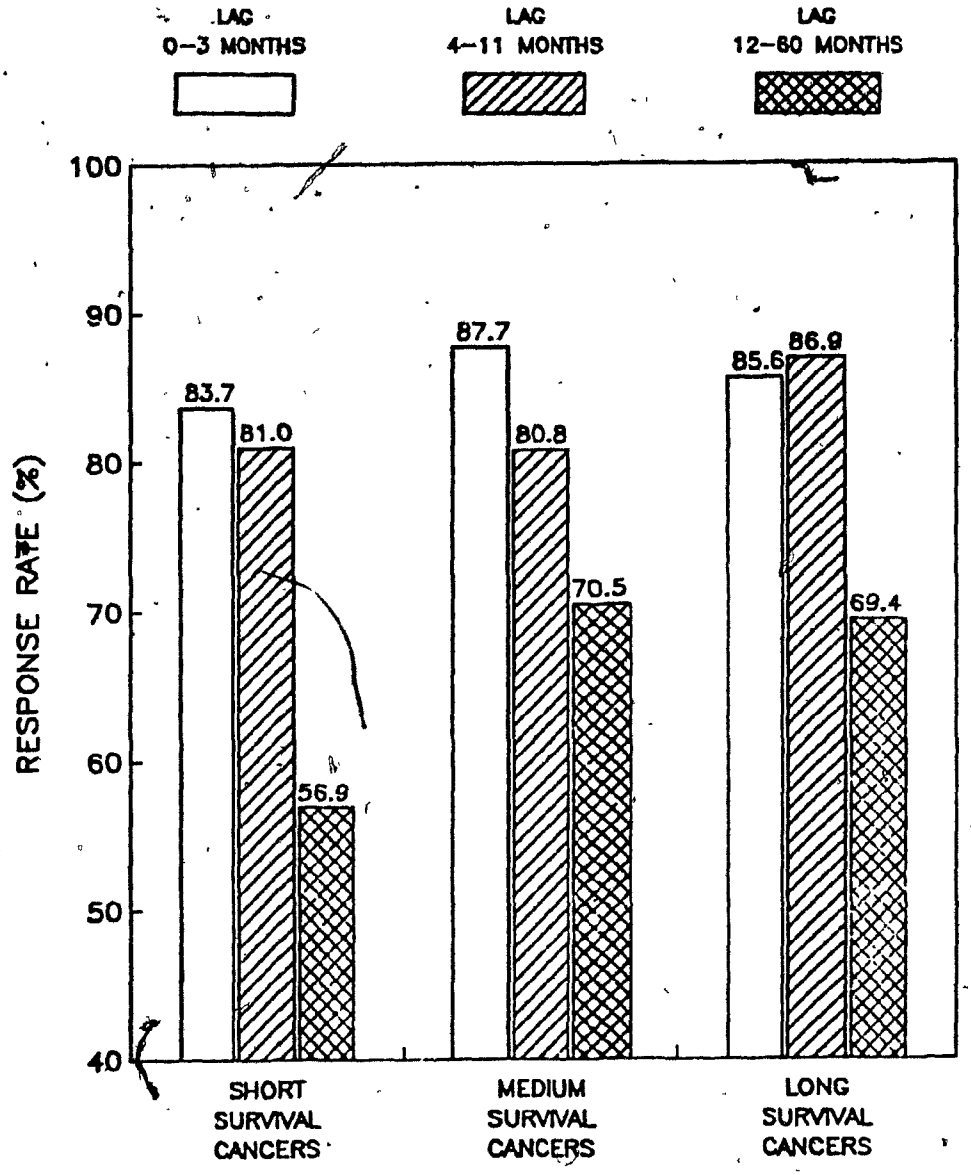
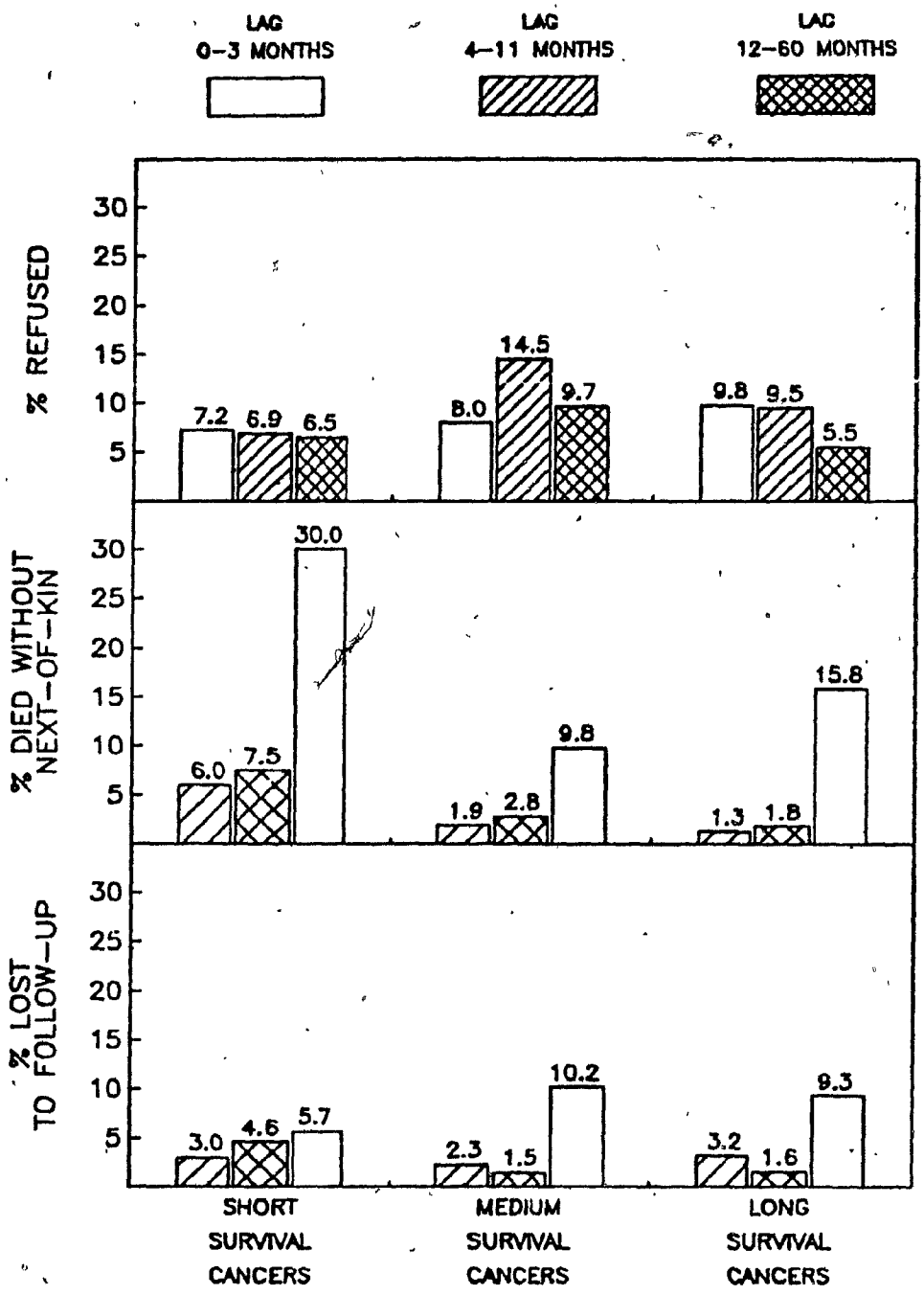


FIGURE B2

REASONS FOR NON-RESPONSE IN EACH OF THREE LAG TIMES FOR SITES OF CANCER WITH SHORT, MEDIUM AND LONG SURVIVAL



Interestingly the lowest value occurred in the group which was comprised largely of proxy respondents - namely sites with short survival and a lag of 12-60 months. Within each of the three survival groupings there were no differences between the 0-3 months and 4-11 months lags in percentage of subjects who died without next-of-kin or were lost to follow-up.

B.4.5 Quality of questionnaire data and lag

The response rates presented in the preceding tables included both self-and proxy respondents. On the reasonable assumption that subjects provide as good or better information about their job histories as do either their spouses or children, the most usual proxies, an important index of data quality is the percentage of all responses obtained from the subject himself. Thus, we compared the proportions of self-respondents obtained in each of the three lags. A second, complementary index of quality was the evaluation by chemist coders of the work histories provided by respondents. Table B17 shows the percentage of all completed questionnaires in which the patient himself provided the information. 76.4% of all respondents were self-respondents. Of the subset of completed questionnaires whose quality was scored by the chemists, 70.4% overall were judged to be of good quality.

Table B18 compares the proportion of self-respondents across the three lags and the proportion of work histories judged to be good. The effect of lag is immediately apparent. The proportion of self-respondents drops rapidly from 82.7% in the shortest lag to 68.8% in the second lag. Only 41.5% of responses in the longest lag were obtained from the subject himself. Similarly, the proportion of work histories judged to be of good quality decreases across the lags from 71.2% in the first lag to 67.6% in the second to 59.2% in the third. Because of the expected relationship between the proportion of self-respondents and the proportion of good work histories,

Table B17

INDICES OF QUALITY OF RESPONSE AMONG RESPONDENTS

Index of quality of response		
a)	Self-response:	
	Total number of respondents	3,322
	Number of self-respondents	2,538
	% of self-respondents	76.4
	S.E.**	0.7
b)	Quality of work history:	
	Number of work historical evaluated*	1,775
	Number considered to be of good quality	1,250
	% considered to be of good quality	70.4
	S.E.	1.1

* The chemists evaluated the subset of all work histories which were obtained between 1981 and 1983.

** SE: standard error based on binomial distribution.

Table B18

INDICES OF QUALITY OF RESPONSE AMONG RESPONDENTS BY LAG*

Index of quality of response	Lag time		
	0 - 3 months	4 - 11 months	12 - 60 months
a) Self-response			
Total number of respondents	2,540	356	430
Number of self-respondents	2,101	245	179
% of self-respondents	82.7	68.8	41.5
S.E.++	0.8	2.5	2.4
b) Quality of work histories			
Number of work histories evaluated**	1,521	189	65
Number considered to be of good quality	1,083	128	39
% considered to be of good quality+	71.2	67.6	59.2
S.E.	1.2	3.4	6.1

* Lag: time from date of diagnosis to first attempt to interview subjects.
** The chemists evaluated the subset of all work histories which were obtained between 1981 and 1983.
\+ These estimates were adjusted for year diagnosis.
++ S.E.: standard error based on binomial distribution.

we examined the relationship between lag and quality separately for self- and proxy respondents. Table B19 shows these findings.

Although part b of Table B18 showed a dramatic decrease in quality (i.e. "good" job descriptions) with increasing lag, the evidence from Table B19 suggests that this was largely a result of the confounding of lag with self-/proxy response, since for each of self- and proxy type of respondents, the variation in quality across lag periods is, at most, modest. In fact, among proxy respondents the quality was slightly higher in the longest lag group, though the numbers on which this was based were small and the estimates therefore imprecise.

B.4.6 Relationship between expected median survival, lag and type of respondent

Table B20 shows the proportion of self-respondents obtained in each lag for the short survival sites, medium survival sites and long survival sites, respectively. Among sites with less than six months expected median survival (short survival), the proportion of self-respondents decreased dramatically from 76.6% in the first lag to 53.9% in the second, to only 13.0% in the longest lag. For the two longer survival groups, the proportions of self-respondents were considerably higher in all three lags with only a marginal fall off in the frequency of self-respondents in the second as compared with the first lag and a larger fall off in the third (longest) lag period.

Table B19

PERCENT OF GOOD QUALITY WORK HISTORIES* BY

TYPE OF RESPONDENT AND LAG** TIME

Type of respondent		Lag time 0 - 3 months	4 - 11 months	12 - 60 months
Self:	N+	1,252	136	36
	%	76.1	73.0	68.6
	S.E.	1.2	3.8	7.7
Proxy:	N	269	53	29
	%	47.7	54.0	51.8
	S.E.	3.1	6.8	9.2

* The chemists evaluated the subset of all work histories which were obtained between 1981 and 1983.

** Lag: time from date of diagnosis to first attempt to interview subjects.

\+ N: denominator equals number of work histories evaluated by type of respondent and lag time.
%: % of N with good quality of work histories, adjusted for year of diagnosis.
S.E.: standard error based on binomial distribution.

Table B20

PERCENT OF SELF-RESPONDENTS BY LAG* FOR CANCERS OF SHORT, MEDIUM AND LONG SURVIVAL**

Site grouping**		Lag time		
		0 - 3 months	4 - 11 months	12 - 60 months
Short survival:	N+	989	163	164
	%	76.6	53.9	13.0
	S.E.	1.4	3.9	2.6
Medium survival:	N	546	57	88
	%	85.2	82.1	48.8
	S.E.	1.5	5.1	5.3
Long survival:	N	1,002	137	178
	%	87.4	81.5	62.4
	S.E.	1.1	3.3	3.6

* Lag: time from date of diagnosis to first attempt to interview subjects.

** Short survival: oesophagus, stomach, liver, pancreas, lung (expected median survival less than 6 months).
Medium survival: colon, rectum, kidney (expected median survival between 6 months and 2 years).
Long survival: prostate, bladder, non-Hodgkin's lymphoma, Hodgkin's lymphoma, melanoma of skin (expected median survival greater than 2 years).

\+ N: denominator equals total number of respondents in this category.
%: % of self-respondents among N.
S.E.: standard error based on binomial distribution.

B.5 DISCUSSION

B.5.1 The effect of lag on response rates

In the framework of our fieldwork protocol, the lag time had an important effect on response rates and response quality. For all 13 sites combined, there was little difference in response rates between patients contacted in lag 0-3 months and those contacted in lag 4-11 months; however, there was a 20% fall off in response if the lag exceeded 12 months. Furthermore the quality of data collected after 12 months lag, as judged by the percentage of self-response and the percentage with "good" quality work histories, declined dramatically. These declines in response rate and response quality were observed for sites of cancer with long survival as well as for those with short survival, although they were most pronounced for sites with short survival. It would seem, therefore, that for an interview-based cancer case-control study, such as the Montreal study, every effort should be made to achieve a lag of less than 12 months.

While the overall response rates did not differ much between lag 0-3 months and lag 4-11 months, this does not imply that the quality of data was equivalent. In fact the difference in quality was dependent on the type of tumour: For medium and long survival tumours, there was a minor reduction in data quality from lag 0-3 months to lag 4-11 months. However, for short survival tumours the reduction was very considerable. For the short survival sites therefore, it would clearly be preferable to aim at a short lag time between diagnosis and interview. It is of course not entirely surprising that losses due to death would occur more frequently if the lag were long. However, the potential argument in favour of a longer lag, namely that refusal rates would be higher in the early lag when a patient had just learned of his condition, did not turn out to be true. Or at least the slightly lower refusal rate after 12 months lag

compared with less than 12 months lag does not at all balance the opposite difference due to deaths and losses to follow-up.

In fact, the proportion of refusals was remarkably constant in the 5% to 10% range (with one outlier, probably due to chance) for the nine combinations of three groupings of sites and the three lags. This is in line with findings from most other cancer case-control studies among males in North America (listed in Table B1) and lends credence to the notion that there is a hard core refusal group. Since the psychological impact of the diagnosis of cancer and the imperative to deal with utmost sensitivity towards patients and their families make it unethical to engage in aggressive attempts to pursuade unwilling subjects to participate in research it would seem that the upper limit of response is around 95% for an interview-based study of incident cases. The beneficial impact of shorter lags is to reduce the number of nonrespondents due to "death without next-of-kin" and "lost to follow-up".

That higher nonresponse rates increase the likelihood of nonresponse bias is self-evident, and will be addressed more explicitly in Section C. However, it is worth considering here the potential for bias introduced by higher proportions of subjects who die without next-of-kin or who are lost to follow-up. Namely, it has been reported that subjects who are hard to trace because of residential mobility are more likely to be of the lower socio-economic class (Bright, 1969). In our data set, subjects who were lost to follow-up in fact were more likely to be from the low socio-economic group and were less likely to be married than those who responded. Subjects who died without next-of-kin also tended to be from the low socio-economic group, not married and heavy consumers of alcohol as compared with responders. It is these types of bias which may be reduced by means of a rapid case-ascertainment system and short lag.

B.5.2 Limitations to the generalizability of these findings

There are limitations to the generalizability of these findings. As noted in section A.1.2 there were limits to our patient tracing procedures. Most of the available resources were devoted to the case-ascertainment system, verification of diagnoses and interviewing. We were unable to engage in extensive tracing through the use of other data sources for patients who moved or the families of patients who died with no next-of-kin information noted in the medical record. Investigators who can afford to invest in this aspect of fieldwork should be able to improve on the response rates reported here, and the degree of improvement may differ according to lag. For instance, it is quite plausible that an intensive follow-up of relatives of dead patients would have substantially increased the response rate in the longest lag period from the 64% observed whereas such follow-up would only marginally have improved the response rate from the 86% observed in the shortest lag period.

The second limitation of generalizability concerns the relationship between self-/proxy response and quality of data. In our data, self-respondents provided better quality occupational descriptions than did proxy respondents. The relationship between self-/proxy response and quality of response may be quite specific to the type of questionnaire information being sought. For some situations the relative quality of proxy response would likely be even worse than in the Montreal study. As was argued in the Literature Review, for a study in which the respondent is requested to enumerate specific chemicals to which the subject was exposed at work, the quality of proxy response would be very questionable (Pershagen and Axelson, 1982; Selevan, 1980), whereas for studies like the Montreal study in which the respondent is requested to list the jobs a subject held with some nontechnical description of the nature of each job, the proxy may give more useful information. In other situations (e.g. diet histories) the relative quality of proxy response may yet be better than for the type of

questions on which the Montreal study was based (Enterline and Capt, 1959; Humble et al., 1984; Kolonel et al., 1977; Marshall et al., 1980). In the first situation, the need for a short lag, and consequently, less proxy response would be even greater than in the Montreal study. In the latter situation, the need could be relaxed somewhat, as long as the overall response rate were high combining self- and proxy response.

A third limitation concerns a specific condition of case-ascertainment in Quebec. Since there is a national health insurance system which provides hospitalization and medical care to all citizens with no out-of-pocket charges to the patient, there is no incentive for hospitals to maintain up-to-date records of addresses and next-of-kin information for billing purposes. In many other parts of North America, this would not be the case and an investigator could probably count on better information in hospital records for tracing. In our study, many of the lost to follow-up might have been recouped in the respondent's column, had the medical records been more up-to-date.

The fourth limitation concerns the study population. It is likely that the findings have direct relevance to the case series in case-control studies of adult males diagnosed with cancer in urban North America. Extrapolating further afield would be risky.

The final limitation is not so much a limitation of generalizability as a limitation of applicability which is obvious but nevertheless bears reiterating. The issues raised in this section are only of relevance to a case-control study in which the investigator has a choice about lag, that is, a study with prospective case-ascertainment.

3.5.3 Costs and benefits of a rapid case-ascertainment system

The logistics of obtaining a sample of cancer cases for an interview-based case-control study invariably entail time and money, regardless of the source of the cases. If a single source such as a Tumour Registry is used, rather than a network of hospitals, the costs of creating the sample frame can be kept to a minimum. In general, costs will increase as the number of sources for the cases increase. However, because of turnaround time, national or provincewide tumour registries are not typically able to provide investigators with patient identification before several months after diagnosis. Thus case-ascertainment via such a central registry does not usually permit a short lag option. The possibility of establishing a rapid case-ascertainment system will vary from place to place. In Montreal it took a year of negotiations and diplomacy to obtain the agreement and participation of the various hospitals (19 in all). Herrman et al. (1981) documented a similar experience for a study of colon cancer. This involved a great deal of the principal investigator's time plus about four months full-time equivalent of a research assistant's time.

There are considerable ongoing expenses involved in maintaining a rapid case-ascertainment system, which will in part be determined by the size of the population in the study and the number of hospitals involved. In the Montreal study the liaison with each pathology department and verification of pathology logs, tumour registry records and medical records took approximately 1.5 person years for each year of the study. Adding to this the cost of paying the pathology secretaries for reported cases, the approximate total cost of ascertainment and verification per case was $50 (Cdn). These costs were for the ascertainment of 13 sites of cancer in 19 hospitals. For studies involving fewer sites and/or hospitals, the unit costs might be quite different.

It is important to build good relations with the pathology department staff as rapidly as possible. From the start of the second year when our staff visited the hospitals regularly (sometimes two or three times a month in the larger institutions) we put a great deal of effort into developing relations with the pathology and records staff which paid off in the tremendous interest that they developed in the study. The case-ascertainment system improved steadily with time, as the staff in the hospitals became increasingly familiar with the eligibility criteria for the study and integrated the reporting into their routine. Certain small courtesies are very much appreciated such as Christmas cards, receiving copies of articles published on the study, etc. If we had started building these relations from the beginning of the study we would have had far fewer cases in the longer lag group. In our experience, the investigator must be actively involved in monitoring the case-ascertainment regardless of the quality of relations with the hospital staff. In the Montreal study the number of cases not reported by hospital staff and picked up in subsequent checks by our staff averaged out to one case per hospital per month.

In conclusion, we believe that the cost and effort involved in setting up and maintaining a rapid case-ascertainment system are well worth the increase in both quantity and quality of data that a strategy based on short lag can provide.

PART C

RESPONSE RATES AS A FUNCTION OF SIX SOCIO-DEMOGRAPHIC CHARACTERISTICS, AND NONRESPONSE BIAS

C.1 INTRODUCTION

The objective of this part of the study was to determine whether the level of nonresponse and socio-demographic characteristics of nonrespondents observed in an actual case-control study do in fact lead to bias in estimates of disease-exposure associations.

Nonresponse bias is a function of two parameters: the proportion of the target population that does respond (the response rate) and the extent to which respondents and nonrespondents differ. The closer an overall response rate is to 100% the less opportunity there is for nonresponse bias. Table C1, abstracted from Table B1 and representing those studies generated by a Medline search for cancer case-control studies among males in urban North America, shows the distribution of response rates. Response rates among case series have ranged from 50% to 90% with a majority in the 65% to 85% range. While it is possible to devise hypothetical situations where such levels of response combined with differential response among cases and controls in different categories of some putative risk factor would lead to substantial biases in estimates of association, it is generally unknown whether this actually occurs or not. It would thus be of interest to demonstrate empirically the presence or absence of nonresponse bias in an actual case-control study.

As shown above in Table B12, the response rates for the various sites in the Montreal study ranged from 60% to 90%, which corresponds to the range observed in other case-control studies. Thus the presence or absence of nonresponse bias in the Montreal study may be a useful guide to the dimension of the problem in many other studies.

Table C1

DISTRIBUTION OF RESPONSE RATES ACHIEVED AMONG CANCER CASE SERIES FROM SELECTED CASE-CONTROL STUDIES*

Response rate range	Number of studies with these rates
Less than 54%	6
55% - 59%	2
60% - 64%	2
65% - 69%	2
70% - 74%	5
75% - 79%	7
80% - 84%	4
85% - 89%	1
90% - 94%	1
95% - 100%	0

* A Medline search was carried out to identify all case-control studies published from 1970 to 1985 concerning cancer among males in urban North America. Only studies which reported response rates are included. For two multi-center studies, each study center was counted as a distinct study.

C.2 LITERATURE REVIEW

There has been some methodological work on the issue of factors related to nonresponse in various fields, notably marketing, sociology, public policy, public health and epidemiology. Almost all of this research has been among general populations of mainly healthy subjects. It is debatable whether this research is of any relevance for case-control studies. Certainly the context in which case-control studies are conducted, especially when dealing with life-threatening conditions such as cancer, differs radically from most other types of study. These differences may create reasons for nonresponse unlike those in a health survey. For example, the subject may be seriously ill. He may die before the investigator can reach him to request an interview or move away because of his condition. He may be depressed and despondent on having learned of his condition. In such a context the research team must approach sick subjects with extreme sensitivity, extending well beyond common courtesy. This may militate against the use of more insistent approaches that would be appropriate and that may effectively increase response rates in other types of study. On the other hand, the subject may have increased interest and motivation to participate in a study of the disease he has. He may in any case be a more captive audience for an interview request than would be a subject selected for a general population survey. Thus both the investigators' strategy for obtaining responses and the study subjects' reactions to a request to participate are likely to differ between the case-control situation and the general population survey. For these reasons it would be unwise to assume that the findings on nonresponse bias reported by researchers dealing with general populations can routinely be transferred to the cancer case-control study situation.

Unfortunately, however, there is virtually no published literature on nonresponse in cancer case-control studies. Therefore, we extended our review of nonresponse to the general health survey and epidemiologic literature despite the questionable relevance of findings in these areas for the case-control situation. In this chapter we will first review the major findings in interview-based health surveys concerning socio-demographic factors and patterns of nonresponse. We will omit from consideration the literature concerned with mail surveys, since the determinants of response to this format are likely very different. For the interested reader, useful reviews of determinants of response rate in mail surveys have been provided by Scott (1961), Kaplan and Cole (1970), and Siemiatycki (1976). We will then discuss the theoretical framework developed by Criqui (1979) and Criqui et al. (1979) which clarifies the mechanism by which nonresponse may bias risk estimates derived from a fourfold table.

C.2.1 Response rates as a function of socio-demographic characteristics in health related research

In order to assess the impact of socio-demographic factors on response rates, the researcher must have access to some information on all subjects in the target population. Typically, the health survey investigator knows little about the individual members of the target population until they are interviewed and thus there is little opportunity to compare respondents and nonrespondents. In a case-control study, some background information may sometimes be available from medical records. We found reference to only two published investigations comparing respondents with nonrespondents in case-control studies. These are presented in Tables C2 and C3.

The Third National Cancer Survey (TNCS) conducted by the US National Cancer Institute, attempted to establish the frequency and distribution of incident

Table C2

DISTRIBUTION OF DESCRIPTIVE VARIABLES FOR INTERVIEW RESPONDENTS VERSUS 10% TARGET POPULATION IN THE THIRD NATIONAL CANCER SURVEY (U.S.)*

Variable	Target population %	Respondent population %
Sex:		
Male	49.6	47.1
Female	50.4	52.9
Race:		
White	88.3	87.5
Black	10.1	10.9
Other	1.6	1.0
10 year age groups:		
35 - 44	6.5	7.0
45 - 54	16.6	17.6
55 - 64	24.2	24.1
65 - 74	25.8	25.2
75 - 84	18.0	16.8
85 +	4.1	3.7
Marital status:		
Married	61.6	62.4
Widowed	22.3	21.8
Separated	1.3	1.1
Divorced	4.8	5.1
Single	9.2	9.0
Unknown	0.7	0.6
Vital status:		
Alive	48.0	54.4
Dead	52.0	45.6

* Source: Williams et al., 1977. Patient interview study from the Third National Cancer Survey: overview of problems and potential of these data. J.N.C.I. 58(3):519-524.

Table C3

PERCENT OF BLADDER CANCER CASES INTERVIEWED
BY SEX AND AGE IN THE
NATIONAL BLADDER CANCER STUDY (U.S.)*

Variable	Cases interviewed	
	%	Number
Sex:		
Male	75	3,016
Female	69	1,070
Age (years):		
21-34	68	57
35-44	82	111
45-54	85	396
55-64	79	997
65-74	75	1,375
75-84	61	1,150
Total	73	4,086

* Hartge et al. (1983). Design and methods in a multi-center case-control interview study. Am. J. Publ. Hlth. 74(1):52-56.

cancer in the United States (Williams et al., 1977). Incident cases of all sites (excluding superficial skin cancer) were ascertained in nine geographic areas of the US, between 1969 and 1971. Within the TNCS a case-control interview study was conducted. A 10% representative sample of all cases reported to the TNCS was selected as the target population for the study. The overall response rate for eight centres was 57% (the New Jersey response rates were not included). Table C2 compares respondents to the interview study with the case-control target population on selected socio-demographic factors that had been collected from medical records for all subjects in the TNCS study. There appears to be no important difference between interviewed subjects and the entire target population on those socio-demographic factors presented. The authors interpreted this as suggesting that despite the overall low response rates there is little likelihood of nonresponse bias, at least on these factors. However, this interpretation, based on response rates by risk factor characteristics, is not a foolproof guide to nonresponse bias in odds ratios, as will be discussed in section C.2.3.

A second case-control study, the National Bladder Cancer Study (Hartge et al., 1984), was able to examine response rates in relation to sex and age. There was a somewhat higher response rate for male cases (75%) than female cases (69%), and higher rates among subjects aged 35-64 (81%) than for those older than 65 (68%). Neither of these two studies analysed these data further to assess whether estimates of risk were affected by the response rates, leaving the question of nonresponse bias open.

The one type of epidemiological design which does provide the requisite material and which in fact has been the main area of empiric research into factors related to nonresponse in epidemiology is the prospective follow-up study. Typically

data have been collected at some baseline point in time and subsequent periodic attempts to interview the same subjects have been made. Although there may be some nonresponse at the very first stage, this would not be formally assessed. Rather, investigators have taken the respondents at the first stage as the entire target sample for subsequent stages and assessed response rates and levels of nonresponse in subsequent stages as a function of socio-demographic and health related characteristics of this initial target sample. The terms participation and nonparticipation will be reserved for those studies in which subjects were asked to undergo clinical observation or to engage in health enhancement activities. The terms response and nonresponse will have a more general usage; response will encompass both participation as defined above and response to a questionnaire. The most consistently observed factor associated with nonresponse in the studies appears to be cigarette smoking (Burgess and Tierney, 1970; Criqui et al., 1978; Doll and Bradford Hill, 1964; Oakes et al., 1973; Seltzer et al., 1975). Smokers tend not to respond at all or to respond only after repeated attempts to elicit participation. Another factor associated with nonresponse was age. In three studies (Criqui et al., 1978; Napier, 1962; Wilhelmsen et al., 1976), the older age groups participated significantly less than younger subjects. The Swedish primary prevention trial (Wilhelmson et al., 1976), the Framingham Heart Study (Gordon et al., 1959) and the Honolulu Heart Program (Heilbrun et al., 1982) compared mortality amongst participants and nonparticipants and found higher rates of mortality amongst nonparticipants from heart disease, cancer and all causes. These findings may be a reflection of the aforementioned association of both smoking and older age with nonparticipation.

Only three studies (the Swedish study, NHANES II (Forthoffer, 1983; Cobb et al., 1957)) reported differential participation by socio-demographic characteristics other than smoking and older age. In Sweden (Wilhelmson et al., 1976) subjects who

consumed more alcohol, were unmarried, or had lower incomes were more likely not to participate (i.e. more likely to refuse or be untraceable). In the NHANES II project (Forthoffer, 1983) unmarried subjects, those who lived in the Northeast and those living in cities were less likely to participate, while in Pittsburgh (Cobb et al., 1956) nonparticipants were more likely to be from single person or large families.

Each of these prospective studies comprised follow-up of a generally "healthy" population. The researchers wished either to elicit information relating to health from the subjects, to conduct a clinical examination or to enlist participation in some activity designed to improve the health status of the subjects. The association between nonparticipation and those factors which are strongly associated with increased morbidity and early death, smoking in particular, may merely reflect a general attitude towards health related matters. In fact the phenomenon of overrepresentation of health conscious subjects in the participants' group has come to be known as the "worried well" phenomenon (Criqui et al., 1978). This phenomenon is not relevant to a study of subjects who are already seriously ill.

The Commission on Chronic Illness Morbidity Survey in Baltimore (Bright, 1969) was specifically able to investigate one form of nonresponse: subjects lost to the study because of residential mobility. They compared the proportions of subjects who proved difficult to trace in different socio-economic groups. Those subjects who had moved and proved untraceable were more likely to be from the lower socio-economic group.

Although the evidence from these prospective studies indicates that respondents differ from nonrespondents, and constrasts with the findings from the two case-control studies which did not provide any evidence of difference on the factors

reported, the data are limited and therefore fragile. Nonresponse patterns in case-control studies clearly need further investigation.

C.2.2 Estimating nonresponse bias

It was Berkson (1946) who first discussed the concept of bias in the use of 2 x 2 tables to infer associations. The particular example he cited demonstrated how selection bias in the choice of cases and controls could create a spurious association. However, his purpose was to raise the more general issue which Mantel and Haenszel (1959) articulated as follows: "The fundamental assumption underlying this technique (the case-control study) is that the assembled cases and controls are representative of the universe defined for investigation". In other words the odds of being exposed among respondent cases must reflect the odds among all cases in the universe under study and similarly the odds of being exposed among respondent controls must reflect that among all controls in the universe under study. For the purpose of this report we will assume that the target population as defined by the study design is representative of the universe and that bias would ensue only if the sample of subjects for whom responses are obtained are not representative of the target population.

Nonresponse bias was not addressed in theoretical terms until Greenland (1977) broached the subject in relation to cohort studies. He showed that although lost subjects might be evenly distributed across exposure categories in a cohort study, the relative risk extimates could be biased if the lost subjects were not equally distributed across the disease outcome categories.

In a series of papers Criqui (1979), and Greenland and Criqui (1981) developed a theoretical framework within which to consider nonresponse bias in both case-control and cohort studies. Before proceeding it will be useful to introduce the

following notation. Let the 2 x 2 table for the target population in a case-control study be denoted as follows:

	Case	Control	
Exposed	a_t	b_t	$a_t + b_t$
Unexposed	c_t	d_t	$c_t + d_t$
	$a_t + c_t$	$b_t + d_t$	

and the 2 x 2 table for the respondents as follows:

	Case	Control	
Exposed	a_r	b_r	$a_r + b_r$
Unexposed	c_r	d_r	$c_r + d_r$
	$a_r + c_r$	$b_r + d_r$	

The target odds ratio: $$OR_t = \frac{a_t d_t}{b_t c_t}$$

The respondent odds ratio: $$OR_r = \frac{a_r d_r}{b_r c_r}$$

If OR_r departs from OR_t there is nonresponse bias.

By means of a series of hypothetical examples, Criqui (1979) showed that equality or inequality of marginal response rates has no direct implication for the

likelihood of nonresponse bias. That is, if response rates are equal for cases and controls,

$$\frac{a_r + c_r}{a_t + c_t} = \frac{b_r + d_r}{b_t + d_t},$$

or if response rates are equal for the exposed and unexposed,

$$\frac{a_r + b_r}{a_t + b_t} = \frac{c_r + d_r}{c_t + d_t},$$

this does not imply that there will be nonresponse bias. The following hypothetical example shows that even if both sets of marginal response rates are equal, it does not guarantee lack of nonresponse bias. Suppose that $a_t = b_t = c_t = d_t = 100$, so that the true $OR_t = 1.0$. Suppose that the interview attempt produces the following configuration: $a_r = 80$, $b_r = 60$, $c_r = 60$, $d_r = 80$. It is easily verified that all four marginal response rates equal 70% but that the odds ratio based on respondents $OR_r = 1.8$.

In a similar fashion it can be shown that it is possible to have inequality of marginal response rates but no nonresponse bias in the odds ratio. The reader can verify that the following configuration will have such an effect: $a_r = 90$, $b_r = 60$, $c_r = 60$, $d_r = 40$.

The condition under which bias does occur can be derived from the relationship

$$OR_r / OR_t = \frac{a_r d_r}{b_r c_r} \Big/ \frac{a_t d_t}{b_t c_t}$$

$$\text{Thus, } OR_r/OR_t = \frac{a_r}{a_t} \times \frac{d_r}{d_t} \Big/ \frac{b_r}{b_t} \times \frac{c_r}{c_t} = \frac{Pa \times Pd}{Pb \times Pc}$$

$$\text{where } Pa = \frac{a_r}{a_t}, \quad Pb = \frac{b_r}{b_t}, \quad Pc = \frac{c_r}{c_t}, \quad Pd = \frac{d_r}{d_t}.$$

Thus, there is an error term which we will refer to as the "bias factor" which equals:

$$\frac{PaPd}{PbPc}$$

This bias factor is, in effect, an odds ratio of the response rates in the fourfold table. It is clear that when this bias factor equals 1.0, the OR_r will equal the OR_t and no bias is present. When the error term is less than 1.0 the respondent odds ratio is an overestimate of the "true" association present in the target population; conversely an error term greater than 1.0 will indicate an underestimate of the "true" association.

These theoretical developments have shown that we cannot assume an unbiased estimate will be derived from respondents because lost subjects are equally distributed across either the exposure or the disease categories. Nor can we assume that inequality of marginal response rates by disease status or by exposure status will necessarily lead to biased odds ratio estimates. Therefore an evaluation of non-response bias should be based not simply on marginal response rate differences in the exposure or disease categories but rather must take into consideration the effect of differences in response rates in each cell of the fourfold table. This is the principle upon which our evaluation of nonresponse bias will be based.

C.3 METHODS

C.3.1 Collection of data on six socio-demographic factors for all eligible subjects in the Montreal study

To compare nonrespondents and respondents on certain key variables and to estimate the extent of possible nonresponse bias, we abstracted information from the medical records of all subjects eligible for the Montreal case-control study regardless of their response status. Certain information was available for all these individuals and included the following variables: site and histologic type of cancer; age at diagnosis; and a crude estimate of socio-economic status based on average income of the census tract of residence*.

Further information sought from the medical records concerned ethnicity, marital status, smoking habits and alcohol consumption. However, because such information is not routinely recorded in all medical records, we could not use all target subjects to compute response rates by these subcategories. Table C4 shows the percentage of the target population for whom information was available for each variable. Because information on marital status, ethnicity and cigarette and alcohol use was collected solely for the purpose of this thesis and only began in the second year of the Montreal study first year patients are excluded from the comparisons of respondents and nonrespondents on these variables.

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* The census tract for each patient is derived from his address. For each census tract a mean income is calculated by Statistics Canada. Since one of the criteria for delineation of census tracts is social homogeneity of the population, we feel that the latter is an adequate, albeit imprecise, indication of socio-economic status.

Table C4

SUMMARY OF SOCIO-DEMOGRAPHIC VARIABLES ON WHICH THE RESPONDENTS ARE COMPARED TO NONRESPONDENTS

Factor	% of target population with information	Subgroups for each factor
Age	100	35-59 60-70
Mean census tract income	100	less than $17,999 $18,000 - 26,999 more than $27,000
Marital status	80	married not married (divorced, separated, widowed, single),
Ethnic group	84	French English Italian Jewish Other
Cigarette smoking	70	nonsmoker smoker
Alcohol consumption	64	never social heavy

C.3.2 The influence of socio-demographic characteristics on response rates

To assess the influence of the six socio-demographic factors on response rates, we established different subgroups for each variable. The guiding principle was to create the fewest possible subgroups, so as to optimise the statistical precision of our comparisons, while keeping separate subgroups that should not be lumped together.

The median age in our population was 61 and we simply dichotomised the population into those aged 35-59 and those aged 60-70. Income was divided into three groups based on the income distribution in the target population using a ratio 25:50:25. Marital status was also dichotomised: all married subjects were compared to a group comprised of all who were not married because there were too few subjects in each of the individual "unmarried" categories (single, widowed, divorced, separated) to enable meaningful comparisons. The ethnic group categories were chosen to reflect the two main linguistic groups in Montreal - French and English - and the two most prominent cultural/linguistic minority groups - Italians and Jews. People of all other linguistic and cultural origins were classified together. Unfortunately, the data available from medical records on both cigarette smoking and alcohol consumption were quite crude. Thus we were only able to distinguish "ever smokers" from "never smokers"; and "never consumed alcohol" from "ever social consumption" and "ever heavy consumption". Table C4 shows the cutpoints used for each variable.

Response rates were computed for the socio-demographic subgroups of patients for each cancer site separately. Because of potential confounding between any of the socio-demographic variables and the lag time between diagnosis and attempt to interview, we computed response rates for different subgroups after adjusting for lag. The adjustment procedure was based on the additive model described in section B.3.3

and was carried out using the SPSS ANOVA Multiple Classification Analysis (Nie et al., 1975). Analogous estimates were made for all sites combined, adjusting simultaneously for both lag and site distributions in the different socio-demographic subgroups. Standard errors were derived from the crude response rates, based on the assumption of a binomial distribution, since there was very little difference between the crude and adjusted rates.

C.3.3 Determining nonresponse bias

In contrast with the conventional approach of comparing marginal rates between cases and controls, or between exposed and not exposed, which as was shown in section C.2.2, can be a misleading guide to nonresponse bias, we addressed directly the issue of nonresponse bias in the estimates of association between risk factors and each site of cancer in the study. The most commonly used measure of association between disease and exposure in a case-control study is the odds ratio. If the odds of exposure among cases and controls for respondents do not differ from those in the target population then the odds ratio estimated in the respondent group will equal that in the target population and thus, the ratio of the two odds ratios, which we will refer to as the bias factor, should equal 1. Under these conditions one could conclude that nonresponse bias is absent. We may define the bias factor as: $B = OR_r/OR_t$.

To assess nonresponse bias we considered each socio-demographic subgroup as a distinct exposure (risk factor) and chose one level of each characteristic as the referrent category. Table C5 shows the exposure and referrent categories for each socio-demographic factor. There were 11 exposure/referent category combinations for risk factors. Only the nine cancer sites with at least 100 subjects interviewed were included in this analysis (Table C6), thereby yielding a total of 99 associations. For each cancer site series, all other cancer sites served as controls.

Table C5

LEVELS FOR "EXPOSED" AND "REFERRENT" SUBGROUPS WITHIN THE SIX SOCIO-DEMOGRAPHIC FACTORS USED IN THE ANALYSIS OF NONRESPONSE BIAS

Socio-demographic factor	"Exposed"		"Referrent group"
Age	less than 60	vs	greater than 60
Income	low	vs	medium
	high	vs	medium
Ethnic group	English	vs	French
	Italian	vs	French
	Jewish	vs	French
	Other	vs	French
Marital status	married	vs	not married
Smoking	smokers	vs	nonsmokers
Alcohol consumption	social drinkers	vs	nondrinkers
	heavy drinkers	vs	nondrinkers

Table C6

SITES INCLUDED IN THE ANALYSIS OF NONRESPONSE BIAS

Stomach
Colon
Rectum
Lung
Prostate
Bladder
Kidney
Lymphoma
Melanoma

Using a program designed to handle large numbers of odds ratio calculations (Dewar and Siemiatycki, 1985), we calculated the 99 odds ratios first for the respondent population only and then for the entire target population. For each of the 99 associations we then computed the bias factor, OR_r/OR_t. The distribution of the bias factors was examined next.

Some of the odds ratio estimates were unstable (that is they had large standard errors) because of small numbers in one or more of the cells of the 2 x 2 tables. We therefore excluded from further consideration any estimates based on 2 x 2 tables with less than 15 cases in any of the cells or for which the log of the variance of the odds ratio exceeded 0.1. The bias factors were calculated and the distribution of bias factors was examined for those associations which provided stable odds ratio estimates.

Estimation of standard errors, or any other form of formal statistical inference for the bias factors themselves has not been discussed in the literature. The development of such methods was considered beyond the scope of this research, in which we have preferred to rely on an informal approach to statistical inference, facilitated by the exclusion of unstable odds ratios as described above.

The total respondent population includes both self- and proxy respondents. The use of proxy respondents may not be advisable for all study designs. If only self-respondents are accepted then overall response rates may be considerably lower and the opportunity for nonresponse bias possibly higher. To assess the risk of nonresponse bias under a self-respondent rule, we therefore repeated the above analyses excluding proxy respondents from the respondent population.

C.4 RESULTS

Table C7 shows for all sites combined the overall response rates for each subgroup of the six socio-demographic variables. Examining the adjusted response rates, and keeping in mind the corresponding standard errors, we make the following observations. Response rates were very slightly higher among the young than the old. The poor had lower response rates than the wealthy and middle income groups. Jewish subjects had particularly low response rates, while subjects of Italian origin had particularly high response rates. Detailed analyses showed that the nonresponse among Jewish subjects was concentrated in the "refusal" category (20%) rather than in "dead" (0%) or "lost to follow-up" (2.8%) categories. Married subjects provided much higher response rates than unmarried, with the difference being concentrated in the "dead" and "lost to follow-up" categories. There were no differences between smokers and nonsmokers and a slight suggestion of lower response among heavy alcohol drinkers.

Case-control studies of cancer are typically carried out among patients with tumours at a specific site as the case series. Therefore we looked at patterns of response for specific sites of cancer. Appendix Tables 1 through 9 are analogous to Table C7 and present for each of the nine sites with over 400 eligible cases, the response rates by socio-demographic subgroups. Where the numbers in the subgroup were sufficiently large to provide reasonably precise estimates, the patterns of response rates by socio-demographic subcategories were similar for the individual sites to those observed in Table C7 for all sites combined.

However, the comparisons of response rates in the various subgroups of each socio-demographic factor do not provide a reliable guide to potential nonresponse bias.

Table C7

RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION

Socio-demographic characteristic	N***	Unadjusted response rate* %	Adjusted response rate** %	S.E.
Age:				
35 - 59	1,264	83.2	82.5	1.1
60 +	1,729	80.5	80.9	1.0
Mean census tract income:				
$15,999	886	72.3	77.9	1.5
16,000 - 26,999	1,476	86.2	83.8	0.9
27,000	632	83.8	81.7	1.5
Ethnic group:				
French	1,589	82.1	82.5	1.0
English	397	78.2	79.2	2.1
Italian	155	90.3	88.7	2.4
Jewish	172	74.1	70.6	3.3
Other	228	84.1	83.3	2.4
Marital status:				
Married	1,903	83.7	83.7	0.9
Non married	536	74.2	74.1	1.9
Cigarette smoking:				
Nonsmokers	289	80.7	80.6	2.3
Smokers	1,875	81.7	81.8	0.9
Alcohol consumption				
Never	259	82.7	83.0	2.4
Social	411	84.6	83.3	1.8
Heavy	586	79.8	79.8	1.7

* Crude response rate in each subcategory.

** Response rate estimates were adjusted for site and lag.

*** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

As explained in section C.3.3, we computed odds ratios between 11 "risk factors" and nine sites of cancer, and we did this first for all eligible subjects and then for respondents only. Tables C8 through C16 (one table per site of cancer) present the two sets of odds ratios and the corresponding ratio of odds ratios, or bias factor. The absolute values of the odds ratios themselves are not the items of concern; rather it is the ratio of the two odds ratios that addresses the issue of bias. A ratio of 1.0 indicates no bias, while a departure from 1.0, in either direction indicates some bias.

Some of the 99 pairs of odds ratios were based on very small numbers and consequently the difference between the OR_t (odds ratio for the entire target population) and the OR_r (odds ratio among respondents only) might easily have been due to the instability of the OR estimates, rather than to nonresponse bias per se. As described in section C.3.3 to minimize the impact of sampling variation we decided to ignore the bias factor estimates which were based on unstable odds ratios - the criteria for instability were described in section C.3.3. The associations which were thus eliminated from further consideration are denoted in Tables C8 through C16 by parentheses. Seventy-five associations remained.

Figure C1 synthesizes the results of Tables C8 through C16 by showing the distribution of the 75 bias factors based on "stable" odds ratio estimates. It should be emphasized that the direction of the difference in the OR_r/OR_t ratio is immaterial here; it is merely a reflection of the choice of risk factor categories designated as "exposed" and "unexposed". Simply switching them around would have the effect of producing a bias factor which is the reciprocal. Thus, what we are interested in is how often the bias factor falls outside some symmetric range about 1.0. None of the bias factors were outside the range from 1/1.4 to 1.4. This is highlighted in Table C17

Table C8

ASSOCIATIONS BETWEEN STOMACH CANCER AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
Age:			
Over 60 vs under 60	0.90	0.88	1.02
Income:			
Low vs medium	0.60	0.69	0.87
High vs medium	0.85	0.91	0.93
Ethnic group:			
English vs French	0.89	0.98	0.91
Italian vs French	(1.46)*	(1.81)	(0.81)
Jewish vs French	(0.98)	(0.99)	(0.99)
Other vs French	1.97	2.39	0.82
Marital status:			
Married vs non married	1.24	1.34	0.93
Cigarette smoking:			
Smokers vs nonsmokers	0.80	0.64	1.25
Alcohol consumption:			
Social vs never	0.73	0.60	1.22
Heavy vs never	0.71	0.63	1.13

* If any cell contained less than 15 cases or the log odds variance was greater than 0.1, the resulting estimate was considered to be unstable. Estimates in brackets were eliminated from further consideration in the distribution of bias factors.

Table C9

ASSOCIATIONS BETWEEN COLON CANCER AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
Age:			
Over 60 vs under 60	1.20	1.20	1.00
Income:			
Low vs medium	1.14	1.05	1.09
High vs medium	1.24	1.22	1.02
Ethnic group:			
English vs French	1.33	1.44	0.92
Italian vs French	1.37	1.45	0.94
Jewish vs French	1.38	1.83	0.75
Other vs French	0.98	0.86	1.14
Marital status:			
Married vs non married	1.06	1.10	0.96
Cigarette smoking:			
Smokers vs nonsmokers	0.55	0.53	1.04
Alcohol consumption:			
Social vs never	0.84	0.82	1.02
Heavy vs never	0.69	0.72	0.96

Table C10

ASSOCIATIONS BETWEEN RECTAL CANCER AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
Age:			
Over 60 vs under 60	0.87	0.87	1.00
Income:			
Low vs medium	1.06	0.96	1.10
High vs medium	1.07	0.99	1.08
Ethnic group:			
English vs French	1.18	1.20	0.98
Italian vs French	(1.58)*	(1.71)	(0.92)
Jewish vs French	(0.91)	(0.83)	(1.10)
Other vs French	(1.36)	(1.17)	(1.16)
Marital status:			
Married vs non married	0.83	0.94	0.88
Cigarette smoking:			
Smokers vs nonsmokers	0.55	0.53	1.04
Alcohol consumption:			
Social vs never	(1.37)	(1.40)	(0.98)
Heavy vs never	(1.16)	(1.14)	(1.02)

* If any cell contained less than 15 cases or the log odds variance was greater than 0.1, the resulting estimate was considered to be unstable. Estimates in brackets were eliminated from further consideration in the distribution of bias factors.

Table C11

ASSOCIATIONS BETWEEN LUNG CANCER AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
Age:			
Over 60 vs under 60	1.01	1.02	0.99
Income:			
Low vs medium	0.77	0.82	0.94
High vs medium	0.60	0.60	1.00
Ethnic group:			
English vs French	0.75	0.66	1.14
Italian vs French	0.51	0.47	1.09
Jewish vs French	(0.27)*	(0.21)	(1.29)
Other vs French	0.91	0.79	1.15
Marital status:			
Married vs non married	0.77	0.72	1.07
Cigarette smoking:			
Smokers vs nonsmokers	(17.46)	(17.49)	(0.94)
Alcohol consumption:			
Social vs never	0.75	0.82	0.91
Heavy vs never	1.68	1.85	0.91

* If any cell contained less than 15 cases or the log odds variance was greater than 0.1, the resulting estimate was considered to be unstable. Estimates in brackets were eliminated from further consideration in the distribution of bias factors.

Table C12

ASSOCIATIONS BETWEEN PROSTATE CANCER AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
Age:			
Over 60 vs under 60	3.15	3.06	1.03
Income:			
Low vs medium	1.05	0.90	1.17
High vs medium	0.88	0.83	1.06
Ethnic group:			
English vs French	1.05	1.03	1.02
Italian vs French	(0.46)*	(0.46)	(1.00)
Jewish vs French	0.98	1.04	(0.94)
Other vs French	(0.49)	(0.71)	(0.69)
Marital status:			
Married vs non married	1.32	1.15	1.15
Cigarette smoking:			
Smokers vs nonsmokers	0.62	0.65	0.95
Alcohol consumption:			
Social vs never	1.61	1.67	0.96
Heavy vs never	0.71	0.71	1.00

* If any cell contained less than 15 cases or the log odds variance was greater than 0.1, the resulting estimate was considered to be unstable. Estimates in brackets were eliminated from further consideration in the distribution of bias factors.

Table C13

ASSOCIATIONS BETWEEN BLADDER CANCER AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
Age:			
Over 60 vs under 60	0.98	0.96	1.02
Income:			
Low vs medium	1.27	1.05	1.21
High vs medium	1.34	1.38	0.97
Ethnic group:			
English vs French	0.98	0.95	1.03
Italian vs French	1.10	1.09	1.01
Jewish vs French	1.39	1.66	0.84
Other vs French	1.14	1.19	0.96
Marital status:			
Married vs non married	1.32	1.38	0.96
Cigarette smoking:			
Smokers vs nonsmokers	1.54	1.31	1.18
Alcohol consumption:			
Social vs never	1.05	1.11	0.95
Heavy vs never	1.05	0.86	1.22

Table C14

ASSOCIATIONS BETWEEN KIDNEY CANCER AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
Age:			
Over 60 vs under 60	0.69	0.73	0.95
Income:			
Low vs medium	0.84	1.12	0.75
High vs medium	1.10	1.20	0.92
Ethnic group:			
English vs French	1.08	1.01	1.07
Italian vs French	(1.18)*	(0.95)	(1.24)
Jewish vs French	(2.05)	(1.74)	(1.18)
Other vs French	(1.26)	(1.17)	(1.08)
Marital status:			
Married vs non married	1.05	1.16	0.91
Cigarette smoking:			
Smokers vs nonsmokers	0.45	0.49	0.92
Alcohol consumption:			
Social vs never	1.55	1.26	1.23
Heavy vs never	1.15	1.03	1.12

* If any cell contained less than 15 cases or the log odds variance was greater than 0.1, the resulting estimate was considered to be unstable. Estimates in brackets were eliminated from further consideration in the distribution of bias factors.

Table C15

ASSOCIATIONS BETWEEN MELANOMA AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
Age:			
Over 60 vs under 60	0.41	0.39	1.05
Income:			
Low vs medium	0.93	0.91	1.02
High vs medium	1.79	2.10	0.85
Ethnic group:			
English vs French	2.73	3.10	0.88
Italian vs French	(2.45)*	(2.41)	(1.02)
Jewish vs French	(4.01)	(4.41)	(0.91)
Other vs French	(1.63)	(1.80)	(0.91)
Marital status:			
Married vs non married	1.30	1.74	0.75
Cigarette smoking:			
Smokers vs nonsmokers	0.16	0.17	0.94
Alcohol consumption:			
Social vs never	(1.01)	(1.24)	(0.81)
Heavy vs never	(0.16)	(0.14)	(1.14)

* If any cell contained less than 15 cases or the log odds variance was greater than 0.1, the resulting estimate was considered to be unstable. Estimates in brackets were eliminated from further consideration in the distribution of bias factors.

Table C16

ASSOCIATIONS BETWEEN NON-HODGKIN'S LYMPHOMA AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
Age:			
Over 60 vs under 60	0.58	0.58	1.00
Income:			
Low vs medium	1.04	1.18	0.88
High vs medium	1.34	1.32	1.02
Ethnic group:			
English vs French	0.91	0.92	0.99
Italian vs French	(0.94)*	(0.79)	(1.19)
Jewish vs French	(1.48)	(1.06)	(1.40)
Other vs French	(0.89)	(0.59)	(1.51)
Marital status:			
Married vs non married	1.55	1.28	1.21
Cigarette smoking:			
Smokers vs nonsmokers	0.67	0.62	1.08
Alcohol consumption:			
Social vs never	0.60	0.56	1.07
Heavy vs never	0.49	0.44	

* If any cell contained less than 15 cases or the log odds variance was greater than 0.1, the resulting estimate was considered to be unstable. Estimates in brackets were eliminated from further consideration in the distribution of bias factors.

FIGURE C1

DISTRIBUTION OF BIAS FACTORS DUE TO NON-RESPONSE IN 75 ASSOCIATIONS FOR ALL RESPONDENTS

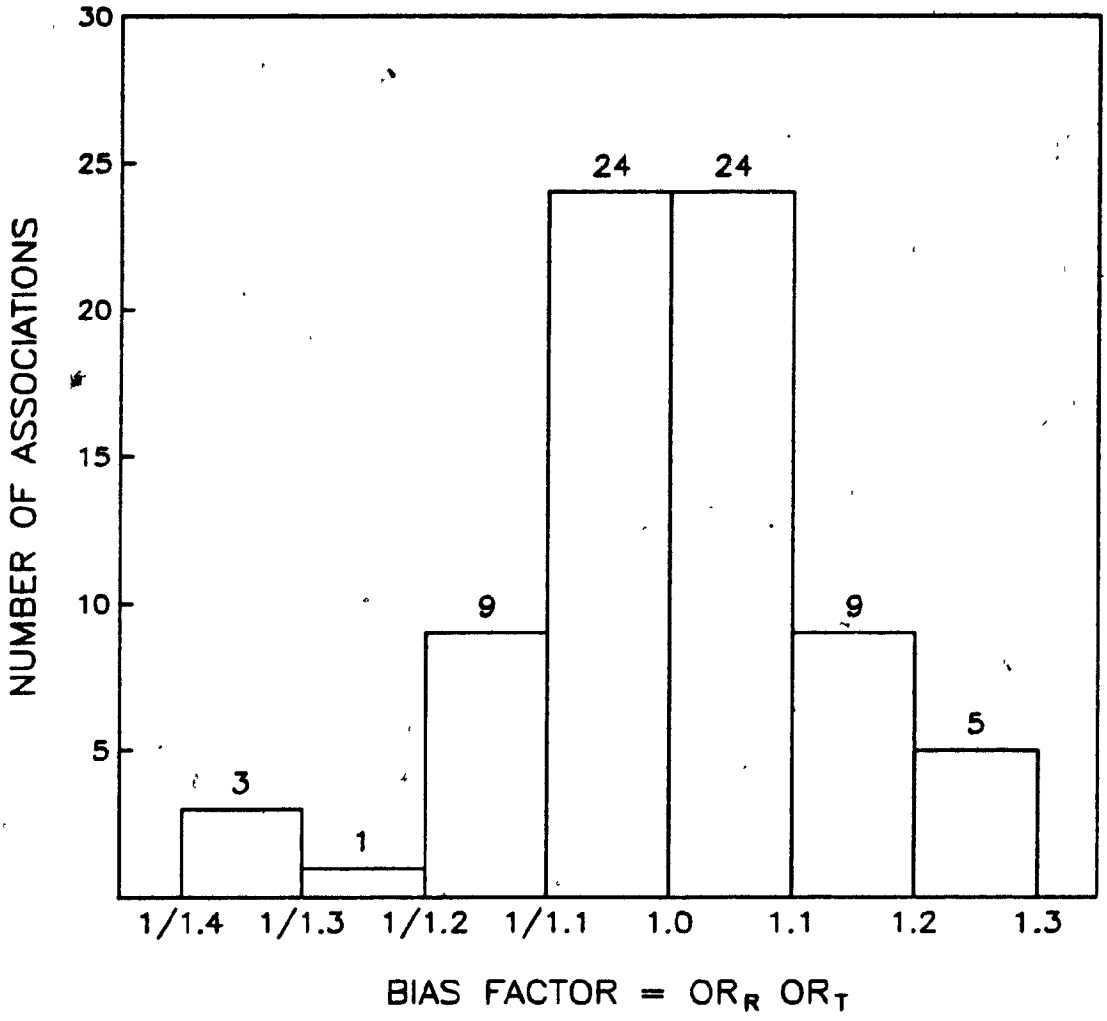

Table C17

PERCENTAGE OF 75 SELECTED* BIAS FACTORS

FALLING IN SPECIFIED RANGES

Range	% of bias factors falling within this range
1/1.1 - 1.1	64.0
1/1.2 - 1.2	88.0
1/1.3 - 1.3	96.0
1/1.4 - 1.4	100.0

* Odds ratios between 9 sites of cancer and 11 risk factors were estimated. If any cell contained less than 15 cases or the log odds variance was greater than 0.1, the resulting estimate was considered to be unstable. Tables C8 to C16 show which associations were included in the above distribution and gives the odds ratios from which the bias factors were derived. Estimates in brackets were eliminated from further consideration in the distribution of bias factors.

which also shows that two thirds (64%) of the OR_r's were within 10% of the OR_t's, 88% were within 20%, and 96% were within 30%.

It is generally accepted that even in well designed studies with large sample sizes it is impossible to rule out random variation or uncontrolled confounding as an explanation for odds ratios in the range 1/1.3 to 1.3 (Monson, 1980; Day, 1985; Robins et al., 1985). On the other hand, conventional wisdom holds that an odds ratio equal to or greater than 1.5 in a well designed study with large enough sample sizes is unlikely to reflect a false association resulting from bias or confounding. On this basis, therefore, we considered that only a bias factor outside the range 1/1.3 - 1.3 was an indication of nonresponse bias, since a bias factor greater than 1.3 (or less than 1/1.3) could distort a null association into the range where it would become "remarkable" or a "remarkable" association would be pushed into the null range.

The three associations that had bias factors outside the 1/1.3 to 1.3 range are shown in Table C18. Although none of these three were eliminated by the criteria mentioned above, they were nonetheless among the least stable of the 75 associations retained, and it seems likely that sampling variation played at least some role in the difference between OR_r and OR_t.

In the cancer study, proxy responses were accepted as a last resort if self-response was not possible, and the preceding analyses were based on all respondents. Had we only accepted self-response (as is done in many studies, quite defensibly), the response rates would have been lower and the opportunity for nonresponse bias higher. To evaluate nonresponse bias had we enforced a "self-response rule", the analyses carried out above for all respondents were repeated for self-respondents only. Table C19 shows the response rates for each subcategory of the socio-demographic variables

Table C18

ASSOCIATIONS FROM FIGURE C1 FOR WHICH THE BIAS FACTOR WAS LESS THAN 1/1.3 OR GREATER THAN 1.3

Association		OR_r and 95% C.L.	OR_t and 95% C.L.	OR_r/OR_t
Site	Risk factor			
Colon	Jewish vs French	1.38 (0.9 - 2.1)	1.83 (1.3 - 2.6)	0.75
Kidney	low vs medium income	0.84 (0.6 - 1.3)	1.12 (0.8 - 1.6)	0.75
Melanoma	married vs non married	1.30 (0.7 - 2.5)	1.74 (0.9 - 3.3)	0.75

Table C19

RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SELF-RESPONDENTS ONLY

Socio-demographic characteristic	N***	Unadjusted response rate* %	Adjusted response rate** %	S.E.
Age:				
35 - 59	1,047	69.7	68.8	1.4
60 +	1,375	63.7	64.4	1.3
Mean census tract income:				
$15,999	689	53.8	64.3	1.9
16,000 - 26,999	1,218	72.4	67.8	1.3
27,000	516	69.1	65.2	2.0
Ethnic group:				
French	1,277	66.7	67.4	1.3
English	318	62.4	64.6	2.7
Italian	130	78.4	74.2	3.6
Jewish	146	63.2	57.8	4.0
Other	172	63.7	62.0	3.7
Marital status:				
Married	1,523	67.6	67.6	1.2
Non married	445	61.3	61.2	2.3
Cigarette smoking:				
Nonsmokers	251	71.1	71.5	2.9
Smokers	1,502	65.5	65.4	1.2
Alcohol consumption				
Never	217	66.8	68.3	3.2
Social	349	69.8	68.5	2.5
Heavy	166	58.6	59.4	3.8

* Crude response rate in each subcategory.

** Response rate estimates were adjusted for site and lag.

*** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

when proxy respondents are considered as nonrespondents. Focussing in particular on the column of response rates adjusted for lag and site, we observe similar patterns to those manifest in Table C7 for self- and proxy respondents combined; namely, slightly higher response rates among the younger than the older subjects, higher rates among Italian subjects and lower rates among Jewish respondents and higher response rates among married than unmarried subjects. At variance with the patterns for all respondents, nonsmokers had higher rates of self-response than smokers and heavy alcohol consumers had much lower rates of self-response than non and low alcohol consumers. Whether these patterns translate themselves into biased estimates of disease-exposure relationships depends on patterns of response rates in cases and controls for each site under consideration. We therefore repeated the same series of analyses of odds ratios (OR_r and OR_t) for each site, but this time included only self-respondents in the computations of OR_r. Because of fewer respondents, there were smaller numbers in the cells of the fourfold tables for OR_rs and consequently higher variances. Many more associations failed to satisfy the criteria outlined above for inclusion of an OR estimate. Of the 36 associations involving the variables age, income and marital status (income had two "risk factor" levels and the other variables one each), 34 produced sufficiently "stable" estimates; of the 63 associations involving the remaining variables (ethnic group, cigarette smoking and alcohol consumption), only 29 produced "stable" estimates. Therefore, without loss of much information and for simplicity of presentation, we decided to base the evaluation of nonresponse bias among self-respondents on the four "risk factors" defined by the age, income and marital status variables. Tables C20 through C28 show, for each site, the OR_r, OR_t and bias factor for the four risk factors. For the sake of comparison, each table also shows the corresponding bias factors for the same four "risk factors" based on all respondents. (This is simply abstracted from the corresponding rows in Tables C8 to C16.)

Table C20

ASSOCIATIONS BETWEEN STOMACH CANCER AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS: ALL RESPONDENTS COMBINED AND SELF-RESPONDENTS ONLY

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
a) Self and proxy respondents combined			
Age:			
Over 60 vs under 60	0.90	0.88	1.02
Income:			
Low vs medium	0.60	0.69	0.87
High vs medium	0.85	0.91	0.93
Marital status:			
Married vs non married	1.24	1.34	0.93
b) Self-respondents only			
Age:			
Over 60 vs under 60	0.94	0.88	1.07
Income:			
Low vs medium	0.55	0.69	0.80
High vs medium	0.85	0.91	0.93
Marital status:			
Married vs non married	1.18	1.34	0.88

Table C21

ASSOCIATIONS BETWEEN COLON CANCER AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS: ALL RESPONDENTS COMBINED AND SELF-RESPONDENTS ONLY

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
a) Self and proxy respondents combined			
Age:			
Over 60 vs under 60	1.20	1.20	1.00
Income:			
Low vs medium	1.14	1.05	1.09
High vs medium	1.24	1.22	1.02
Marital status:			
Married vs non married	1.06	1.10	0.96
b) Self-respondents only			
Age:			
Over 60 vs under 60	1.15	1.20	0.96
Income:			
Low vs medium	1.19	1.05	1.13
High vs medium	1.27	1.22	1.04
Marital status:			
Married vs non married	1.22	1.10	1.11

Table C22

ASSOCIATIONS BETWEEN RECTAL CANCER AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS: ALL RESPONDENTS COMBINED AND SELF-RESPONDENTS ONLY

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
a) Self and proxy respondents combined			
Age:			
Over 60 vs under 60	0.87	0.87	1.00
Income:			
Low vs medium	1.06	0.96	1.10
High vs medium	1.07	0.99	1.08
Marital status:			
Married vs non married	0.83	0.94	0.88
b) Self-respondents only			
Age:			
Over 60 vs under 60	0.89	0.87	1.02
Income:			
Low vs medium	1.31	0.96	1.36
High vs medium	0.93	0.99	0.94
Marital status:			
Married vs non married	0.82	0.94	0.87

Table C23

ASSOCIATIONS BETWEEN LUNG CANCER AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS: ALL RESPONDENTS COMBINED AND SELF-RESPONDENTS ONLY

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
a) Self and proxy respondents combined			
Age:			
Over 60 vs under 60	1.01	1.02	0.99
Income:			
Low vs medium	0.77	0.82	0.94
High vs medium	0.60	0.60	1.00
Marital status:			
Married vs non married	0.77	0.72	1.07
b) Self-respondents only			
Age:			
Over 60 vs under 60	0.96	1.02	0.94
Income:			
Low vs medium	0.61	0.82	0.74
High vs medium	0.69	0.60	1.15
Marital status:			
Married vs non married	0.79	0.72	1.10

Table C24

ASSOCIATIONS BETWEEN PROSTATE CANCER AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS: ALL RESPONDENTS COMBINED AND SELF-RESPONDENTS ONLY

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
a) Self and proxy respondents combined			
Age:			
Over 60 vs under 60	3.15	3.06	1.03
Income:			
Low vs medium	1.05	0.90	1.17
High vs medium	0.88	0.83	1,14
Marital status:			
Married vs non married	1.32	1.15	1.15
b) Self-respondents only			
Age:			
Over 60 vs under 60	3.21	3.06	1.05
Income:			
Low vs medium	1.12	0.90	1.24
High vs medium	0.78	0.83	0.94
Marital status:			
Married vs non married	1.25	1.15	1.09

Table C25

ASSOCIATIONS BETWEEN BLADDER CANCER AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS: ALL RESPONDENTS COMBINED AND SELF-RESPONDENTS ONLY

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
a) Self and proxy respondents combined			
Age:			
Over 60 vs under 60	0.98	0.96	1.02
Income:			
Low vs medium	1.27	1.05	0.83
High vs medium	1.34	1.38	0.97
Marital status:			
Married vs non married	1.32	1.38	0.96
b) Self-respondents only			
Age:			
Over 60 vs under 60	1.06	0.96	1.10
Income:			
Low vs medium	1.57	1.05	1.49
High vs medium	1.17	1.38	0.85
Marital status:			
Married vs non married	1.38	1.38	1.00

Table C26

ASSOCIATIONS BETWEEN KIDNEY CANCER AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS: ALL RESPONDENTS COMBINED AND SELF-RESPONDENTS ONLY

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
a) Self and proxy respondents combined			
Age:			
Over 60 vs under 60	0.69	0.73	0.95
Income:			
Low vs medium	0.84	1.12	0.75
High vs medium	1.10	1.20	0.92
Marital status:			
Married vs non married	1.05	1.16	0.91
b) Self-respondents only			
Age:			
Over 60 vs under 60	0.67	0.73	0.92
Income:			
Low vs medium	0.84	1.12	0.75
High vs medium	1.20	1.22	0.98
Marital status:			
Married vs non married	1.09	1.16	0.94

Table C27

ASSOCIATIONS BETWEEN MELANOMA AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS: ALL RESPONDENTS COMBINED AND SELF-RESPONDENTS ONLY

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
a) Self and proxy respondents combined			
Age:			
Over 60 vs under 60	0.41	0.39	1.05
Income:			
Low vs medium	0.93	0.91	1.02
High vs medium	1.79	2.10	0.85
Marital status:			
Married vs non married	1.30	1.74	0.75
b) Self-respondents only			
Age:			
Over 60 vs under 60	0.50	0.39	1.28
Income:			
Low vs medium	1.11	0.91	1.22
High vs medium	1.97	2.10	0.94
Marital status:			
Married vs non married	(1.15)*	1.74	----

* If any cell contained less than 15 cases or the log odds variance was greater than 0.1, the resulting estimate was considered to be unstable. Estimates in brackets were eliminated from further consideration in the distribution of bias factors.

Table C28

ASSOCIATIONS BETWEEN NON-HODGKIN'S LYMPHOMA AND SEVERAL SOCIO-DEMOGRAPHIC CHARACTERISTICS IN THE RESPONDENT POPULATION AND THE TARGET POPULATION, AND BIAS FACTORS: ALL RESPONDENTS COMBINED AND SELF-RESPONDENTS ONLY

Socio-demographic characteristic	Odds ratio in the respondent population OR_r	Odds ratio in the target population OR_t	Bias factor OR_r/OR_t
a) Self and proxy respondents combined			
Age:			
Over 60 vs under 60	0.58	0.58	1.00
Income:			
Low vs medium	1.04	1.18	0.88
High vs medium	1.34	1.32	1.02
Marital status:			
Married vs non married	1.55	1.28	1.20
b) Self-respondents only			
Age:			
Over 60 vs under 60	0.53	0.58	0.91
Income:			
Low vs medium	1.06	1.18	0.90
High vs medium	1.18	1.32	0.89
Marital status:			
Married vs non married	(1.55)*	1.28	----

* If any cell contained less than 15 cases or the log odds variance was greater than 0.1, the resulting estimate was considered to be unstable. Estimates in brackets were eliminated from further consideration in the distribution of bias factors.

Figure C2 shows for self-respondents only and for all respondents, the distribution of bias factors for the same set of 34 associations. Clearly the distribution is more spread out for the self-respondents ostensibly indicating greater nonresponse bias. However, because sample sizes were smaller in the self-respondent analysis than in the analysis of all respondents combined, we cannot exclude the possibility that the greater spread of bias factors simply reflects the smaller precision of bias factor estimates. Table C29 synthesizes the range of values for each of the two sets of bias factors. For all respondents combined 73% were within 10% of the OR_t and 94% were within 20% of the OR_t. Among self-respondents, only half of the odds ratios were within 10% of the target odds ratio and 76% were within 20%. Thus, nearly one quarter of the odds ratios among self-respondents differed from the target odds ratios by more than 20%. There were four associations among self-respondents only with bias factors outside the range 1/1.3 to 1.3. These are shown in Table C30. All four involve the comparison of low income and middle income groups and are not therefore independent observations.

FIGURE C2

DISTRIBUTION OF BIAS FACTORS DUE TO NON-RESPONSE
IN 34 ASSOCIATIONS FOR ALL RESPONDENTS AND SELF-RESPONDENTS ONLY

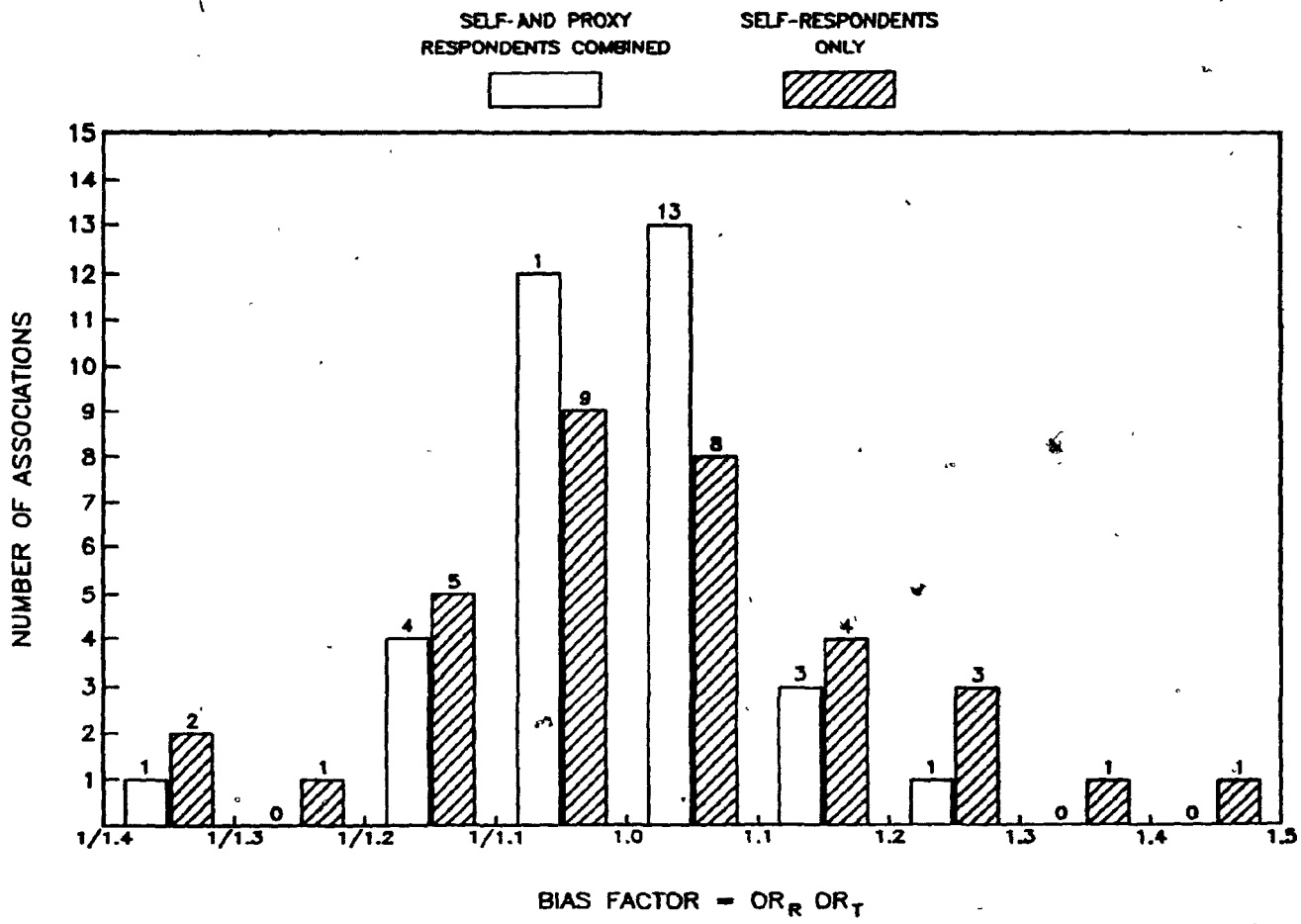

Table C29

PERCENTAGE OF 34 SELECTED* BIAS FACTORS FALLING IN SPECIFIED RANGES FOR SELF AND PROXY RESPONDENTS COMBINED AND SELF-RESPONDENTS ONLY

Range	% of bias factors falling within this range for self + proxy combined	% of bias factors falling within this range for self-respondents only
1/1.1 - 1.1	73.5	50.0
1/1.2 - 1.2	94.1	76.0
1/1.3 - 1.3	97.1	88.0
1/1.4 - 1.4	100.0	100.0

* Odds ratios between 9 sites of cancer and 4 risk factors were estimated. If any cell contained less than 15 cases or the log odds variance was greater than 0.1, the resulting estimate was considered to be unstable. Tables C20 to C28 show which associations were included in the above distribution and gives the odds ratios from which the bias factors were derived. Estimates in brackets were eliminated from further consideration in the distribution of bias factors.

Table C30

ASSOCIATIONS FROM FIGURE C2 AMONG SELF-RESPONDENTS ONLY
FOR WHICH THE BIAS FACTOR WAS LESS THAN 1/1.3 OR GREATER THAN 1.3

Association		OR_r and	OR_t and	
Site	Risk factor	95% C.L.	95% C.L.	OR_r/OR_t
Rectum	low vs medium income	1.31	0.96	1.36
		(0.9 - 2.0)	(0.7 - 1.3)	
Lung	low vs medium income	0.61	0.82	0.74
		(0.5 - 0.8)	(0.7 - 1.0)	
Bladder	low vs medium income	1.57	1.05	1.49
		(1.2 - 2.0)	(0.8 - 1.3)	
Kidney	low vs medium income	0.84	1.12	0.75
		(0.5 - 1.3)	(0.8 - 1.6)	

C.5 DISCUSSION

Most epidemiologic studies that have assessed nonresponse bias simply compared response rates in different socio-demographic subgroups or, equivalently, compared socio-demographic characteristics of respondents and nonrespondents. If the purpose of the study is to estimate some parameter based on a single variable in the target population (e.g. mean blood pressure, percentage of smokers, distribution of number of days of hospitalization in the past year) then this approach is an appropriate guide to nonresponse bias. In the case-control situation the parameter of interest is some measure of association (usually the odds ratio) between two variables: disease status and exposure status. In this situation nonresponse bias is not directly related to the differences in marginal response rates between cases and controls or between exposed and unexposed. Rather it depends on response rates for the different combinations of the two variables (Criqui, 1979; Greenland and Criqui, 1981). For this reason we used as the prime parameter for assessing nonresponse bias the bias factor defined as OR_r/OR_t. Nevertheless the examination of response rates by risk factor characteristics may be of some interest, if for no other reason than the fact that it has been the main approach taken in the literature.

C.5.1 Differences in response rates by socio-demographic variables

For the most part the variation in response rates by socio-demographic subgroup was minor, and perhaps predictable. The most important difference observed was the lower response rates among older, unmarried and poor subjects; specifically, rather more of these patients died before we could reach them for interview. Ehrlich et al. (1975) have reported that significantly more members of these groups do not receive diagnosis and treatment for their cancer, are often seen in hospital for the first time only days before death, and as a consequence the cancer diagnosis is made

only at autopsy. This poses a problem for the investigator from several points of view. An active case-ascertainment system will not improve self-response rates among patients diagnosed on the verge of death or after death. In addition, if the next-of-kin belongs to the same social class as the case (as would seem likely) then the next-of-kin would be difficult to trace as well (Bright, 1969). Imaginative solutions are required to find ways to achieve higher response rates in this group.

The findings of high response rates among subjects of Italian origin as compared notably with Jewish subjects may be due to the fact that two of our interviewers happened to be of Italian origin and spoke Italian whereas we had no Jewish interviewers. It may be that minority groups are more responsive to a member of their own group (Aday et al., 1980; Vernon et al., 1984), or these differences may merely reflect different cultural attitudes to illness or participation in health related research.

The most commonly reported difference between respondents and nonrespondents in health survey research concerns smoking habits, with higher response rates found among nonsmokers (Burgess and Tierney, 1970; Criqui et al., 1978; Doll and Bradford Hill, 1964; Oakes et al., 1973; Seltzer et al., 1975). These results were all derived from studies conducted in nondiseased populations. In the Montreal study cancer series, there was no such smoker/nonsmoker difference in overall response rates. However, when proxy respondents were excluded, there was a small difference in self-response rates between smokers and nonsmokers, in the same direction as suggested by the literature. If there really are differential response patterns by smoking status for cancer cases as opposed to healthy subjects, this may have implications for selection of appropriate control groups in case-control studies. This will be expanded upon below.

The findings in relation to alcohol were somewhat similar to those for smoking. There was little evidence of difference when proxy respondents were included but a noticeable difference when they were excluded. Lower response rates among heavy alcohol drinkers are similar to findings in other studies. The lower rates among drinkers may reflect a personality that is less health conscious and consequently less interested in participating in a study. Alternatively, heavy alcohol consumption may be associated both with some of the more rapidly fatal cancers - liver, oesophagus and lung - as well as characteristics that might make them or their families more difficult to trace.

C.5.2 Nonresponse bias

We were encouraged to find that there was a concentration of bias factors around 1.0. There was not a single bias factor as great as 2.0 (or less than its reciprocal) and only three out of the 75 examined were greater than 1.3 (or less than its reciprocal), and, in fact, very few of the bias factors were greater than 1.2 (or less than its reciprocal). The following generalization would seem to be warranted. If a study is conducted of a type of cancer and a risk factor that are in some sense similar to the ones we examined, and if response rates over 75% are achieved, and if an odds ratio greater than, say 1.5, is observed, then such a result is unlikely to be an artefact of nonresponse bias. This is not to say that such a result could not be due to other potential biases; only that nonresponse bias is unlikely to cause as much as a 50% distortion in odds ratios.

When examining nonresponse bias under a "self-response rule" there was somewhat more spread of the bias factors away from the value of 1.0 than under the self- plus proxy rule. Four of 34 bias factors fell outside the range 1/1.3 to 1.3. However, this probably reflects only two or perhaps three truly deviant bias factors

since the same risk factor (low income in this case) was involved in all four apparently deviant bias factors. Because of the Montreal study design where for each cancer site all other sites were used as controls a couple of bias factors leaning away from 1.0 in one direction may tip one or two others to the opposite extreme. In any case with self-response rates in the 60%-75% range for different cancer sites, there were no bias factors greater than 1.6, and the vast majority were less than 1.2.

It should be noted that among the 75 associations for which the bias factors were calculated there were several that had odds ratios that were significantly different from 1.0. It is our belief that the bias factors can be interpreted independently of the odds ratios on which they are based. That is, there should be no difference in interpretation whether a bias factor of 1.3 changed the odds ratio from 1.0 to 1.3 or from 2.0 to 2.6.

Based on conventional wisdom that an odds ratio less than 1.3 not be taken as serious evidence of association, we have used 1.3 as a guideline for deciding whether the bias factor was significant or not (in the nonstatistical sense of "significant"). While there may be situations where a bias factor of 1.3 may mislead an investigator in his or her conclusions, in fact it is most unlikely that odds ratios of 1.0 or 1.3 would lead to different conclusions (given the variability and opportunity for other types of bias). The same would hold for odds ratios of 2.0 or 2.6, 4.0 or 5.2, etc. Of course it must be remembered that nonresponse is unlikely to be the only source of bias in a given study. Therefore, even small bias factors, when taken in conjunction with other sources of bias, may create sufficient distortion to bias the overall measures of association.

So far as we know, this approach to ascertaining and describing nonresponse bias as a function of the bias factors has never been used in a case-control study. It is therefore impossible to compare our experience with that of other investigators in this regard. However, Austin et al. (1981) published a set of bias factors due to nonresponse in the context of a prospective follow-up study of subjects who were healthy at the initial examination and who agreed to participate at the baseline contact. The range of bias factors observed was in fact similar to ours: 88% of the 24 bias factors were within the range 1/1.3 - 1.3, and none were greater than 1.6 (or smaller than its reciprocal). It is of interest that despite the different study design, the different associations being measured (diseases and risk factors), the distribution of bias factors in the Montreal study should so closely resemble those reported by Austin et al. (1981).

C.5.3 Some problems in the interpretation of these results

In the analyses of each of the thirteen sites of cancer in the Montreal study, the controls consist of all other cancer cases. There are two aspects to this that require comment. First, the fact that the estimates of association obtained from comparisons of one case series with a control group comprised of all other case series combined means that the whole set of odds ratios computed are not mutually independent. Secondly, our findings in relation to nonresponse bias may not be generalizable to studies using some other source of controls such as "healthy" members of the general population. We will address these two issues separately.

The analyses of each set of site/risk factor combinations are in some ways analogous to a proportional mortality analysis whereby if there is a strong positive relation between a given risk factor and one or more sites this may diminish the effect seen in others. There is no apparent theoretical reason why the lack of mutual

independence should cause a systematic distortion of the distribution of bias factors in one direction or another, i.e. to be more compressed around 1.0 or to be more spread out. It does, however, imply that the strength of the evidence we have presented of lack of nonresponse bias is not as great as would be implied by 75 independent observations. It is impossible, with the theoretical tools currently available to quantify how many independent observations would be equivalent to our 75 mutually dependent ones.

The second issue is whether the distribution of bias factors would have been as concentrated as it was around 1.0 had a different source of controls been used. The present findings of little nonresponse bias essentially reflect the fact that the pattern of response rates by levels of the six socio-demographic factors examined were relatively stable across the different sites of cancer. That is, where response rates did not vary by characteristic, as for smoking status, this tended to hold across all cancer sites for which there were adequate numbers. Where response rates did vary by characteristic, as for marital status, this tended to hold across all cancer sites.

It may be argued that from the point of view of likelihood of response by risk factor status, other seriously ill patients would behave as cancer patients. If so, using other hospital controls would lead to a nonresponse bias distribution similar to that obtained from cancer controls. However, it is less clear that our findings on the distribution of bias factors would hold when a general population sample is used as the control group. The patterns of response by risk factor characteristic may differ between ill patients and healthy controls. For example, the response patterns amongst our cases showed no difference by smoking status whereas in most reports in the health survey literature it appears that healthy nonsmokers are more likely to respond than healthy smokers. Thus, it is conceivable that nonresponse bias in relation to

smoking may arise in a case-control study using general population controls if the response patterns amongst cases were the same as in the Montreal study (i.e. no difference in response between smokers and nonsmokers) and where the pattern amongst controls were the same as in the general survey literature (i.e. higher response rates amongst nonsmokers than smokers).

The question of the appropriate choice of controls for cancer case-control studies has been widely discussed from many perspectives such as overmatching and differential quality of information. Perhaps the issue of different response rate patterns in different types of control groups should be added to the debate. From our results it would appear that the use of cancer patients as controls involves little risk of nonresponse bias. We suggest that the same may hold if other seriously ill patients are used. However, the risks of nonresponse bias may be greater if population controls are used.

Another potential limitation of inference is related to the particular variables and sites of cancer available for analysis. It is of course possible that the findings on nonresponse bias in relation to the various associations studied here are not "representative" of nonresponse bias potential with respect to other risk factors. This is difficult to evaluate. However, the six socio-demographic variables are important epidemiological variables in their own right and findings in relation to them are not unimportant. Furthermore, they are correlated with many other socio-psycho-environmental factors and in this way may provide a window on potential bias with respect to other factors.

The final problem to be commented on concerns the quality and quantity of the available data on socio-demographic characteristics. Information was not always

available on each socio-demographic characteristic for each subject. The age and mean census tract income variables were always available because the date of birth and the address of the patient are always recorded. There would inevitably be some random human error in recording and abstracting this information. This random misclassification may lead to some small attenuation of odds ratios. Inasmuch as mean census tract income is an imperfect measure of socio-economic status, this too would induce random misclassification and any putative association between socio-economic status and cancer would be attenuated.

Ethnic group and marital status are items that were once routinely recorded on admission to all hospitals in Quebec, but have become part of the "voluntary" medical history since 1980. History of cigarette smoking and alcohol consumption should be a standard feature of a good medical history. Unfortunately this does not guarantee that this information is in fact recorded in medical records. The over 4,000 subjects ascertained come from 19 different hospitals. The quality of the records tends to vary by type of hospital, by whether the patient is an in- or outpatient and by the habits of the individual treating physician. We noted some tendency for university based hospitals to have better records: this may be due to the presence of "enthusiastic" interns and residents. Inpatients' records tend to be more complete than outpatients' records. The likelihood of this type of information being recorded in a patient's file undoubtedly varies according to his diagnosis. For example, nearly all lung cancer patients had some notation in their records about cigarette smoking, whereas only a minority of melanoma cases had this information recorded. Furthermore it is reasonable to assume that someone who smoked or drank was more likely to have his practice recorded than the nonpractitioner. Thus the proportions of smokers and drinkers as derived from the medical records are unlikely to reflect accurately the true patterns of these habits among cancer patients. This might very well bias an odds

ratio between smoking and some particular cancer. However, it would not, in itself, distort the findings of this methodologic study of bias factors. There were cases whose medical record contained the information that the case was a nonsmoker and there were cases denoted as smokers. Even if the distribution of persons into these two groups was unrepresentative of all cancer cases, the difference in subsequent response rates between these two groups is still meaningful. It may be that there was misclassification in the attribution of cigarette smoking or even that the misclassification was not random (e.g. lung cancer cases were more likely to be "upgraded" to smokers than their controls). This would certainly affect the odds ratio estimates, but it would affect the OR_r and OR_t estimates equally. Thus, the bias factor should not be much affected by the vagaries of the missing data or the differential misclassification. In this respect it is worth noting that many of the ORs did depart from the null value in directions that would be expected from the literature.

Thus, despite the defects of such information as abstracted from medical records, we feel that it is useful for the present purpose and does allow for reasonable comparisons between respondents and the target population.

C.5.4 Overall response rates as guides to nonresponse bias

It has been an accepted truism in case-control studies as well as in other survey research that the higher the response rate achieved, the less the likelihood of nonresponse bias in results. The fact that this belief is well-founded can be illustrated by hypothetical examples in the case-control situation.

Suppose that in the target population there are 100 subjects in each cell of the 2 x 2 table such that the odds ratio equals 1.0:

	CASES	CONTROLS	
Exposed	$a_t = 100$	$b_t = 100$	
			$OR_t = 1.00$
Unexposed	$c_t = 100$	$d_t = 100$	

Following are three sets of results that might come from the attempt to interview this population. The overall response rates are 80%, 50% and 20% respectively. However, the variation in response rates within the cells of the table is identical for all the three tables. That is, exposed cases have 20% higher response rate than subjects in the other three cells. The resulting odds ratios and corresponding bias factors demonstrate that greater distortion is engendered when the response rates are lower.

Hypothetical table with overall 80% response rate

	CASES	CONTROLS
Exposed	$a_r = 95$	$b_r = 75$
Unexposed	$c_r = 75$	$d_r = 75$
	$OR_r = 1.27$	Bias factor = 1.27

Hypothetical table with overall 50% response rate

	CASES	CONTROLS
Exposed	65	45
Unexposed	45	45
	$OR_r = 1.44$	Bias factor = 1.44

Hypothetical table with overall 20% response rate

	CASES	CONTROLS
Exposed	35	15
Unexposed	15	15
	OR_r = 2.33	Bias factor = 2.33

Of course one can make up examples in which a 20% overall response rate provides perfectly representative figures in the cells and a true odds ratio estimate, whereas an overall response rate of 80% provides an imperfect representation and a biased odds ratio. The point, as implied by the three examples, is that for a given pattern of cell-specific deviations from the overall response rate, the lower the overall response rate the higher will be the bias factor. Furthermore, if one devises a set of cell-specific deviations which maximizes the bias factor (i.e. maximize a_r and d_r, minimize b_r and c_r) then the upper limit of the bias factor can be shown to be related to the overall response rate. There is an upper limit to the amount of bias that can be engendered by nonresponse and this upper limit is greater when the response rate is lower. That is, the possibility of a large bias factor is greater with lower response rates.

C.5.5 Conclusion

In a cancer case-control study among males in which other cancer patients served as controls for each case series, in which proxy response was accepted as a last resort, and in which site specific response rates were in the range 75%-85%, there was no evidence of important bias in odds ratios resulting from differential patterns of response by disease status and exposure status. Even when proxy response was excluded and the self-response rates ranged from 60% to 75%, there was little indication of important distortion in odds ratios. These findings would seem to

indicate that nonresponse bias is not in itself a major source of distortion in this study. Nevertheless, even a small distortion due to nonresponse bias, if combined with some other potential bias(es), could result in major bias(es) in odds ratio estimates. Further, the generalizability of our findings to other circumstances, such as the use of population controls, remains open to speculation. The best protection against nonresponse bias remains the achievement of very high response rates in all study groups.

ACKNOWLEDGEMENTS

The work presented here would not have been possible without the support and collaboration of the many individuals and organizations who made possible the Montreal study as well as those more directly concerned with this thesis.

Funding for the Montreal study has been provided by: Conseil de la recherche en santé du Québec, Health and Welfare Canada, National Cancer Institute of Canada, and the Institut de recherche en santé et en sécurité du travail du Québec.

We received invaluable cooperation from the pathology department, tumour registry and archive staff in the following hospitals: Cité de la Santé, Fleury Hospital, Hôtel-Dieu of Montreal, Jean-Talon Hospital, Jewish General Hospital, Lakeshore General Hospital, Maisonneuve-Rosemont Hospital, Montreal Chest Hospital, Montreal General Hospital, Notre-Dame Hospital, Queen Elizabeth Hospital, Reddy Memorial Hospital, Royal Victoria Hospital, Sacré-Coeur Hospital, St-Luc Hospital, St-Mary's Hospital, Ste-Jeanne d'Arc Hospital, Santa Cabrini Hospital, and Verdun Hospital who notified us of cases, and assisted in the verification of eligibility criteria for all cases.

Thanks must go to our enthusiastic team responsible for interviewing and collecting data from the medical records: D. Bourbonnais, Y. Céré, L. Felicissimo, H. Sheppard, V. Vacarelli, M. Vinet. Special thanks to D. Bourbonnais whose meticulous work in searching for missing cases, data entry and clean-up of data is greatly appreciated.

The chemical coding for the Montreal study was carried out by D. Bégin, H. Kemper, R. Lakhani, L. Nadon and L. Laroche under the supervision of Dr. M. Gérin. Coding the quality of work histories added to an already heavy burden, and the author is extremely grateful for their cheerful collaboration.

J. Pellerin provided valued assistance with data management and C. Richer prepared the manuscript and provided much needed moral support.

I would like to thank the Centre de recherche en épidémiologie et médecine préventive of the Institut Armand-Frappier which made it possible for me to pursue this research while I was employed as a research asssistant, providing both materials and facilities.

My thesis supervisor, Dr. A. Lippman, has been a tremendous help, providing encouragement and constructive criticism throughout. Dr. J. Hanley helped in the development of the statistical analysis. Dr. B. Armstrong provided valuable criticism of the final draft of the manuscript.

Finally, it must be acknowledged that without my husband and mentor, Dr. J. Siemiatycki, this work would have been impossible. He encouraged me to develop a project within the context of the Montreal study and granted permission to use the data. He provided the intellectual stimulus to develop the questions and methods, he bullied me to continue in dark days of despair, and provided the domestic support necessary for such a task to be completed. Thanks too to Harriet and Toby for coping with and supporting a preoccupied and distant mother for so many months.

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APPENDICES

APPENDIX - Table 1

RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH STOMACH CANCER

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	90	85.0	3.7
60 +	110	86.8	3.2
Mean census tract income:			
<$15,999	50	66.0	6.6
16,000 - 26,999	104	95.2	2.1
>27,000	46	87.0	5.0
Ethnic group:			
French	98	87.7	3.3
English	19	84.1	8.4
Italian	14	80.9	10.5
Jewish	8	95.1	7.6
Other	27	77.1	8.1
Marital status:			
Married	126	87.3	3.0
Non married	29	77.7	7.7
Cigarette smoking:			
Nonsmokers	24	70.7	9.2
Smokers	115	87.8	3.1
Alcohol consumption			
Never	24	75.4	8.8
Social	23	100.0	6.3
Heavy	37	81.5	6.4

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 2

RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH COLON CANCER

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	189	87.8	2.4
60 +	317	82.3	2.1
Mean census tract income:			
< $15,999	141	76.6	3.6
16,000 - 26,999	250	86.8	2.1
>27,000	115	88.7	3.0
Ethnic group:			
French	244	85.7	2.2
English	79	77.2	4.7
Italian	32	90.6	5.2
Jewish	40	67.5	7.4
Other	36	94.4	3.8
Marital status:			
Married	316	86.2	1.9
Non married	89	74.2	4.6
Cigarette smoking:			
Nonsmokers	69	85.5	4.2
Smokers	270	85.9	2.1
Alcohol consumption			
Never	42	90.5	4.5
Social	63	87.3	4.2
Heavy	74	81.1	4.6

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 3

RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH RECTAL CANCER

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	82	93.9	2.6
60 +	104	87.5	3.2
Mean census tract income:			
<$15,999	54	83.3	5.1
16,000 - 26,999	94	91.5	2.9
>27,000	38	97.4	2.6
Ethnic group:			
French	91	89.1	3.3
English	27	85.2	6.8
Italian	14	92.9	6.9
Jewish	8	87.5	11.7
Other	18	88.9	7.4
Marital status:			
Married	122	90.2	2.7
Non married	39	84.6	5.8
Cigarette smoking:			
Nonsmokers	30	90.0	5.5
Smokers	111	90.1	2.8
Alcohol consumption			
Never	16	93.8	6.0
Social	34	91.2	4.9
Heavy	39	89.7	4.9

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 4

RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH LUNG CANCER

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	284	86.6	2.0
60 +	366	86.3	1.8
Mean census tract income:			
<$15,999	177	75.1	3.3
16,000 - 26,999	368	90.8	1.5
>27,000	105	90.5	2.9
Ethnic group:			
French	379	84.4	1.9
English	72	91.7	3.3
Italian	22	95.5	4.4
Jewish	10	90.0	9.5
Other	39	94.9	3.5
Marital status:			
Married	413	90.1	1.5
Non married	144	81.3	3.3
Cigarette smoking:			
Nonsmokers	8	87.5	11.7
Smokers	547	87.6	1.4
Alcohol consumption			
Never	40	92.5	4.2
Social	49	93.9	3.4
Heavy	145	85.5	2.9

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 5

RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH PROSTATE CANCER

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	57	87.7	4.4
60 +	250	86.4	2.3
Mean census tract income:			
<$15,999	97	84.5	3.7
16,000 - 26,999	156	87.8	2.6
>27,000	54	87.0	4.6
Ethnic group:			
French	190	88.4	2.3
English	46	84.8	5.3
Italian	8	100.0	0
Jewish	21	71.4	9.9
Other	16	93.8	6.0
Marital status:			
Married	196	87.8	2.3
Non married	45	75.6	6.4
Cigarette smoking:			
Nonsmokers	37	89.2	5.1
Smokers	157	86.6	2.7
Alcohol consumption			
Never	28	96.4	3.5
Social	72	87.5	3.9
Heavy	50	84.0	5.2

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 6

RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH BLADDER CANCER

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	181	87.3	2.5
60 +	239	86.2	2.2
Mean census tract income:			
<$15,999	131	87.0	2.9
16,000 - 26,999	183	88.0	2.4
>27,000	106	84.0	3.6
Ethnic group:			
French	214	87.4	2.3
English	53	86.8	4.7
Italian	21	100.0	0
Jewish	36	66.7	7.9
Other	37	86.5	5.6
Marital status:			
Married	282	87.6	2.0
Non married	61	82.0	4.9
Cigarette smoking:			
Nonsmokers	32	78.1	7.3
Smokers	265	87.2	2.1
Alcohol consumption			
Never	41	80.5	6.2
Social	60	86.7	4.4
Heavy	73	91.8	3.2

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 7

RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH KIDNEY CANCER

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	77	87.1	3.8
60 +	69	76.8	5.1
Mean census tract income:			
<$15,999	46	63.0	7.1
16,000 - 26,999	68	95.6	2.5
>27,000	32	81.3	6.9
Ethnic group:			
French	77	79.2	4.6
English	22	72.7	9.5
Italian	8	100.0	0
Jewish	12	100.0	0
Other	13	84.6	10.0
Marital status:			
Married	100	81.0	3.9
Non married	22	77.3	8.9
Cigarette smoking:			
Nonsmokers	26	84.6	7.1
Smokers	77	79.2	4.6
Alcohol consumption			
Never	12	75.0	12.5
Social	24	83.3	7.6
Heavy	26	76.9	8.3

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 8

RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH MELANOMA

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	63	85.7	4.4
60 +	35	85.7	5.9
Mean census tract income:			
<$15,999	21	81.0	8.6
16,000 - 26,999	42	90.5	4.5
>27,000	36	80.6	6.6
Ethnic group:			
French	30	90.0	5.5
English	22	77.3	8.9
Italian	7	100.0	0
Jewish	13	76.9	11.7
Other	7	85.7	13.2
Marital status:			
Married	58	84.5	4.8
Non married	11	90.9	8.7
Cigarette smoking:			
Nonsmokers	18	94.5	5.4
Smokers	24	87.5	6.8
Alcohol consumption			
Never	9	88.9	10.5
Social	18	77.8	9.8
Heavy	3	66.7	27.2

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 9

RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH NON-HODGKIN'S LYMPHOMA

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	94	90.4	3.0
60 +	74	85.1	4.1
Mean census tract income:			
< $15,999	50	78.0	5.9
16,000 - 26,999	75	93.3	2.9
> 27,000	43	90.7	4.4
Ethnic group:			
French	94	85.1	3.7
English	22	81.8	8.2
Italian	8	100.0	0
Jewish	11	90.9	8.7
Other	11	90.9	8.7
Marital status:			
Married	110	90.9	2.7
Non married	25	68.0	9.3
Cigarette smoking:			
Nonsmokers	24	87.5	6.8
Smokers	100	90.0	3.0
Alcohol consumption			
Never	28	85.7	6.6
Social	26	84.6	7.1
Heavy	28	89.3	5.8

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 10

SELF-RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH STOMACH CANCER

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	90	67.3	4.9
60 +	110	66.7	4.5
Mean census tract income:			
< $15,999	50	90.0	4.2
16,000 - 26,999	104	57.1	4.9
>27,000	46	64.4	7.1
Ethnic group:			
French	98	63.0	4.9
English	19	89.2	7.1
Italian	14	52.8	13.3
Jewish	8	56.3	17.5
Other	27	68.4	9.0
Marital status:			
Married	126	65.4	4.2
Non married	29	70.8	8.4
Cigarette smoking:			
Nonsmokers	24	69.9	9.4
Smokers	115	65.4	4.4
Alcohol consumption			
Never	24	68.7	9.5
Social	23	57.1	10.3
Heavy	18	79.8	9.5

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 11

SELF-RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH COLON CANCER

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	189	60.6	3.6
60 +	317	74.3	2.5
Mean census tract income:			
$15,999	141	78.7	3.5
16,000 - 26,999	250	65.9	3.0
27,000	115	64.4	4.5
Ethnic group:			
French	244	62.9	3.1
English	79	78.9	4.6
Italian	32	59.6	8.7
Jewish	40	87.1	5.3
Other	36	56.8	8.3
Marital status:			
Married	316	64.8	2.7
Non married	89	80.1	4.2
Cigarette smoking:			
Nonsmokers	69	69.1	5.6
Smokers	270	71.2	2.8
Alcohol consumption			
Never	42	70.7	7.0
Social	63	68.3	5.9
Heavy	27	97.2	3.2

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 12

SELF-RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH RECTAL CANCER

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	82	71.1	5.0
60 +	104	79.5	4.0
Mean census tract income:			
<$15,999	54	79.4	5.5
16,000 - 26,999	94	78.7	4.2
>27,000	98	77.9	4.2
Ethnic group:			
French	91	73.5	4.6
English	27	75.3	8.3
Italian	14	70.8	12.2
Jewish	8	86.9	11.9
Other	18	77.1	9.9
Marital status:			
Married	122	75.3	3.9
Non married	39	77.2	6.7
Cigarette smoking:			
Nonsmokers	30	81.3	7.1
Smokers	111	76.2	4.0
Alcohol consumption			
Never	16	80.0	10.0
Social	34	84.7	6.2
Heavy	17	73.0	10.8

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 13

SELF-RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH LUNG CANCER

Socio-demographic characteristic	Response rate*		S.E.
	N**	%	%
Age:			
35 - 59	284	59.3	2.9
60 +	366	63.6	2.5
Mean census tract income:			
<$15,999	177	58.6	2.9
16,000 - 26,999	368	55.5	2.6
>27,000	105	50.1	4.9
Ethnic group:			
French	379	60.3	2.5
English	72	58.8	5.8
Italian	22	29.0	9.7
Jewish	10	39.9	15.5
Other	39	81.5	6.2
Marital status:			
Married	413	60.7	2.4
Non married	144	67.0	3.9
Cigarette smoking:			
Nonsmokers	8	75.0	15.3
Smokers	547	62.3	2.1
Alcohol consumption			
Never	40	71.9	7.1
Social	49	59.8	7.8
Heavy	43	78.9	6.2

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 14

SELF-RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH PROSTATE CANCER

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	57	68.1	6.2
60 +	250	73.7	2.8
Mean census tract income:			
< $15,999	97	77.2	4.3
16,000 - 26,999	156	76.9	3.4
>27,000	54	76.8	5.8
Ethnic group:			
French	190	71.0	3.3
English	46	69.1	6.8
Italian	8	100.0	3.5
Jewish	21	83.3	8.1
Other	16	70.2	11.4
Marital status:			
Married	196	68.8	3.3
Non married	45	75.8	6.4
Cigarette smoking:			
Nonsmokers	37	73.8	7.2
Smokers	157	75.0	3.5
Alcohol consumption			
Never	28	63.6	9.1
Social	72	73.5	5.2
Heavy	18	84.7	8.5

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 15

SELF-RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH BLADDER CANCER

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	181	73.8	3.3
60 +	239	72.6	2.9
Mean census tract income:			
<$15,999	131	72.2	3.9
16,000 - 26,999	183	68.6	3.4
>27,000	106	82.0	3.7
Ethnic group:			
French	214	71.1	3.1
English	53	75.1	5.9
Italian	21	56.3	10.8
Jewish	36	91.3	4.7
Other	37	76.7	7.0
Marital status:			
Married	282	72.0	2.7
Non married	61	76.9	5.4
Cigarette smoking:			
Nonsmokers	32	74.9	7.7
Smokers	265	73.2	2.7
Alcohol consumption			
Never	41	78.9	6.4
Social	60	74.6	5.6
Heavy	34	70.2	7.8

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 16

SELF-RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH KIDNEY CANCER

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	77	61.7	5.5
60 +	69	77.5	5.0
Mean census tract income:			
<$15,999	46	94.9	3.3
16,000 - 26,999	68	57.5	6.0
>27,000	32	57.1	8.8
Ethnic group:			
French	77	72.9	5.1
English	22	69.7	9.8
Italian	8	50.4	17.7
Jewish	12	46.2	14.4
Other	13	76.3	11.8
Marital status:			
Married	100	70.3	4.6
Non married	22	66.6	10.1
Cigarette smoking:			
Nonsmokers	26	60.9	9.6
Smokers	77	71.6	5.1
Alcohol consumption			
Never	12	89.3	8.9
Social	24	68.5	9.5
Heavy	6	64.3	19.6

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 17

SELF-RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH MELANOMA

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	63	77.1	5.3
60 +	35	66.9	8.0
Mean census tract income:			
< $15,999	21	78.8	8.9
16,000 - 26,999	42	71.7	7.0
> 27,000	36	70.5	7.6
Ethnic group:			
French	30	77.6	7.6
English	22	71.6	9.6
Italian	7	44.3	18.8
Jewish	13	75.1	12.0
Other	7	72.9	16.8
Marital status:			
Married	58	78.3	5.4
Non married	11	59.8	14.8
Cigarette smoking:			
Nonsmokers	18	83.3	8.8
Smokers	24	83.3	7.6
Alcohol consumption			
Never	9	89.3	10.3
Social	18	67.1	11.1
Heavy	2	44.8	35.2

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.

APPENDIX - Table 18

SELF-RESPONSE RATES BY AGE, MEAN CENSUS TRACT INCOME, ETHNIC GROUP, MARITAL STATUS, CIGARETTE SMOKING, AND ALCOHOL CONSUMPTION FOR SUBJECTS WITH NON-HODGKIN'S LYMPHOMA

Socio-demographic characteristic	Response rate* N**	Response rate* %	S.E. %
Age:			
35 - 59	94	59.9	5.1
60 +	74	75.2	5.0
Mean census tract income:			
<$15,999	50	77.3	5.9
16,000 - 26,999	75	57.3	5.7
>27,000	43	70.6	7.0
Ethnic group:			
French	94	65.2	4.9
English	22	80.1	8.5
Italian	8	55.1	17.6
Jewish	11	48.3	15.1
Other	11	57.4	14.9
Marital status:			
Married	110	61.6	4.6
Non married	25	76.9	8.4
Cigarette smoking:			
Nonsmokers	24	70.4	9.3
Smokers	100	68.1	4.7
Alcohol consumption			
Never	28	56.3	9.4
Social	26	70.6	8.9
Heavy	14	49.2	13.4

* Crude response rate in each subcategory.

** Denominators were all eligible subjects in each group for which information was available. Because of missing information for some of the variables, the total numbers for ethnic group, marital status, cigarette smoking and alcohol consumption did not equal the total number in the study.