Mortality Study Critique

Eric Mintz, Ph. D.

February 2004

DRAFT ONLY

I. Background

Port Hope is a small community with a current population of about 12,000. It follows that the study of rare diseases is limited by the small numbers of cases that would be expected to occur in a limited time period. This is a constant and crucial consideration. Many of the diseases that might be of concern in Port Hope are normally rare ones like brain cancer and leukemia. Any study of rare but important outcomes in Port Hope would want to maximize the number of cases available for study.

A. Mortality Data vs. Incidence Data

Even serious diseases like cancer may have a considerable long-term survival rate. Therefore a mortality study will result in many fewer cancers to study in a time period than would an incidence study. The degree of the difference is related to the case-fatality rate of the cancer. Lung cancer mortality and incident event numbers would not differ markedly because lung cancer is usually fatal. Breast cancer incidence rates are much higher than fatality rates, however, since the case-fatality rate is about 50 percent. Overall, there were a total of 589 incident cancers diagnosed (using postal code for residence) from 1986-1996. During the period 1986-1997 there were 339 cancer deaths. There were over 53 incident cancers and only about 28 cancer deaths that occurred per year during these most closely corresponding periods. Clearly when we use mortality data we lose a large proportion of the cases. This is crucial given the small numbers and the resulting low statistical power available to analyze most cancers, even when using incidence data. It is important that with mortality data many more of the computations will be confidential, since the overall number of deaths will more likely be less than 5.

The bottom line is that the lower number of mortality cases results in a serious limitation for studying cancer in Port Hope, since the mortality study will generally have fewer cases for each disease in each time period. This seriously limits the statistical power associated with the SMR analyses and subsequent conclusions that can be made.

Obviously the time from cancer initiation to death is longer than the time to diagnosis. This occurs because in addition to the time between exposure to disease diagnosis; there is an additional period from diagnosis to death. The longer the period from exposure to an outcome, the more difficult it is to make associations and particularly causal connections. Also, people may be more likely to move between diagnosis and death. The residence is assigned at the time of death. Again in this regard, incidence data is superior. It should be noted that because the time intervals are rather long; that many deaths would occur in the same time interval as the diagnosis.

Incidence is a measure directly rated to risk (if surveillance biases are not large) whereas mortality is related to two measures; the risk of getting the disease and the risk of dying from the disease once you get it. Clearly earlier detection and better medical care may lower mortality but will not usually affect disease risk. It is the risk of getting disease that is most important in Port Hope since risk is most closely related to causation.

The mortality study covers a period of 42 years compared to 26 years in the incidence study. Taken by its itself, of course, the greater follow-up period would appear to at least partially balance the lower mortality numbers per time period.

But the study in specific time periods (e.g. 10 year periods) will have less power in the mortality study due to smaller numbers. This is very important because the entire study period includes times of higher and lower exposures which when combined will dilute any negative health effects. In other words, trends in time may be masked when we only have sufficient data to look at the entire time period.

This is particularly evident for childhood cancers where mortality data is only presented for the entire period, presumably due to the small numbers resulting in time specific data being of limited use. Since children generally have greater exposures and shorter induction times, the childhood data is of particular interest. Looking at Table 1, it is quite evident that the incidence data for children is much more revealing than the mortality data (e.g. brain cancer).

B. Ecological environmental studies

This mortality study utilizes environmental epidemiology. Environmental epidemiology investigates whether environmental exposures are associated with subsequent excess rates of disease. Ecological studies in particular, such as this one, are blunt tools. There are many limitations and biases that make it difficult to obtain an accurate picture of the relationship between exposure and disease, some of which are described below.

C. Biases

1. a). misclassification by disease

a) i). misdiagnosis

There is considerable misdiagnosis of cancer. The diagnosed cancer may not represent the primary site (where the cancer originated). The degree of misdiagnoses depends on the tumour type as well as other factors. This may be a smaller problem for mortality data when compared to incidence data.

b) ii). coding errors

There will inevitably be some death certificate coding errors of the tumour type by The Cancer Registry.

2. b). misclassification by exposure

Misclassification by exposure is most likely far more important than misclassification by disease.

a) i. migration

Any ecological study such as this one, makes an implicit assumption that those who lived in Port Hope when they died had lived there long enough to have been exposed there. This is often not the case. Lee's incidence study found that nearly 1/3 did not live long enough in the community to receive a meaningful radon dose. On the other hand, some people move away to live in a different community at the time of diagnosis. Their tumour that may have been acquired due to exposures in Port Hope, will not be attributed to Port Hope. People may be even more likely to move by the time of their death. These biases may be important. This bias will generally be nondifferential that means it results in an underestimating of risk (towards the null).

b) ii. residency coding

Residence at death may not be completely or accurately coded. This is discussed at some length in the report.

3. standard rates

The standard rates used to determine the expected number of cancers are based on provincial rates. These rates include other areas close to nuclear facilities as well as many urban areas that may have multiple exposures to various industrial and environmental contaminants. Therefore many of the communities included in the standard may have elevated rates. Therefore we could be comparing "dirty" areas to "dirty" areas and may be falsely underestimating risk in Port Hope.

D. Limitations

1. This being a descriptive SMR (Standardized Mortality Ratio) study, there is no information on individual exposures. The principal exposure is living in Port Hope. There is no way to control for confounding for individuals; that is we don't know what other factors besides radiological and heavy metal exposures in Port Hope may have caused cancers or other diseases. Certainly many other common causes are acting besides the one(s) of interest in this study. For these reasons, firm conclusions regarding cause and effect for such studies are generally not possible. The main purpose of this type of preliminary study is to provide leads for further research.

2. Statistical results can only be used as a guidepost. Since so many SMRs were calculated, many (5 or 10% depending on the significance level) would appear to be statistically significant even if there were no unusual exposures in Port Hope. On the other hand, small numbers result in very low statistical power (ability to detect SMRs that are truly elevated). This is even more of a problem in the mortality study. Therefore elevated but non statistically significant results cannot provide reason for comfort. The pattern of elevated SMRs must be judged as to its suggestibility of problems. On interpretation of this pattern, reasonable people may disagree.

3. We are dealing mainly with chronic diseases such as cancer and circulatory disease, most of which have very long periods from diagnosis to death. It is difficult to assign causation for a chronic disease to an exposure that may have occurred 25 years ago. These problems are less important for some of the cancers such as leukemia that have a shorter induction period.

4. The accuracy of the census data for Port Hope is another limitation. Census data inherently will have some under or overcounts.

E. Burden of Proof

The statistical burden of proof is very high. Traditionally we have to be 95% or at least 90% certain (confidence level) that differences are not due to chance before we state they are "likely not chance findings" or statistically significant. That leaves the area of high but less than 90% confidence as a gray zone where results are likely real, but not statistically significant.

The arguments for using a 95% confidence level (5% significance level) centre on it being the historical standard for the burden of proof. There is, however, no logical basis for choosing the 95% level of confidence. In fact, in was originally arrived at based on the cost-benefit associated with agricultural decision making. It is arbitrary. Most people use it simply because others have, not because of its appropriateness. It was not designed with the limitations of environmental epidemiology in mind.

The 95% level would appear unrealistically stringent here for a number of reasons including the following:

1. The confidence level assumes that the data is of high quality. High levels of misclassification by exposure (people are placed in the incorrect exposure categories) and some misclassification by disease (people are incorrectly classified as either being

free from or having a given cancer) will usually decrease the chance of finding significant differences between groups. This sets the burden of proof much higher than the stated level. We are dealing with highly inexact data here. Most of the biases are non directional errors that would increase the burden of proof by adding noise to the data. The misclassification may be quite large in this study due to the serious sources of bias discussed above.

2. The ramifications of incorrectly finding a significant relationship between an exposure and a cancer is not great since conclusions in a study of this type will be based mainly on patterns rather than individual associations.

3. The ability to detect true excesses (statistical power) is very low for many cancers in the mortality study. Using a high confidence level decreases the power.

For these reasons, I advocate a less stringent burden of proof of 90% if one is to be chosen at all.

In any case, the choosing of a significance level is largely a red herring. Significance levels are chosen when we are investigating whether an exposure (or a few) is related to a disease (or a few diseases). They are used to make decisions.

This study (and the incidence study) is not to be used for decision making. It is a preliminary study searching for likely leads. We are looking at hundreds of SMRs. It is not useful to rely on a stringent, strict statistical cutoff as a standard of proof. In so doing, we would be imagining that the quality of evidence is far superior than the reality and not taking into account serious issues affecting the true statistical significance of each finding.

The 95% confidence level, or any other, is not magical. For example, a study comparing leukemia rates in children living around the Pickering plant to lower risk children found approximately a doubling of the risk for children living near the plant. The probability of this finding being due to chance was about 5.5%. Therefore the study was interpreted as being "negative", that is not statistically significant. If the p-value was 4.9% the study would have been seen as "positive". Clearly these divisions are arbitrary and somewhat foolish.

The only statistical measure that really matters is the p-value, which is based on the results obtained. Interpretation of the results should be based on the p-value, an estimate of the biases affecting the p-value and clinical information, other information (such as the patterns over time and demographic groups) and common sense. Interpreting study results as negative based on arbitrary significance points is nonsensical in my view, for all of the above reasons.

The choosing of important findings is an art as well as a science. The p-value along with the consistency of the finding and its plausible relationship to exposures in Port Hope should be taken into account.

For example, in the incidence study, brain cancer was found to be elevated in all time periods for women in Port Hope. It is statistically significant at the 5% level for the

period 1986-1996 using MOH data only (p-value < .05). It is also highly significant for the total study period (p<.01). This cancer is elevated in men for the 1986-1996 period, but the p-values are not low (could well be a chance finding). Taken alone the male data would not be strongly suggestive of excess brain cancer.

Brain cancer was found to be highly elevated in Port Hope children during the period 1971-1985 (p < .05). These findings taken together show a pattern that is quite suggestive of there being a problem with brain cancer in Port Hope, even though only some of the findings were statistically significant at the 5% level. This is because excesses were found in all three groups and in all time periods.

Children generally have greater exposures and shorter latency periods. That the brain cancer excesses were greatest in children and appeared earlier is supportive of a real excess that is environmental related.

The above example shows that statistical significance (at any level) should be used only as a guidepost or screen for diseases which require further scrutiny. There will be significant results that are due to chance because of the large number of SMR calculations. On the other hand, because of low statistical power, many of the nonsignificant elevations may be important particularly if they are part of a pattern of excess rates.

F. IV - Other Issues

1. Time Window

As previously stated there are long periods between exposure and death for most cancers and other chronic diseases. This period between initial exposure and death will vary by disease. It becomes obvious that one will not uncover excesses if one is looking in the wrong time window. For example, most leukemias have short latency periods of less than 10 years. If it is true that exposure was greatest before the mid 1970s then we would expect the greatest leukemia rates to occur in the 1971-1985 time period.

The expected pattern of excess is one of the tools we can employ to separate perhaps spuriously elevated rates from ones which require further scrutiny.

G. Background Summary

Most of the biases discussed above serve as white noise masking any real effect between exposure and disease. The result is that most environmental epidemiological studies are biased towards producing "negative" results due to the inherently low quality of the evidence (data) being evaluated. This should be taken into account when interpreting the findings.

II. Text Review and Discussion

1 b. Port Hope Background

The Lee study result did show an association between radon levels and lung cancer risk in Port Hope after smoking was controlled for. This is minimized in the report, here, and in the discussion.

The report tells us that models show that "an observed excess of cancer would not be expected because the cumulative doses were low." But such models are of dubious worth since they are based on very inexact cumulative doses of exposure and "existing knowledge of dose-response relationships of radiation risk." Also, logically, the main values of models is to predict the future, not the past. If a model says that excess cancer should not be occurring but our findings show that it is occurring, it is only logical to put more weight on the actual data rather than a theoretical and limited prediction.

Similarly, while it is noted that heavy metals that are of concern in Port Hope are human carcinogens, the Ontario Ministry of the Environment reported that levels observed in Port Hope (in 1991) "were not of sufficient magnitude to expect increases in cancer". Here we have the additional limitation that exposures were measured at only one point in time.

The increases of circulatory disease found with radiation doses of one Gy or higher is a finding that is potentially very important. Circulatory disease is extremely common, being the leading cause of death in Western Society. Even a weak association between radiation exposure and circulatory disease would have a greater effect than a strong association between radiation and a rare disease. For example, the greater than 20 fold (2000 percent) increase in lung cancer deaths associated with heavy smoking has a lesser public health impact than the 1.4 fold (40 percent) increase in heart disease caused by heavy smoking.

2. Methods

A test for trend in over the time period of the study was done for most causes of death. But why would one expect a trend in time over the study period, if the exposures in Port Hope were (are) significant health predictors?

Its true that there were remediations done in the late 70s that would hopefully reduce the burden of some contaminants. But the long latency of many cancers would result in the effects (especially for the additional time inherent in mortality data) not appearing, for the most part, by the terminal study year of 1997. It is also not clear if exposures were greatest in the 50s and 60s. Therefore, I would not necessary expect most cancers to follow a trend line showing a decreasing rate in time from the 1950s to the 1990s.

The report , throughout, appears to ignore this long latency period from exposure to diagnosis and then to death that we know exists for many cancers. For example, the report states when referring to providing SMRS starting in 1956 "the importance of going back as early as possible is based on providing results for the time period before remediation actions were initiated to determine if greater effects were observed than in later periods." But for cancer, even mortality cases from the 70s would almost universally reflect cases that were initiated years and even decades earlier, before remediation took place.

3. Results

3a. Port Hope residence assignment

There were pockets of very low all cause mortality in Northumberland County; namely Hope Township and Hamilton Township. Both had just over half the expected number of deaths in the period 1986-1997. This contrasts with an SMR of 1.13 or 13% more deaths for all Port Hope residents over that period. However the entire county had an all cause SMR for all residents of 1.01 for the entire period. Assuming that Northumberland included Port Hope, the Northumberland all resident SMR (excluding Port Hope) would have been noticeably lower than Port Hope's.

3b. Mortality for Cancers Frequently Associated with Radiation and Childhood Cancer

Tables 3a-c are supposed to present SMRs for all cancers combined and radiosensitive cancers. Only lung, breast and leukemia were considered radiosensitive. Notable by omission were brain cancer (where radiation is certainly a suspected cause) colon cancer, stomach and rare cancers such as NHL, Hodgkin's disease and other rare cancers associated with radiation.
Since there are a smaller number of cases in each time period, censoring due to confidentiality concerns, reduces the value of the data in this study. In these cases the actual number of cases and the associated confidence intervals are not released. The result is still flagged as "statistically significant" at the %5 or lesser level, but no other information is given.

The mortality data is certainly much less useful in assessing childhood cancer in Port Hope. There were only 19 incident cases that occurred in the 26 year period from 1971-1996. Numbers were very small for most cancers resulting in a low ability to detect any high cancer rates that did exist (low statistical power). But the mortality data was much more limiting. Only 11 cancer related deaths occurred during the 42 year period covered by the mortality study. Statistical power, already a problem, is much lower here. For example, for all childhood cancers there was a 48% increase over expected rates and for leukemia a 63% elevation over what might be expected. We cannot say that these two results are not chance happenings, however, due to the low power. Given the lack of information available to us in this data, statements about statistical significance are of little value.

While the report emphasizes that all SMRS in these tables of "sentinel" sites for radiosensitivity were near one, actually lung cancer was elevated for men and women in different periods. The results were near statistically significant at the 10% level. In fact over the entire study period females showed an SMR for lung cancer of 1.15.

What is notable are the radiosensitive data not highlighted in this section. Brain cancers in females appear at more than 2 times the expected rate in the 1986-1997 period ($p<.05$) similar to the incidence results. Children showed a near 50% excess of brain cancer over the mortality study period ($p>.05$). Colorectal cancer rates were high in women during the same period (SMR = 1.38 p**) which closely matches the corresponding incidence results using postal code (1.42 $p<.05$). I cannot see a valid reason for colorectal and brain cancer data to be ommitted from this table.

The small percentage excess rates for circulatory disease noted are highly significant because of the great importance of this cause of death. Even small rises in rates have large impacts. Male rates all high over the enitire study period while female rates are higher in the later periods. They are the main reason that some of the all cause mortality rates are significantly high.

3e. Comparison of Morbidity and Mortality

While mentioning the high brain cancer rate for women state that "brain cancer was not significantly elevated in any other time period, or among men". True enough, but this passes by the fact that the childhod brain cancer incidence rate was highly elevated (SMR = 4.17 , $p<.05$) during the 1971-1985. (Add text from incidence**)

4. Discussion

4a. Summary of Main Results

This section begins by saying "the mortality rates for all cancers were within expected values, based on provincial rates, for all periods examined and among both males and females". In fact, for males during 1956-1965 the SMR was 1.12 ($p>.05$). Again the authors limit 'sentinel" cancers to lung, breast, leukemia and thyroid. This conflicts with the literature and even their own earlier discussion (section 1c.) which shows many more cancers associated with radiation exposure.

Nasal cancers are associated with heavy metal carcinogenetic exposures in Port Hope, but are not discussed as a cancer "important in examining possible adverse health effects of industrial activity in Port Hope". Nasal cancer incidence rates were significantly high for males, most notably in the 1971-1985 period with rates 5 times higher than expected. The mortality study does not indicate excess rates. Most probably this indicates that most of the small number of cases survived. This points out the weakness of mortality data for studying rare cancers that are not usually fatal.

Regarding leukemia, both the incidence and mortality results show a markedly (but not statistically significant) increase over expected rates in the order of 50% over the entire

study period. In addition, rates were lower than expected since remediation which indicates that in the period 1971-1985 they must have been even higher. The statistical power, or the ability to detect true excesses is very limited for childhood cancers, which is acknowledged in the report. Yet later in the discussion we are told that "the absence of excess leukemia cancer rates is particularly reassuring". This latter statement is inreconcilable with the findings of an excess noted with low power The fact that we cannot prove that the excesses noted were not due to chance fluctuations, is hardly grounds for rejoicing.

Then there is the major consideration of brain cancer in children. There was a markedly high rate before remediation found in the incidence study. The mortality study does not contradict the incidence study. It shows an excess in brain cancer over the entire period which is not statistically significant. However, the data is very limited by the very small numbers and the fact that the results are not shown for each time period.

When one considers all of these factors, the discussion of the childhood cancers does not accurately reflect the findings and the inherent limitations of the studies.

The small percentage increases in circulatory deaths, noted in this section, is very significant in terms of number of lives this represents. A small increase in a very common disease may be more important than a very large increase in a rare disease. For, example, during the 42 year study period there was a modest 15% excess over expected in circulatory deaths. But this represents over 300 excess deaths (more than 7 a year). Clearly, more study of the circulatory disease risk factor profile in Port Hope is warranted in an attempt to determine if lifestyle or environmental contamination is most likely responsible for the findings.

4b. Strengths and Limitations of the Report

The authors continue "The absence of an increase in leukemia rates, and other radiosensitive sites, does not support the hypotheses that radiation exposures in the community impact on residents' health. The absence of excess leukemia cancer cancer rates among chidren is particularly reassuring, because the minimum latency for childhood leukemia is short and the radiation risk coefficent relatively high".
This is misplaced ****

On page 10 there is a thorough discussion of the effects of misclassification on epidemiological studies. Misclassification occurs when individuals are placed in the wrong exposure or disease categories. Generally, misclassification biases results towards the null. This means that real excesses in rates are more likely to go undetected. The results of misclassification will normally lead the observed SMR to be lower than the true one. As the report states, the possibility for misclassification is even greater for mortality data since there is additional time (and possibly reasons) for individuals to migrate between the time of diagnosis and death.

Since radiation exposre is a factor of interest, it is not a confounder. Therefore it shouldn't be discussed here as a confounder for brain cancer. Similarly, radon is discussed here with respect to lung cancer when it is a known risk factor rather than a confounder.

The public health importance of the high circulatory disease rates in Port Hope and the lack of information regarding the cause of the high rates make it a priority for investigation. Given these conditions; it is inappropriate that this is dismissed out of hand as not due to exposure. The reasons given are the low exposures and the high rates in the rest of Northumberland County. But the effects of prolonged low radiation exposures are not known, particularly in conjunction with heavy metal exposures. ** are the rates in the rest of the county as high.

4d. Concluding Remarks

The first paragraph in this section misrepresents the results. Suprisingly we are told that "the absence of an increase in leukemia rates and other radiosensitive sites, does not support the hypothesis that radiation exposures in the community impact on residents' health. The absence of excess leukemia rates amongst children is particularly reassuring". It depends on how you define "excess" and "radiosensitive sites". As discussed earlier, the leukemia rates in children are well above those expected. The fact that they are not statistically significant is far from reassuring given the low statistical ability to detect real excesses due to small number (low power). Radiosensitive sites are defined in a limited fashion, not including brain cancer and colon cancer which both show some disturbing patterns. Certainly the raised leukemia rates, which were even higher before remediation support an effect on residents's health. Along with the brain cancer and colon cancer results and some of the rare cancers, the available evidence points to their being problems in Port Hope. The fact that this evidence, due to its limited nature is not definitive should not be taken as reassuring. Again strict criteria of statistical significance is used for decision making when information available in this report show such a method to be inadequate and inappropriate.

. add last sentence in paragraph one ..comment on the rate really being higher in the first period..we dont know what they speculate on is true.

Are the results of the mortality and incidence childhood cancer studies reassuring? Actually the available data, having the limitations alluded to, points strongly in the opposite direction. Firstly, in the mortality study, all 4 cancers looked at, showed SMRs greater than one. There is only 1/16 probability that this would occur by chance if there was in reality no problem with childhood cancer in Port Hope.

Referring to brain cancer, the increases noted in women are discounted since "the lack of any excess among men in any period does not provide suport for an environmental hypothesis". This assumes that men and women have been subjected to the same environment. But through personal communication, I hav learned that the women were more likely to play with children in some of the high risk areas. Men were more likely to be working. Ignored are children where in an earlier period the incidence was

several times the expected rate. The pattern of childhood and female breast cancer increases is consistent with an environmental effect.

The incidence data provides much more information for rare cancers or those with low death rates. The incidence report showed brain cancer to be elevated in all time periods for women in Port Hope. It is statistically significant at the 5% level for the period 1986-1996 using MOH data only (p-value < .05). It is also highly significant for the total study period (p<.01). This cancer is elevated in men for the 1986-1996 period, but the p-values are not low. Taken alone the male data would not be strongly suggestive of excess brain cancer. Brain cancer was found to be highly elevated in Port Hope children during the period 1971-1985 (p < .05). These findings taken together show a pattern which is quite suggestive of there being a problem with brain cancer in Port Hope, even though only some of the findings were statistically significant at the 5% level. This is because excesses were found in all three groups and in all time periods. The sum of this data is not likely to be due to chance.

The above example shows that statistical significance (at any level) should be used only as a guidepost or screen for cancers which require further scrutiny. There will be significant results that are due to chance because of the large number of SMR calculations. On the other hand, because of low statistical power, many of the nonsignificant elevations may be important particularly if they are part of a pattern of excess rates. It is harder to discern patterns in the mortality data since so many results are censored or based on smaller numbers.

The second paragraph makes the point that cancer mortality rates were close to Ontario rates. As noted, the patterns of several cancers rates show cause for concern in that the patterns are consistent with environmental contamination. The standard rates used to determine the expected number of cancers are based on provincial rates. These rates include other areas close to nuclear facilities as well as urban areas which may have multiple exposure problems and elevated rates. Urban areas generally have higher cancer rates than small communities like Port Hope. Therefore we could be comparing "dirty" areas to "dirty" areas and may be falsely underestimating risk in Port Hope. This problem is not totally alleviated by comparisons to similar communities because of the limitations of these comparisons. It is nearly certain that the Ontario standard rates overestimate the risk that a community like Port Hope should have in the absence of major unusual environmental contaminants. It follows that the SMRS that have been calculated generally underestimate the risk in Port Hope. Under normal conditions, because of a "healthy community effect" we would expect most SMRS to be lower than one. Along with misclassification bias, which is probably larger in mortality studies, the calculated SMRS may be considerably larger than the true values would be. Given these arguments, there is nothing about the results here that could be deemed reassuring unless your criteria is that there be no obvious gross excesses of cancer in Port Hope.

III. Analyses of Results

Brain cancer was discussed at length in the Incidence Study Review (1) because the pattern of elevated rates suggest strongly that there may be a problem. The mortality data are more sparse, particularly for children where data are only presented for the entire time period where nonsignificant but higher than expected death and case rates are found. Where there is corresponding data, there are not great disparities. For example, women show statistically significant and similarly elevated brain cancer rates in the 1986-1996,7 periods whether considering deaths or incident cases. The only possible disparity is that males show high incident rates in 1986-1996 but lower than expected mortality rates. Men and women combined show similarly increased (not statistically significant) incidence and mortality rates over the entire period.

Lung Cancer

Lung cancer death SMRs are generally lower than the corresponding SIRS for some unexplained reason. The incidence and mortality patterns are similar for women, however, as the rates are high in the 1986-1996,7 period.

Colorectal

The incidence study showed high rates for women in the 1986-1996 period. The mortality study showed a similar 38% higher number of deaths than expected. The only difference, is that as has often occurred, the incidence results are statistially significant while the mortality ones are not due to the lower power. Men do not show a marked increase in this cancer in either study, although the mortality rates are higher in the two later time periods.

Breast Cancer

There is a hint of elevated female breast cancer incidence rates (not statistically significant) but the mortality rates are close to expected values.

Rarer Cancers
(Lip/nose and sinuses/bone)

All of these rarer cancers showed statistically significantly elevated rates for men in at least one time period. Nasal cancer is associated with the heavy metal exposures of Port Hope. This is not reflected in the corresponding mortality results where there were no significant elevations and all SMRs were displayed as <1 or >1 due to confidentiality restrictions. Clearly the mortality data is not very useful for looking at very rare cancers because of universally small numbers.

Leukemia

This cancer which has a relatively large impact on children and known to be radiation sensitive; is of interest for both reasons. Adults show no evidence of problems. As noted in the incidence review, children demonstrate a 41% elevated rate for the entire incidence study time period. This result while suggestive, is not statistically significant. The mortality results are only available summed over the time periods and shows a similar but slightly higher SMR.

NHL

Children showed statistically significantly elevated incidence rates for the 1986-1996 period and for the entire period. The mortality study again gives little information, showing a confidential computation for the entire study period only. It shows a rate over one that is not statistically significant. Less data provides less information that limits interpretations and conclusions.

Esophageal

There is suggestive evidence that male esophageal cancer rates are elevated in Port Hope. For the earliest incidence period and the nearest corresponding mortality study period; the SIR and SMR are both well over 2. The incidence result is statistically significant. The mortality SMR shows a 50% increase over expected rates during this period at borderline statistical significance at the 10% level **test. The incidence study showed women to have higher than expected rates in all periods and a 50% excess rate for the entire period which was not statistically significant. The mortality rates were near expected ones for women.

For men and women combined, both incidence and mortality rates were statistically significantly high for the 1971-1985-1976-1985 periods. The SMR for th e 66-75 period was 1.86 (Nss test). For the entire time period, both rates were greater than one, but not statistically significant test.

IV. Conclusions

1. Regarding cancer, when we use mortality data instead of incidence data, we lose a large proportion of the cases. ~~This is crucial~~ given the small numbers and the resulting low statistical power available to analyze most cancers, even when using incidence data The ability to detect real increases in many cancer (statistical power) is inadequate and much lower than in the incidence study.

2. It is important that with mortality data many more of the SMR computations will be confidential, since the overall number of deaths will more likely be less than 5. For a large proportion of SMRs, the actual number of cases and the p values are not released. We only know if the results were statistically significant or not. This censoring due to confidentiality concerns, further reduces the value of the data in this study.

3. It follows from 1. and 2. that for the study of cancer in Port Hope, incidence data is more useful than mortality data since there is no reason to believe that the mortality data is of greater quality.

4. Most of the analyses, presentations and interpretations are based primarily on strict statistical criteria (statistical significance at the 95% level). Results are important and noted if they meet this requirement and are dismissed if they do not. This is inappropriate for several reasons discussed in this report.

5. Tables 3a-c are supposed to present SMRs for all cancers combined and radiosensitive cancers. Only lung, breast and leukemia were considered radiosensitive. The definition of cancers "sentinel" for radiosensitivity is arbitrary as several radiosensitive cancers are not highlighted.

6. The incidence and mortality results cancer results generally show close agreement. Despite this, the incidence results are more likely to be statistically significant due to the limited information contained in the mortality data.

7. The results of the mortality study do not in any way contradict the main conclusions of the Incidence Study Review (1). These major conclusions are listed below:

   - For several common cancers the evidence from this study suggests that females have high rates (lung cancer, colorectal cancer, all cancers). The SIRs were generally higher than the corresponding ones for males. These findings suggest differential exposures by gender.

   - If confounding explains the pattern of lung cancer and colorectal rates it would have to be greater for females. Such a scenario is not a likely one.

   - The findings suggest that children have experienced high cancer rates particularly before 1986. The pattern of cancer rates in children is consistent with effects from the higher exposures before remediation.

- The findings taken together show a pattern which is quite suggestive of there being an excess of brain cancer in Port Hope.

- The Canadian Cancer Registry confidentiality restrictions when there were less than five cancers further constrained a study which relied on limited data.

- Further research should look into the feasibility of a case-control study for suggestive sites.

8. The small percentage excess rates for circulatory disease noted are highly significant because of the great importance of this cause of death. Even small rises in rates have large impacts. Male rates all high over the enitire study period while female rates are higher in the later periods. They are the main reason that some of the all cause mortality rates are significantly high.

9. The reasons for the high circulatory death rates are not clear. It is important to determine if the radiation and heavy metal exposures in Port Hope are contributing factors for the reasons outlined in 8..

10. When one considers all of the inherent biases and limited data, the discussion of the childhood cancers does not accurately reflect the findings and the inherent limitations of the studies. The term "reassuring" to characterize these findings is not appropriate.

11. The report , throughout, appears to ignore the long latency period from exposure to diagnosis and then to death that we know exists for many cancers and other chronic diseases. For example, for cancer, even mortality cases from the 70s would almost universally reflect cases that were initiated years and even decades earlier, before remediation took place. This contrasts with assertions made in the report.

		66-75		0.57test			0.89				0.75
			SMRS - Selected Cancers								
			Incidence	Mortality		Incidence	Mortality		Incidence	Mortality	Incidence	Mortality
Cancer	Time Period	Time Period	Men			Women			Children		Overall	
	Incidence	Mortality										
	71-85	76-85	0.93	1.18test		1.03	0.72				0.99	0.93
	86-96 PC	86-97	1.03	1.20test		**1.42****	1.38test				**1.23****	1.29borde
	86-96 MOH		1.08			1.26*1/2					1.17	
	Total	Total	1.01	1.05		1.13	1				1.07	1.02
Nose/sinuses		56-65		<1			<1					<1
		66-75		<1			<1					<1
	71-85	76-85	**5.61****	<1		<1 nc	<1				2.86*	<1
	86-96 PC	86-97	<1nc	<1		>1 nc, ns	<1				<1 nc, ns	<1
	86-96 MOH		>1nc,ns			>1 nc, ns					>1 nc, ns	
	Total	Total	**>1 nc ****	<1		<1 nc, ns	<1				>1 ** nc	<1
Lip		56-65		<1			<1					<1
		66-75		<1			<1					<1
	71-85	76-85	1.12	<1		<1 nc	<1				0.95	<1
	86-96 PC	86-97	**2.35***	<1		<1 nc	<1				1.78	<1
	86-96 MOH		**2.75****			<1 nc					2.07*	
	Total	Total	1.71	<1		<1 nc	<1				1.39	<1
NHL children		56-65		<1			>1					1.62test
		66-75		<1			<1					<1
	71-85	76-85		<1			<1		>1 nc, ns			0.78
	86-96 PC	86-97		<1			1.68test		**>1 ****			>1
	86-96 MOH								**>1 ****			
	Total	Total		0.71			1.40check		**>1 ****	>1		1.06
Leukemia		56-65		>1			<1					0.93
		66-75		<1			>1					>1
	71-85	76-85		<1			<1		**>1 nc, ns**			<1
	86-96 PC	86-97		0.78			0.89		<1			0.83
	86-96 MOH								<1			
	Total	Total		0.63			0.85		1.41	1.63test		0.73
Breast		56-65		<1			1.06					
		66-75		<1			0.99					
	71-85	76-85		<1		1.17 borde	1.01					
	86-96 PC	86-97		<1		1.01	0.96					
	86-96 MOH					0.93						
	Total	Total		<1		1.09	1					
Esophageal		56-65		>1			<1					<1
		66-75		>1			>1					1.86test
	71-85	76-85		2.48			>1					>1**
	86-96 PC	86-97		<1			<1					0.72
	86-96 MOH						<1					
	Total	Total		1.52*?			1.02					1.35test

Table 1 - Incidence and Mortality Results

SMRS - Selected Cancers

Cancer	Time Period Incidence	Time Period Mortality	Incidence Men	Mortality	Incidence Women	Mortality	Incidence Children	Mortality	Incidence Overall	Mortality
All Causes										
		56-65		**1.10****		**0.97**		**0.81**		**1.04test**
		66-75		**1.10****		**1.03**		**1.1**		**1.07**
	71-85	76-85		**1.12****		**1**		**1.02**		**1.06**
	86-96 PC	86-97		**1.09****		**1.16****		**1.18 test**		**1.13*****
	86-96 MOH									
	Total	Total		**1.10****		**1.06****		**0.98**		**1.08*****
All Cancer										
		56-65		1.12		0.93		>1		1.02
		66-75		0.89		0.89		>1		0.89
	71-85	76-85	0.99	1	1.01	0.96	1.76*	>1	1	0.98
	86-96 PC	86-97	0.93	0.98	1.07	1.09test	0.82	>1	1	1.03
	86-96 MOH		1.01		1.11		0.98		1.06	
	Total	Total	1	0.99	**1.06***	0.99	1.41 .5*	1.48test		0.99
Brain		56-65		>1		<1			>1	>1
		66-75		>1		>1				1.52test
	71-85	76-85	<1	<1	1.73 (.97, 3	<1	**4.17****		nc, ns>1	<1
	86-96 PC	86-97	1.31ns	<1	1.61	**2.39****	<1		1.45	>1
	86-96 MOH		1.49 ns		**2.21****		<1			
	Total	Total	<1	1.03	**1.96*****	1.47 check	>1 nc ns	>1 nc??	1.23 ??do	1.23test
Bone		56-65		>1		<1				>1
		66-75		<1		<1				<1
	71-85	76-85	>1 nc,ns	>1	<1 nc	<1	.		>1 nc,ns	>1
	86-96 PC	86-97	<1 nc	>1	<1 nc	<1	.		<1 nc	>1
	86-96 MOH		>1 nc, ns		<1		.		>1 nc, ns	
	Total	Total	**2.58***	>1	<1	<1	.		1.38	>1
Lung		56-65		1.27		>1				>1
		66-75		0.92		>1				NA
	71-85	76-85	1.13	1.02	0.93	0.86			1.08	0.97
	86-96 PC	86-97	1.05	0.96	**1.35***	1.28test			1.16	1.07test
	86-96 MOH		1.13		**1.44****				1.24**	
	Total	Total	1.13 near 1	1	**1.24***	1.15test			1.17**	1.02
Ovary		56-65				<1				
		66-75				<1				
	71-85	76-85			0.92	1.11				
	86-96 PC	86-97			**0.43****	0.61				
	86-96 MOH				**0.43****					
	Total	Total			0.69	0.79				
Colorectal		56-65		1.1		0.85				0.96