HEALTH ASPECTS OF ORGANIC COMPOUNDS IN DRINKING WATER:

EPIEMIOLOGY (H0298CX)

Final Contract Report to the Department of the Environment

Authors:
Shirley A A Beresford*
Lucy M Carpenter*
P Powell

April 1982

307-M

RESTRICTION: This report has the following restricted distribution:

External: DOE Nominated Officer – 20 copies
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*Royal Free Hospital
School of Medicine
Department of Clinical Epidemiology and General Practice

DOE CONTRACT REFERENCE: DGR/480/294 & PECD7/7/015
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PREFACE

On 1st April 1977 the Department of the Environment placed a contract (Ref. DGR/480/294) with the Water Research Centre to evaluate the possible health effects of the long-term consumption of water from sources containing sewage effluent or industrial effluent. This contract ended on 31st March 1982 but was renewed for three years beginning on 1st April 1982 and ending on 31st March 1984 (Ref. PECD 7/7/015). The work carried out in this study fell into three, broad categories - epidemiology, toxicology and water quality studies.

The work reported here relates to the epidemiological aspects of the contract, the objective of which was to investigate the possibility of an association between the degree of contamination of water sources and long-term disease. The work was undertaken at the Royal Free Hospital, School of Medicine, under sub-contract to the Water Research Centre. This sub-contract ended on 30th September 1981. This is the final report of the work covering the period from April 1977 to September 1981.

The Water Research Centre will produce further reports to fulfil the needs of the other aspects of the original contract.
SUMMARY

A number of epidemiological studies carried out in the United States have found statistical associations between cancer death-rates and the use of river or surface waters as the source of supply.

Epidemiological studies using British data have therefore been undertaken to investigate:

(i) the possibility of an association between the long-term degree of contamination of water sources by sewage effluent and industrial effluent, and cancers of the digestive system and urinary tract,

(ii) whether any such associations with water sources exist with respect to more immediate adverse health indices such as stillbirths and infant mortality,

(iii) whether any adverse health effects are associated with organic chemicals in drinking water, as characterised by the type of water source; groundwater, river, or upland catchment.

The first two objectives, those concerned with the possible effects of re-use, were approached first in a study confined to the London area, where some of the water supplies have for many years contained the highest proportion of sewage effluent in the country. The study with respect to cancer mortality was then extended to all those towns in Great Britain receiving lowland river or underground water. The third objective was approached using data from around
250 urban areas in Britain. Multiple regression techniques were used, with refinements to overcome some of the limitations of aggregate population studies. Throughout the work attention has been paid to the influence of socioeconomic, geographical and other possible confounding factors.

The studies provided some evidence of small adverse health effects associated with (but not necessarily caused by) water supplies. In the case of reused water, the associated health effects were stomach cancer incidence in women, urinary tract cancer incidence in women, and stillbirth rates. Although the sizes of the effects of reuse were small, the evidence is consistent with the results of the epidemiological studies in the United States.

In that part of the study in which different types of water source were contrasted, upland-derived supplies were associated with higher mortality from stomach cancer in women. This is a new finding, and the hypothesis would require further testing before a firm conclusion can be reached.

To investigate any of these matters further in this country it will probably be necessary to move on from studies of aggregated populations to studies of individuals. Possible designs for such studies are being investigated.
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1. INTRODUCTION

1.1. BACKGROUND

With the growth in population and greater industrialisation have come increased demands on the water supply in the United Kingdom. As the limits of availability have been reached of water from the relatively unpolluted upland catchment and underground supplies, increases in demand have been met more and more in recent decades by abstractions from lowland rivers. These rivers are used, not only as water sources, but also as a means of transporting domestic and industrial wastes to the sea. Thus some reuse is taking place, with a downstream community drinking water that is, in part, the waste product of the upstream community, albeit after natural and man-made processes of purification.

The biological and chemical quality of such water supplies are, of course, checked routinely, but such is the diversity of organic chemicals that can enter a river system from domestic and industrial waste and agricultural run-off, that, even with today's most powerful analytical techniques, we can identify only a fraction of the substances present. Traditional treatment methods may remove many of these organic compounds, but not all, and some compounds such as the chlorinated organics are actually created in the treatment process itself. Very little is known about the harmful effects, if any, of these pollutants at the concentrations arising at the consumer's tap.

At the Water Research Centre (WRC), three parallel approaches are being used to investigate the possibility of any
harmful effects from organic micropollutants in water. The first
approach is via the development of more powerful and more varied
techniques for the analysis of trace organic compounds in water,
and the assessment of the possibility of adverse effects in the
light of known toxicological evidence. The second approach is by
the development of tests which directly measure the ability of a
given water to produce changes in living organisms, particularly
bacteria, indicative of the potential to induce cancer. These are
the so called mutagenic screening tests. The third approach, which
is the one described in this report, is the epidemiological study
of human populations. In this case retrospective aggregate
population techniques are used to investigate whether there are
associations between drinking water quality and measures of ill-
health that are routinely available. Statistical techniques are
used to take into account as far as possible the influence of
other environmental and socioeconomic factors. Greater weight can
be given to our findings if they are supported by two or more of
these three avenues of research.

There have been several epidemiological studies which have
shown an association between cancer mortality and river water as
the source of drinking water. These studies have been reviewed in
previous publications (1,2,3) and elsewhere. Different studies have
concentrated on different aspects of water supply (type of supply,
chlorination practice, trihalomethane concentrations), and have
examined cancers in different parts of the body (cancer sites) with
varying positive results. Such evidence as was available in 1976
was conflicting and controversial and justified a carefully planned
investigation in Britain.
1.2. STUDY OBJECTIVES

The objectives of the study were to investigate:

(i) the possibility of an association between the long-term degree of contamination of water sources, by sewage effluent and industrial effluent, and cancers of the digestive system and urinary tract,

(ii) whether any such associations with water sources exist with respect to more immediate adverse health indices such as stillbirths and infant mortality,

(iii) whether adverse health effects such as digestive system or urinary tract cancer or infant mortality, are associated with organic chemicals in drinking water, as characterised by the type of water source (groundwater, river, or upland catchment), or the type of water treatment (chlorination, clarification).

1.3. PROGRAMME OF WORK

The first two objectives, those concerned with the possible effects of reuse, were approached initially in a study confined to the London area, where some of the water supplies have for many years contained the highest proportion of sewage effluent in the country. The initial findings of the London study relating cancer mortality and reuse were reported in a previous WRC publication (2). Since that report further work has been done on this topic, and the results are described in Section 2. In addition, data on morbidity (illness not necessarily resulting in death), infant
mortality and fertility in the London area have been analysed as described in Section 3.

We then widened the study of cancer mortality and reuse to include the urban areas in Great Britain on which data had been collected for an earlier study of cardiovascular disease (4,5). This national study is described in Section 4.

Although these studies were initiated as a result of concern over possible ill-effects of reuse, they have been generalised to consider the role of organic compounds in drinking water, whatever their origin. Not all such compounds arise from man's activities. Indeed, there are many humic and fulvic substances naturally present in surface supplies. Treating these supplies, for example by clarification, should reduce the levels of such substances. Chlorination on the other hand is known to produce chlorinated organic compounds which can be much more biologically active than their precursors.

We therefore looked for possible associations between cancer mortality and the type of water (groundwater, upland catchment, river) supplied to urban areas in Britain. This investigation was then extended to look for possible differences in mortality associated with different chlorination and clarification techniques. These studies are described in Section 5.

Finally, we used infant mortality in Great Britain as an alternative to cancer mortality as the adverse health index, and
the results of looking for possible associations with the type of water supply are given in Section 6.

At all stages, the possible influence of socioeconomic and other factors was investigated, and refinements were used to overcome the limitations of aggregate population studies.

****
2. WATER REUSE AND CANCER MORTALITY IN THE LONDON AREA

2.1. INTRODUCTION

WRC TR 138 (2) gave details of the background, design and method of the study of cancer mortality in the London area. To summarise, data were obtained from the Office of Population Censuses and Surveys (OPCS) for deaths from the following cancers for the 7-year period 1968-74, in men and women:

Gastro-intestinal (ICD* 151-154)
Stomach (ICD 151)
Intestinal (ICD 152-154)
All urinary (ICD 188-189)
Bladder (ICD 188)
Oesophageal (ICD 150)
All cancers (ICD 140-209)

Lung cancer (ICD 162), and bronchitis and emphysema (ICD 490-492) were included as a check on the methodology, since these are diseases one would not expect to be related to water quality. A standardised mortality ratio (SMR) was calculated for each borough, for each cause and each sex. The SMR is the ratio of the actual number of deaths in a borough to the number that would be expected from the England and Wales death rates, given the age distribution of the borough population. The SMRs were calculated using five-year age groups, and were restricted to the ages 25-74 years.

* ICD = International Classification of Diseases, 8th revision
Information was also obtained on a number of socioeconomic factors from the 1971 census. These factors are listed in Table 1. Data were also obtained on the degree of reuse in the rivers supplying drinking water to the London area. Historical and present-day measures of reuse were all so highly correlated that one, the percentage of sewage effluent in the river at average river flow was used throughout. Partly because of the inclusion of lung cancer and bronchitis in the analysis, and partly to check for confounding between air pollution and reuse, air pollution data were also obtained. Multiple regression analysis was used to assess the associations between mortality, reuse, and the social and other factors. TR 138 gives full details of the design of this part of the study.

Since TR 138 was published the work has been extended. Firstly, it proved possible to include in the study four more boroughs, those supplied with New River water. The distribution of supplies within these boroughs was originally thought to be too complex, but further discussions with the the distribution engineers enabled the reuse estimates to be made. The additional boroughs were Camden, Hackney, Haringey and Islington. This brought the total number of study units up to 29. A map of the study area giving the different sources of drinking water is shown in Fig. 1.

Secondly, some further statistical techniques have been developed in order to refine the analysis and reduce the chance of finding false positive results. These developments are described in Sections 2.2 to 2.4. Section 2.5 gives the final results as far as the cancer mortality data are concerned.
### TABLE 1. Socioeconomic variables

**a) Measures of housing conditions:**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Overcrowding</td>
<td>% Households with more than 1.5 persons per room.</td>
</tr>
<tr>
<td>% Lack of amenities</td>
<td>% Households without exclusive use of at least one of: indoor WC, fitted bath or hot water.</td>
</tr>
<tr>
<td>% Lack of inside WC</td>
<td>% Households with no inside WC.</td>
</tr>
</tbody>
</table>

**b) Measures of social class and affluence:**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Manual</td>
<td>% Heads of households who usually work in manual occupations (socioeconomic groups 7-12, 14, 15).</td>
</tr>
<tr>
<td>% Semi or unskilled</td>
<td>% Heads of households* who usually work in semi or unskilled manual occupations (socioeconomic groups 7,10,11,15).</td>
</tr>
<tr>
<td>Mean socioeconomic rank</td>
<td>Average score for the area whose economically active males are scored from 1 to 6 according to socioeconomic group (see Reference 6).</td>
</tr>
<tr>
<td>% Higher education</td>
<td>{N} % Economically active persons with HNC or degree.</td>
</tr>
<tr>
<td>% Unemployment</td>
<td>% Economically active males seeking employment.</td>
</tr>
<tr>
<td>Cars per household</td>
<td>{N} Average number of cars per household.</td>
</tr>
<tr>
<td>% Large families</td>
<td>{N} % Households with married couples with five or more dependent children.</td>
</tr>
</tbody>
</table>

**c) Occupational groups:**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Manufacturing industries</td>
<td>% Economically active males normally employed in a manufacturing industry.</td>
</tr>
<tr>
<td>% Mining industries</td>
<td>{N} % Economically active males normally employed in a mining industry.</td>
</tr>
</tbody>
</table>

**d) Measures of urban growth and spread:**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>% New residents</td>
<td>% Residents who had moved into the area in the last five years.</td>
</tr>
<tr>
<td>Population density</td>
<td>Persons per hectare.</td>
</tr>
<tr>
<td>% Migration</td>
<td>{L} % Change in population not accounted for by births &amp; deaths between 1961 &amp; 1971 censuses.</td>
</tr>
</tbody>
</table>

**e) Index of different cultural groups:**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>% New Commonwealth</td>
<td>% Residents born in the New Commonwealth.</td>
</tr>
</tbody>
</table>

{L} Used in the London studies only.

{N} Used in the national studies only.

* The London study used "Economically active males" rather than "Heads of households" in deriving this variable.
Fig. 1. Sources of water supply in London

Boundaries

- Study area
- Greater London
- Boroughs and districts

I 100% well (until about 1960)
II Thames/well mixture (at least since 1940)
III 100% Thames throughout
IV Over 20% New River throughout
V Over 30% Lee throughout (no New River)
2.2. VARIATIONS IN BOROUGH SIZE

Death rates from any given disease are not constant, but will fluctuate naturally from year to year. Even though we have taken data for several years there will still be some error in the index of mortality. These errors will be greater for smaller boroughs than for the larger ones, since fewer deaths are involved. The classical way of dealing with this problem is to weight each borough by the expected number of deaths \(7, 8, 9, 10\), and this was done in TR 138. However, this approach assumes that, after fitting the multiple regression model, the residual variation is proportional to differences in borough size. Some variation will still, however, be due to factors that we have been unable to measure, for example differences in diet, or in smoking or drinking habits. An alternative approach to the weighting problem that takes account of both possible sources of variation in an additive way has been developed recently (11). This is the weighted regression technique that has been used in this report.

There is, however, a reason why weighting may not be appropriate. The smaller boroughs may have more homogeneous populations and be more similar with respect to socioeconomic factors, sources of water supply and therefore risk of cancer mortality than the larger boroughs. For this reason the results from unweighted regression continue to be presented.

2.3. GEOGRAPHICAL CLUSTERING

Another problem with using geographical areas in mortality
studies arises from the fact that the areas are often contiguous, as is certainly the case in the London study. Neighbouring boroughs tend to have similar water supplies, similar socioeconomic factors, and, in some cases, similar SMRs. More importantly, they may also be similar in respects that we have not been able to quantify, but which could affect mortality. This means that the assumption that the error terms in the regression analysis are independent may not be satisfied (12).

Lazar (13) suggests that the number of independent units for analysis should be reduced by amalgamating similar neighbouring boroughs. This idea is intuitively appealing, but discards much information, weakening still further the power of this type of study. We have chosen rather to adjust for any geographical clustering using an adaptation of a method developed recently by Cook and Pocock (14).

2.4. OTHER METHODOLOGICAL PROBLEMS

When using the regression model as a predictive tool, the fact that many of the social factors are highly correlated with each other, and that the degree of reuse of water is moderately correlated with some of the social factors can give rise to a problem known as multicollinearity. If the correlation between the so-called independent variables is too high, the solution to the regression analysis may not be stable. One possible procedure in such cases is to check the solution using a technique known as ridge regression, where the regression coefficients are disturbed a small amount from their unbiased estimates. This was done in two cases where this was most likely to have been a problem. The effects on the regression coefficients were marginal, with no change in the level of
significance, which indicates that the model is stable, at least with respect to hypothesis testing.

A further difficulty that often besets studies of this type is that of institutional deaths. Deaths are classified according to the usual place of residence of the deceased, so that deaths away from home, even after a short spell in hospital, are correctly accounted for. If, however, a person had been residing at his or her place of death for more than six months, in a hospice or long-term institution, for example, then the death will not be transferred back to the usual place of residence, but will be allocated to the borough containing the institution. Since the mortality rate overall is higher in long-stay institutions than in the general community, borough mortality rates can depend on the presence or absence within the borough of a long-stay institution.

OPCS recognise this problem and do publish adjustments to allow for institutional deaths in each borough, but only for deaths from all causes. There are problems of confidentiality when trying to obtain data to apply corrections for each specific disease that we are interested in, where the numbers involved in a borough are so small that they may represent individual cases in individual institutions.

An examination of the institutional mortality data for England and Wales for 1971, specially requested from OPCS, revealed that cancer mortality represents a lower proportion of the total non-transferrable deaths in institutions than it does in the general population. Other work has also suggested that, in absolute terms,
cancer mortality is lower in certain important classes of institution (15,16). Whereas an excess of deaths in an institutional population can greatly affect the mortality figures for a borough, a deficiency of deaths is only likely to result in a small error. No corrections were therefore made to the data for the effects of institutional deaths.

2.5. RESULTS

Significant simple associations between reuse and the SMRs were found for gastrointestinal cancer (male and female), stomach cancer (m & f), oesophageal cancer (m), all cancers (m) and lung cancer (m), as shown in the columns headed "Reuse alone" in Table A1 in the Appendix. These simple associations take no account of the possible effect of socioeconomic factors.

However, once we had allowed for those social factors that best fitted each cause, reuse ceased to be significant at the 5% level for any of the cancer sites. The most significant association was that between male stomach cancer and reuse (P=.08), and this only with an unweighted analysis. Adjustment for the small degree of geographical clustering present in this case enhanced the association, and the unweighted regression coefficient then became significant at the 5% level. However, when both geographical clustering and the different borough sizes were taken into account simultaneously the partial regression coefficient became non-significant again.

A slight (0.05<P<0.10) negative association between reuse and deaths from bronchitis and emphesema arose after allowing for the
effect of social factors. (A negative association implies decreasing mortality with increasing reuse.)

The regression coefficients, standard errors and levels of significance before and after fitting the social factors, with and without weighting are all shown in Table A1 in the Appendix.

Air pollution data, represented by sulphur dioxide levels for the years 1968-1974, were available for 16 of the boroughs. There was no significant correlation between sulphur dioxide levels and water reuse. There were significant simple associations between SO$_2$ levels and female lung cancer and female bronchitis and emphysema, both of which disappeared when social factors were taken into account. There were no corresponding associations for men.

****
3. WATER REUSE AND OTHER HEALTH INDICATORS IN THE LONDON AREA

3.1. CANCER INCIDENCE

Cancer incidence rates measure the rate of new cases of cancer detected during a defined period of time in different populations. Their accuracy depends on all new cases of cancer being registered. At least as many people contract cancer as die of cancer in any one area or time period, so cancer incidence rates will tend to be larger than cancer mortality rates. In cancers, such as bladder cancer, which are not invariably fatal, the incidence rate can be much larger than the mortality rate. The latency period between the supposed cause and occurrence of cancer will be shorter, but not much shorter than that between cause and death from cancer. Leaving aside the question of data quality, these points mean that, if there is a real effect in operation, it might be more easily discerned from examining incidence rather than mortality.

Since 1962, all patients diagnosed as suffering from cancer and seen in National Health Service (NHS) hospitals in England and Wales should have been entered on a cancer register. This register is administered on a regional basis, but the completeness, and therefore the reliability, varies considerably from region to region. In the London area, the South Thames Cancer Registry is considered to be one of the best, but by contrast the North-West and North-East Thames Registries are probably below the standard for the country as a whole. Therefore, in order to ensure comparability of the data, it was decided to limit cancer incidence studies to the 14 boroughs (from the original 29) in the South Thames Cancer Registry area.

21
A Standardised Incidence Ratio (SIR) for each sex and cancer site was calculated for each borough, being the ratio of the observed number of cases to the number expected as a result of the age distribution within that borough. The age range covered was 25 to 74 years. A more detailed breakdown of intestinal cancers was available compared with the mortality data, so the following nine cancer sites and combination of sites were investigated:

Gastro-intestinal (ICD 151-154)
Stomach (ICD 151)
Intestinal (ICD 152-154)
Colorectal (ICD 153-154)
Colonic (ICD 153)
Rectal (ICD 154)
All urinary (ICD 188-189)
Bladder (ICD 188)
Oesophageal (ICD 150)

3.2. HOSPITAL DISCHARGE RATES

In addition to the cancer registration data described above, information on cancer morbidity is also available from routine returns on hospital discharge rates. There are two sources of information, the Hospital In-Patient Enquiry (HIPE), and the Hospital Activity Analysis (HAA).

The HIPE is intended to cover a 10% sample of in-patient records in NHS hospitals, excluding psychiatric patients. Some hospitals may fail to contribute the whole or part of their quota, so
it may not be quite as much as 10%. The information is collected centrally by OPCS, from whom comparable data were available for all 29 boroughs for the seven-year period 1968-74. Being only a 10% sample meant that in some boroughs in some years there were no recorded discharges for some of the less common cancers.

The HAA system has been introduced more recently. Sponsored by the DHSS, it is an analysis of all hospital discharges and is administered by the Regional Health Authorities. For reasons of comparability and economy of effort, data were again obtained only for those 14 boroughs south of the Thames, for the 5-year period 1974-78. Since the data are not collected centrally, those residents who seek hospital care outside their local Health Authority area will not be included.

A drawback of this type of information is that it relates to hospital events rather than individuals. Patients who have more than one stay in hospital, quite likely in the case of cancer, will produce multiple entries in the records.

The detailed subdivisions of intestinal cancer (colorectal, colonic, rectal) were not available in the discharge data, so the investigation was limited to the other six sites listed in Section 3.1. A Standardised Discharge Ratio (SDR) was calculated for each sex and cancer site, and for each type of data, in an analogous fashion to that used in the calculation of SMR and SIR.

Comparisons of cancer mortality, incidence and the two types of discharge figures showed a number of disagreements, many of which
can be explained by differences in the type or quality of data, or the small numbers involved.

3.3. INFANT MORTALITY AND FERTILITY

If the presence in drinking water of organic micropollutants is harmful to human health, an early warning of this might be detectable in studies of infant mortality, or fertility. Information on the numbers of stillbirths, live births and deaths up to 1 year old was therefore obtained for all 29 study boroughs (except two where stillbirths were not published) for the years 1969-73. Three mortality rates were calculated, the stillbirth rate (stillbirths divided by total births), the 'extended perinatal' mortality rate (stillbirths and deaths up to four weeks divided by total births), and the infant mortality rate (deaths up to 1 year, excluding stillbirths, divided by live births). Information on the mother's parity, that is the number of children she has had prior to the current birth, was also obtained. Using this information the important additional factor, % mothers with parity 3 or more, was added to the list of social factors for this part of the study.

From the numbers of live births and women in the age range 10-55 years, standardised fertility ratios were calculated for each borough, in an analogous fashion to that used in the calculation of SMR, SIR and SDR. The hypothesis here is that the fertility of women drinking reused water could be reduced as a result of the re-cycling of oral contraceptives or their derivatives, although the WRC (unpublished work) has failed to detect such compounds in drinking-water.
3.4. RESULTS

Both unweighted and weighted regression analyses were undertaken, first using the reuse factor alone, and then assessing the effect of reuse after allowing for the social factors.

Using the cancer incidence data, a number of simple associations appeared when the reuse measure was examined alone, namely with gastrointestinal cancer (f), stomach cancer (f), all urinary cancer (m & f) and bladder cancer (m).

After allowing for the effect of social factors, the only association significant at the 5% level was that with female stomach cancer in the unweighted analysis. Figure 2 shows the gradual increase in adjusted SIR with increasing reuse. The two most significant associations that remain in the weighted analysis are with female stomach cancer (P<0.08) and female urinary cancers (P<0.08). There was no evidence of geographical clustering of the residual SIRs for either of these causes.

None of the eleven social factors was related to female bladder cancer incidence or male oesophageal cancer incidence, so the simple slight associations with reuse (P<0.10) could not be reduced.

The regression coefficients relating to cancer incidence, the standard errors and levels of significance before and after fitting the social factors, with and without weighting are all shown in Table A2 in the Appendix.
Fig. 2. London study - female stomach cancer incidence and reuse, adjusted for mean socioeconomic rank
Using the HIPF data, simple associations appeared between reuse and stomach cancer (m), all urinary cancer (f) and bladder cancer (f). There was also a negative association with oesophageal cancer (f).

All these associations disappeared after fitting social factors, with one exception. This was the negative association between reuse and female oesophageal cancer, which could not be explained by any social factors since none were significant. Not much weight should be attached to this association since the numbers involved in this diagnosis (1/2 a discharge per borough per year for women) from the HIPF returns are so small.

The regression coefficients relating to the HIPF data, the standard errors and levels of significance before and after fitting the social factors, with and without weighting are all shown in Table A3 in the Appendix.

Using the HAA data, simple associations with reuse were noted for all urinary cancer (m & f) and bladder cancer (m & f). Once again all these simple associations cease to achieve significance when social factors are fitted first.

The regression coefficients relating to the HAA data, the standard errors and levels of significance before and after fitting the social factors, with and without weighting are all shown in Table A4 in the Appendix.
The results for **infant mortality** are more interesting. All three mortality indices showed significant simple associations with reuse when weighted regression was employed, and for the two strongest ('extended perinatal' mortality and stillbirths, $P<0.01$) the results were equally significant if unweighted regression was used. When social factors were fitted first, the association between reuse and 'extended perinatal' mortality ceased to achieve significance, but the **stillbirth** rate continued to be highly significant ($P<0.01$) when an unweighted regression was performed, $P<0.05$ when weighting was used).

The question of geographical clustering was examined in relation to the **stillbirth** data. Although there was a clear clustering of boroughs with residuals of similar size, when the method of Pocock and Cook (11) was modified to allow for this effect, the partial regression coefficient on reuse, although reduced, was still significant at the 5% level when unweighted regression was used. When both weights and correlated residuals were introduced into the model the partial regression coefficient is reduced ($P=0.06$), but it becomes clear that the simple modified method used to allow for geographical clustering is not necessarily appropriate for stillbirth rates. This is probably because an explanatory variable is missing from the analysis.

The **fertility** analysis showed that, after allowing for social factors, the trend was in the hypothesised negative direction (fewer births per woman in areas of increasing reuse), but the association was not statistically significant ($P>.10$).
The regression coefficients relating to the infant mortality and fertility data, the standard errors and levels of significance before and after fitting the social factors, with and without weighting are all shown in Table A5 in the Appendix.

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4. WATER REUSE AND NATIONAL CANCER MORTALITY

4.1. WATER DATA

The advantage of looking at the national situation rather than just the London area is that a wider range of types of water are used. In particular, upland catchments are found, also river-derived sources where the raw water is not stored for several months before treatment, as is done in London.

A considerable body of data on the water supplies to some 253 urban areas in Great Britain had been collected as part of investigations into water quality and cardiovascular disease (4,5). To this was added information about reuse in the river-derived sources.

When investigating solely the hypothesis that reuse may raise cancer levels, the strong apparent association between upland waters and stomach cancer described in the next section swamped any possible association with reuse. It was therefore necessary to restrict the analysis to only those urban areas receiving less than 10% of their supplies from upland catchments, reducing the number by almost half.

As with the London data, we tried to obtain a number of indices of reuse. The Central Water Planning Unit (CWPU) had abstracted from the River Pollution Surveys of the early 1970's figures for effluent flows and contributing populations upstream of all river abstractions in England and Wales. From the river flow rates at the abstraction points the percentage of effluent in the raw water could be calculated. Also for the period around 1971
values of chloride, nitrate, ammoniacal and albuminoid nitrogen, phosphate and permanganate value, albeit in the treated water, were available from the cardiovascular disease study.

Many studies have shown that there can be a long latent period between the exposure to a cancer-inducing agent and the development of the disease. It is therefore important to try and obtain historical water quality data. Information on the same chemical indicators given above (except phosphate) was available from the British Waterworks Association 1961 Handbook. In addition, the 'contributing population' data obtained by the CWPU could be extrapolated backwards in time, and this was done to 1951, when fewer river abstractions were in use. For each abstraction point the local authorities lying within the catchment area upstream were identified. From the ratio of the 1951 to the 1971 census populations of these areas, an estimate of the 1951 contributing population could be made. Dividing by the mean river flow (this is a long-term average) gives an index of reuse in 1951. This parameter was available for 141 urban areas.

From examination of the correlations with other indices, this last one, the 1951 contributing population divided by the mean river flow, was chosen to represent the reuse factor in the analysis. The distribution of this variable in Great Britain is shown in Fig. 3.

4.2. MORTALITY DATA

Mortality data were obtained from OPCS and the Registrar General for Scotland for the years 1969-1973, broken down by sex and
Fig. 3. National study - reuse in 1951 (1951 contributing population \( \div \) mean river flow in thousands of cubic metres per day)

- Reuse zero
- \( 0 < \) Reuse \( < 100 \)
- \( 100 \leq \) Reuse \( < 400 \)
- Reuse \( \geq 400 \)
- 1951 data missing

London
10-year age group, for the following cancer sites:

- Gastro-intestinal (ICD 151-154)
- Stomach (ICD 151)
- Intestinal (ICD 152-154)
- All urinary (ICD 188-189)
- Bladder (ICD 188)
- Oesophageal (ICD 150)

SMRs were calculated, as before, for the age group 25 to 74 years. The expected number of deaths were calculated using the England and Wales ten-year, age-specific rates for the period 1969-73.

4.3. SOCIOECONOMIC DATA

Data on 15 socioeconomic variables were extracted from the 1971 census. These variables differ slightly from those used in the London study, as shown in Table 1.

4.4. RESULTS

There were simple associations between mortality and reuse, before the fitting of social factors, using weighted regression only for all urinary cancer (m) and bladder cancer (m), and a negative association with intestinal cancer (m). This negative association may simply reflect the distribution of social class in the urban areas in this national study, since here (unlike the London study) reuse and social class are negatively correlated.

Because of the larger number of towns than in the London
study, and an increased diversity of lifestyle, more social factors were often required to model the variation in mortality. After fitting the social factors, none of the simple associations remained. However, an association appeared between male stomach cancer and reuse once the social factors were taken into account, with $P < 0.08$ for the unweighted, and $P < 0.05$ for the weighted regression. Table A6 in the Appendix gives all the regression coefficients, standard errors, levels of significance and social factors used in both weighted and unweighted analyses.

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5. TYPE OF WATER SUPPLY AND NATIONAL CANCER MORTALITY

5.1. INTRODUCTION

In the course of collecting data for the cardiovascular disease study, type of source was recorded in five categories, groundwater, spring, upland catchment, river with pre-treatment storage or river with no pre-treatment storage. For this study these categories were reduced to three, groundwater and spring being combined, and all river supplies being considered as 'lowland', whether or not there was storage before treatment. Where more than one type of water was treated at a works, the proportions of each were estimated. From the source types and the quantities supplied, the proportion of each town's supplies in each of the three categories could be calculated.

In addition to the socioeconomic factors, three other types of data were also used to try and explain the variation in cancer mortality. Blood group 'A' has been found to be associated with stomach cancer (17,18), so information on ABO blood groups was obtained from the National Blood Transfusion Service. It has also been suggested (19,20) that the degree of air pollution may be related to stomach cancer. Sulphur dioxide levels around 1971 were available for 126 of the urban areas from the Warren Spring Laboratory. The third factor introduced simply mapped the towns onto a line running in a north-west to south-east direction. Geographical gradients in mortality, even after adjustment has been made for social class, have been noted before (21). It may be an historical phenomenon as a result, for example, of the geographically
non-uniform advantages (or disadvantages) of industrialisation, or
differences in life-style which are not accounted for by the social
factors used. This north-west to south-east variable may therefore
be interpreted as a substitute for factors not measured, or not
known.

The results of these various investigations into the possible
effects of type of water supply are described in Sections 5.2, 5.3
and 5.4.

Having classified water simply by type, we then tried to
study the possible effects of different types of treatment.
Information gathered during the cardiovascular disease survey had
included qualitative information on the treatment methods and
chemicals used at each source, with dates. In this study we
considered only chlorination and clarification processes, and the
results are described in Section 5.5.

5.2. SIMPLE ASSOCIATIONS

In any given urban area, the percentages of each of the three
types of water (groundwater, upland, lowland river) are not
independent, since the sum of all three must be 100%. Of the 238
urban areas for which data on source proportions were available, 60
were served predominantly (over 90%) by ground or spring water, 53
predominantly by upland water, and 45 predominantly by lowland
supplies.

To study the possible effect of water type alone, that is,
before social and other factors are introduced, we carried out a
multiple regression using both % upland and % lowland as explanatory variables, without any weighting for differences in the town populations. The partial coefficient of % lowland was not statistically significant for any cancer site. The model therefore reduced to a simple regression on % upland. These simple associations were significant for gastrointestinal cancer (m & f), stomach cancer (m & f), intestinal cancer (m & f) and oesophageal cancer (m & f).

Figure 4 shows the geographical distribution of female stomach cancer, one of the cancer sites with the strongest association with reuse. Figure 5 shows the corresponding map for % upland. The north-west to south-east gradient in both is apparent, and Fig. 6 gives the relationship between the two in graphical form. However, the need to include social factors is demonstrated by Fig. 7, which shows that % manual also demonstrates a north-west to south-east gradient.

5.3. MULTIPLE REGRESSION ANALYSIS

Stepwise regression analyses were undertaken for each cause and sex, fitting first those social factors that best explained the variation in mortality. This was done both without any weighting for borough size, and using the weighting method described in Section 2.2. A number of the associations listed in the preceding section disappeared, but some remain, as follows:

$P < 0.001$ Female gastrointestinal cancer (unweighted and weighted analysis)  
Female stomach cancer (   "   "   "   "   )
Fig. 4. National study - female stomach cancer
(Standardised mortality ratios, (%))

KEY
○ <65%
○ 65% -
○ 85% -
○ 105% -
○ >125%
○ MISSING VALUE
Fig. 5. National study - upland catchment supplies (%)
Fig. 6. National study - female stomach cancer and % upland
Fig. 7. National study - % manual workers

KEY
- < 50%
- 50% - 55%
- 55% - 60%
- 60% - 70%
- 70% & over
- MISSING VALUE
P<0.01 Female intestinal cancer (weighted analysis; P<0.05, unweighted analysis)

P<0.05 Male gastrointestinal cancer (unweighted and weighted analysis)
Male stomach cancer (unweighted analysis only)

The regression coefficients, standard errors, social factors used, and levels of significance are all given in Table A7 in the Appendix. The largest partial regression coefficient of % upland, that with female stomach cancer using unweighted regression, is 0.21. The interpretation of this is that if an urban area were to change from zero to 100% upland, the SMR would increase by 21 percentage points. That there is still a lot of scatter amongst the urban areas is demonstrated by Fig. 8, which shows the SMR for female stomach cancer plotted against % upland, after adjustment for social factors.

As a check that the results found were not solely a phenomenon of coincidentally high mortality and high % upland in Scotland, the unweighted analysis for gastrointestinal, stomach and intestinal cancers were re-run, using the same social factors, but without the 21 Scottish burghs. The results were strikingly similar, the coefficients with % upland for male and female gastrointestinal, female stomach and male intestinal cancers being slightly increased.

5.4. OTHER POSSIBLE CONFOUNDING FACTORS

As discussed in Section 5.1, many aspects of the British environment and way of life exhibit a north-west to south-east gradient. The question therefore arises as to whether % upland is merely acting as a substitute for some other factor which we have
Fig. 8. National study - female stomach cancer and % upland, adjusted for socioeconomic factors.
been unable to include. To check for this possibility, a variable was constructed which effectively mapped the urban areas onto a line running in a north-west to south-east direction. Two variables were tried, one using a line at 30° to the north-south line, the other using an angle of 45°. The latter variable, using a 45° angle, was most highly correlated with the SMRs. Analyses were therefore carried out adjusting for both social factors and the 'NW-SE 45°' variable, for those combinations of sex and cancer site listed in Table A7 which remained significant after fitting social factors. The results are presented in Table A8 in the Appendix. The associations that remained significant in the unweighted analysis were between % upland and female gastrointestinal cancer, and % upland and female stomach cancer. In the latter case, the inclusion in the model of the term '% upland' resulted in a non-significant coefficient for the NW-SE 45° variable, implying for this cancer that the NW-SE 45° factor may be explained by % upland, but that the reverse is not true. In the weighted analysis, the only association with % upland was for female stomach cancer (P=0.02). Since the only cancer site to persist in its association with % upland is stomach cancer in women, this is the only site to be considered in the following analyses.

Information on blood groups was then used as a possible explanatory factor. From the data on regional (donor) distributions of blood groups, among A, B, AB and O, the frequencies of the O, A and B genes were estimated. (An individual with blood group A has either two A genes, or one A and one O gene, for example.) These gene frequencies were the three variables used in the analysis. Simple correlations with female stomach cancer yielded a negative
association between A gene frequency and the SMR. This was in the reverse direction from that found in studies on individuals (18). This association remained significant (P<0.05) even after adjustment for three social factors (% manual, % unemployment and % higher education). Inclusion of the NW-SE 45° factor rendered this association non-significant (P>.10), but introduced a significant (P<0.001) association with the B gene frequency, which remained even after % upland was introduced. The coefficient of % upland was increased slightly (to 0.18, P<0.001). This result should be treated with caution, as the B gene association is anomalous when compared with other studies. The point to make is that inclusion of the blood group data does not weaken the association between % upland and female stomach cancer.

Next the possible influence of air pollution was examined. Data on the concentration in air of sulphur dioxide around 1971 were used in preference to Daly's 1951 Index of Domestic Air Pollution, based on the quantity of fuel burnt by area. Although this latter index has the advantage of allowing for a time lag, and predates the dramatic changes in air pollution subsequent to the 1956 Clean Air Act, it is only available for the County Boroughs, whereas 1971 sulphur dioxide levels are available for 126 urban areas. Also, sulphur dioxide levels have changed less radically than smoke between 1951 and 1971 (22).

The result of including the necessary social factors (% manual and % new resident), sulphur dioxide and % upland in the model was that both the latter were significant, the coefficient for % upland being 0.13 (P=0.03). The size of this coefficient (in this
model using only 126 towns) is virtually the same with or without sulphur dioxide, suggesting that % upland and sulphur dioxide operate independently of one another, and certainly sulphur dioxide does nothing to reduce the apparent effect of % upland on female stomach cancer.

Finally an attempt was made to adjust for the effect of geographical clustering, using the method discussed in Section 2.3. Some problems were encountered in applying this relatively new technique, but the indications are that adjustment for geographical clustering is unlikely to reduce the apparent effect of % upland on female stomach cancer.

5.5. TREATMENT PROCESSES: CHLORINATION

An important next step in the investigation of the 'upland' story is to try and identify what it is about this type of source that is resulting in the raised female stomach cancer mortality. One important aspect may be the treatment processes used.

Post-treatment chlorination practices were divided into two categories. Super-chlorination followed by de-chlorination, and breakpoint chlorination were considered to be 'high' post-chlorination, since these are practices designed to deal with possible high levels of contaminants. The use of marginal chlorination or chloramination (or occasionally no chlorination at all), indicating that conditions were perhaps less severe, were classified as 'low' post-chlorination. Pre-chlorination, that is chlorination before other treatment processes have had a chance to
reduce the levels of organic matter, was considered separately. There were thus four possible combinations:

1) No pre-chlorination + 'low' post-chlorination;
2) No pre-chlorination + 'high' post-chlorination;
3) Pre-chlorination + 'low' post-chlorination;
4) Pre-chlorination + 'high' post-chlorination.

Nearly all upland sources fall in the first category, with none at all in the last. It was not possible therefore to compare different chlorination practices in the upland supplies. This comparison was feasible, on the other hand, in the case of lowland river supplies. Of the 67 towns which received some lowland supplies in 1951, 39 were in the first category above, 11 were in the second category, 11 were in the third and only 6 were in the fourth, most extreme category. Using only those towns with less than 10% upland supplies (to eliminate the upland supply effect already reported), the term & lowland was initially fitted and the regression coefficients in respect of the different chlorination categories were examined after adjustment for this term. None of these additional treatment terms were significant for either sex for stomach or bladder cancers, the only sites considered in this part of the analysis.

5.6. TREATMENT PROCESSES: CLARIFICATION

One of two methods is normally used for the removal of colour and/or turbidity from surface supplies: chemical coagulation followed by rapid gravity or pressure filtration; or slow sand filtration which is intended to provide biological as well as physical treatment. Table 2 shows the number of urban areas (classified by
### TABLE 2. Treatment of upland and lowland, 1951

#### UPLAND SUPPLIES

<table>
<thead>
<tr>
<th>% Upland in urban area</th>
<th>Number of urban areas</th>
<th>Number using coagulation</th>
<th>Number using slow sand</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 20%</td>
<td>6</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>20 - 40%</td>
<td>5</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>40 - 60%</td>
<td>7</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>60 - 80%</td>
<td>6</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>80 - 99%</td>
<td>8</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>100%</td>
<td>69</td>
<td>34</td>
<td>28</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td><strong>101</strong></td>
<td><strong>56</strong></td>
<td><strong>47</strong></td>
</tr>
</tbody>
</table>

#### LOWLAND SUPPLIES

<table>
<thead>
<tr>
<th>% Lowland in urban area</th>
<th>Number of urban areas</th>
<th>Number using coagulation</th>
<th>Number using slow sand</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 20%</td>
<td>9</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>20 - 40%</td>
<td>7</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>40 - 60%</td>
<td>8</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>60 - 80%</td>
<td>8</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>80 - 99%</td>
<td>7</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>100%</td>
<td>28</td>
<td>11</td>
<td>24</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td><strong>67</strong></td>
<td><strong>33</strong></td>
<td><strong>45</strong></td>
</tr>
</tbody>
</table>

N.B. In a given town, not all of the water of the same source-type received the same treatment.
proportion of upland, and of lowland) receiving water treated by each of these methods, in 1951.

First we excluded those areas with more than 10% lowland supplies. For male and female stomach and female bladder cancers there were no significant relationships with % upland coagulated or % upland slow sand filtered after adjustment for % upland alone. In the case of male bladder cancer there was a significant negative partial relationship with % upland slow sand filtered (b = -.16, P<0.05). This, however, disappeared once we allowed for the necessary social factor (% large families).

When a similar analysis was repeated for the predominantly (over 90%) lowland and groundwater supplies, only one significant regression coefficient arose after allowance for % lowland, that of a negative relationship between % lowland slow sand filtered and female bladder cancer (b = -.47, P<0.05). This persisted after allowance for the social factor (% lack of inside WC) (b = -.44, P<0.05), suggesting a possible protective effect of slow sand filtration of the lowland supplies. In case this effect might arise because of the extent to which slow sand filtration is used in the London area, the analysis was repeated with the London boroughs excluded. The size of the partial regression coefficient was hardly changed, although its significance was reduced (b= -0.42, P<0.10).

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6. TYPE OF WATER SUPPLY AND NATIONAL INFANT MORTALITY

Data on live births, stillbirths and infant deaths were obtained from OPCS for England and Wales, and from the Registrar General for Scotland. The periods covered varied slightly between the three countries, being 1969-73 for England, 1969-72 for Wales and 1969-74 for Scotland. The same three mortality rates as were used for the London study were calculated, that is the stillbirth rate, the 'extended perinatal' mortality rate, and the infant mortality rate. Information on mother's parity was not available for Scotland, so this variable could not be used. However, parity is highly correlated with the variable % large families, which features prominently in the multiple regression models.

Using each of the mortality rates as dependent variables, an identical analysis to that described in Sections 5.2 and 5.3 was carried out. The regression coefficients, standard errors, social factors used, and levels of significance are all given in Table A9 in the Appendix. The association with % upland is significant for all three mortality measures whether or not weighting is used, even after social factors have been taken into account.

Again, as found with female stomach cancer mortality, the striking north-west to south-east pattern exhibited, for example, by perinatal mortality (Fig. 9), raises the possibility that these relationships with upland supplies may be a result of this pattern being common to both variates. The NW-SE 45° variable described in Section 5.4 was therefore included in the analysis, and the results are presented in Table A10 in the Appendix. The relationship with
Fig. 9. National study – extended perinatal mortality
(rate per 10 000 births)

- Rate < 200
- 200 ≤ Rate < 230
- 230 ≤ Rate < 260
- 260 ≤ Rate < 280
- 280 ≤ Rate
- Missing value
% upland clearly disappears for stillbirths and infant mortality, and is much reduced for perinatal mortality in the unweighted analysis. In this analysis, after the mortality indices were adjusted for both social factors and % upland, the north-west to south-east gradient in mortality ceased to be significant in each case. The relationship between % upland and perinatal mortality disappeared in the weighted analysis after adjustment for the NW-SE 45° variable.

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7. DISCUSSION

7.1. LIMITATIONS OF METHODOLOGY

7.1.1. Units of analysis

One of the major limitations of the studies is that the units available for analysis are either boroughs in the London area or urban areas in Great Britain. There is, therefore, only a small number of units compared to the number in the total population, and these units are aggregates of the units of interest, namely people.

The boroughs or urban areas are assumed to be homogeneous units for much of the analysis. It is the mean value for a borough which is available, and no account is taken of the different amounts of variability that this may hide. As Comstock (23) has pointed out, the larger the geographical unit, the more broadly representative its population is, and the more stable its death rates. However, the source of water supply may be less uniform over a larger area, and using the average value for a borough will conceal the extremes of supply. This will reduce the variation to be explained. In London, for example, Croydon has an associated value of the reuse parameter of 1.39%, but the north-west part of the borough is served by Thames water, reuse value 13.9%, whilst the south-east part is served by well water with zero reuse. The same comment applies to the socio-economic factors. The borough of Kensington and Chelsea is a mixture of affluent middle-class Chelsea, together with the poor housing conditions and general poverty of North Kensington. In this connection, it might be argued that the four boroughs in the London study which are outside Greater London might be more homogeneous than
the others. This is certainly true as far as water supply is concerned. Again, the smaller towns in the national study might be more homogeneous than the large cities. It would be hard, and indeed no attempt has been made, to balance this homogeneity against the smaller weight attached to these boroughs and towns because of their smaller size.

The other problem with areal studies of this type, that of geographical clustering, has been dealt with, as described in Section 2.3. In only one case investigated (stillbirths in the London study) did geographical clustering have any effect on the conclusions reached.

7.1.2. Quality of health measures

Information about cancer risks is available routinely from mortality statistics, hospital discharge diagnoses, and cancer incidence data. Other forms of data that are routinely available and might provide evidence of a more immediate health problem include infant mortality and fertility.

In view of the finality of death, and the completeness with which it is recorded, mortality statistics provide a completely reliable measure when taken as a whole. Problems can arise, however, when they are divided according to the underlying cause of death. Nevertheless, misclassification of an individual person’s cause of death may not have a very great effect on the overall errors in estimates of death rates from a particular cause in a geographical area, since some cancelling out of errors may occur. There is no evidence of differential under- or overrecording from one borough or
The quality of incidence data is not quite as good as that of mortality data. Registration relies firstly on an individual seeking medical care, and secondly on those who provide the medical care reporting the case to the registry. In some cases this does not happen until the person has died. The completeness of registration varies from registry to registry, but is particularly good for the South Thames Registry, to whose regions we limited this part of the study. Data on more detailed cancer sites were available from the registry with respect to intestinal cancers. These were separated into cancer of the colon, cancer of the rectum, and cancer of the small intestine. This latter group was not used on its own because the incidence rates for cancer of the small intestine are so small. The advantage of separating cancer of the colon from those of the rectum is that they are thought to have a different aetiology, but they were also combined into 'colorectal' cancer, acknowledging the likelihood of misallocations of cancers near the rectosigmoid junction. For comparability with the mortality indices, intestinal cancers as a group were examined as well.

The other cancer morbidity information which is routinely available concerns hospital discharges, classified according to the diagnosis at discharge. One disadvantage of this information is that people can be discharged from hospital more than once following treatment for their cancer. The duplication of discharges may vary between boroughs and between sites of cancer. For this reason, together with those discussed in Section 3.2, morbidity measured by hospital discharge rate is probably the poorest quality measure of
health status routinely available.

7.1.3. Lag times and population mobility

In order to add to our understanding of the causes of cancer, information is needed about the environment of the individual with cancer 20 to 30 years before the disease is detectable, since this is the kind of lag time between causal factors and their effect. This could be translated into the statement "information about the environment of each borough or urban area is needed 20 to 30 years before 1971". It has been possible to estimate the quality of the drinking water supply for London, around 1941, although this estimate was not used directly in the analysis, since it correlated so well with current estimates. Water quality was estimated around 1951 for the national disease study. The past social characteristics of the boroughs and urban areas should also be considered. It has been shown that, broadly, housing conditions and social class composition of the London boroughs have remained stable over the past twenty years, but this stability has not been checked in the national study.

Turning to the question of mobility, a measure of the differential mobility of the population of the different boroughs is available from the census variable '% new residents'. Unfortunately, this covers only new residents within the last five years, whereas one would like to know how many have lived in the borough for less than twenty years. Apart from diluting any risks attributable to a particular borough, migrants tend to be a healthier group, especially when migrating long-term towards the large city (24,25). No direct measure of differential in-migration and out-
migration was available in the present study.

The assumption behind a study such as this, is that a 'core group' exists in each borough, which has lived there most of their lives, and which dies there. If this assumption were false, any attempt to examine cancer risk using aggregate data would be a waste of time. One needs also to assume that the core group is large enough for the differences in risk which are hypothesised to be detected. The smaller the core, the larger must be the differences in risk if they are to be detected. It is reasonable to suppose that the core group in the outer boroughs of London is larger than that of the inner London boroughs. For this reason, as well as the argument of homogeneity mentioned earlier in this section, the unweighted regression solution should not be disregarded entirely.

The day to day mobility of the population is another factor to be considered, especially in the London study. A certain proportion of people commute to work outside of the borough in which they live, and this may mean to a different source of water supply. This problem may apply more to men than women, so it would be expected that a difference in risk would be more likely to be detectable in women than in men. However, a recent WRC survey of drinking water consumption in Great Britain (26) shows that on average, over all ages and for both sexes, 79% of the tap water consumed is drunk at home. Further analysis of this data (unpublished) shows that men aged 18 years and over in southern England consume 75% of the tap water they drink at home, whilst the corresponding figure for women is 84%. This indicates that the problem of misclassification of an individual's source of drinking
water is not as great as might have been expected.

7.1.4. Confounding factors

Historically, it was the growth and development of industry which attracted people to an area. Villages sprang up around factories, and the population increased very rapidly (24). The factories were likely to be sited on rivers, which were useful for transport, and the same rivers provided a source of drinking water for the community (27). The factory workers would probably stay living near the river while the more affluent would move away, by coincidence reaping the hypothesised benefit of less polluted water. Housing conditions, standards of diet and clothing and perhaps meteorological effects of certain types of industrial activity would be regarded as components of the general social conditions to which people are exposed (28), and which may be associated with their cancer risk. It may be no coincidence that there is such confounding of poorer social conditions with river water being the source of supply, both in the present London study and in the study of Louisiana (29). By controlling for the measurable social factors first, in the analysis of cancer risk, one is also removing some of the possible effect of water supply. The risk estimated to be attributable to water supply is therefore in a sense a minimum risk.

The inclusion of only a limited number of social variables in the regression equations minimises the problems of multicollinearity discussed in Section 2.4, since many of the available measures of social conditions are highly correlated. It is important to remember that the variables which are included should be interpreted not only in their own right, but also as indicators of other
variables with which they are correlated. A major disadvantage of using grouped information on social conditions from the census is that there is no direct measure of personal factors such as smoking and diet (25). They may be correlated with the measurable factors, but their estimation from the measurable factors is difficult. Therefore, it may not be assumed that the effect of smoking and diet on cancer have been removed completely by adjusting for the set of socioeconomic factors.

7.2. DISCUSSION OF RESULTS

7.2.1. Total cancer, lung cancer and bronchitis (London study)

The association which has been found between populations served by river water and total cancer mortality in men, but not in women, by many studies (8,29,30,31,32) does not persist independent of the social factors in this study. Such an association with total cancer would have been of doubtful value in the search for carcinogens, since it is unlikely that a single factor could play a causative role in cancers in different parts of the body. Positive results with respect to site-specific cancers would be of greater interest.

In order to check that no major factor has been omitted from the analysis, and that the configuration of the 29 boroughs does not have some unexpected properties, additional analyses were performed for mortality from lung cancer and bronchitis. No residual associations were apparent between water reuse and lung cancer mortality in either men or women when adjustments had been made for the social factors. The relationship between reuse and bronchitis
mortality was weakly positive without correction for the social factors, and weakly negative when that correction had been made. The result is quite different from that found in studies of water hardness and cardiovascular disease, where associations between soft water and bronchitis were in the same direction as associations between soft water and heart disease (23). The associations in this study between reuse and bronchitis are not in the same direction as those between reuse and stomach cancer, which gives this latter association a degree of specificity. The conclusions from these extra analyses support the results from the main analyses described in the following sections.

7.2.2. Gastrointestinal cancers

For stomach cancer, there is a strong mortality gradient with social class in England and Wales, with unskilled workers having the highest rates (21). Diet is thought to play an important role. High intakes of starches and lower intakes of fresh produce have been implicated (33), and there is some evidence that vitamin C may be protective (34). There has been a suggestion that the gradual change in storage methods, from brine to refrigeration, may be responsible for the reduction in stomach cancer mortality rates over the last forty years (34).

Dietary factors may also play a role in cancer of the colon, although the evidence is not conclusive. High meat intake has been associated with high incidence (35,36), especially if the meat is beef (37), but the hypothesis that fat intake is important (38) has been challenged (39,40). It has been suggested that dietary fibre (41), in the form of cruciferous vegetables, such as Brussels sprouts
(37), may be protective, although this merits further study (42,43).

Page and Harris (29) found an association between Mississippi river water and mortality from cancers of the **gastrointestinal** system, in both white men and white women, which persisted when adjustments were made for median income, degree of urbanisation, and type of industrial employment. We have found an association between degree of reuse and cancer of the gastrointestinal system in London which is consistent for both mortality and incidence rates, but which ceases to be significant when the social factors are taken into account. There is no evidence of an association with hospital discharge rates.

In the national study of type of water supply, a very highly significant relationship between **female gastrointestinal cancer** and % upland, and a significant relationship between **male gastrointestinal cancer** and % upland persisted even after allowance was made for social factors and the differing population sizes of the urban areas. The associations disappeared after adjusting for those factors represented by the north-west to south-east variable.

The study of the Ohio river basin (8) showed an association between **stomach cancer** and river water for both men and women. We have found an association between **stomach cancer mortality** and reuse which disappears in the London study after both the relative sizes of the boroughs and the social factors are allowed for, although there is some evidence of a persistent association in men in the national study. In London, a significant association between reuse and **stomach cancer incidence** in women persisted even after the social
factors and variation in borough size were taken into account. Only if adjustment is made for multiple significance testing does this result become non-significant, since an individual test is required to be significant at the 0.025 level if four separate tests (two sexes, two principal cancer sites) are performed with overall significance at the 0.10 level.

Any relationship of reuse with cancer was expected to be stronger in women than in men, for the reasons of mobility outlined in Section 7.1.3. This expectation has not been realised with respect to cancer mortality, but there is an indication that this is true with respect to the incidence of stomach cancer in the London area.

In the national study of type of water supply, a highly significant relationship between female stomach cancer and % upland supply persisted even after allowance was made for social factors and the differing population sizes of the urban areas. The association persisted after adjusting for those factors represented by the north-west to south-east variable.

Salg (8) found an association between mortality from cancer of the intestine in men and surface water. We have not been able to reproduce these findings with respect to water reuse once social factors and weighting methods are taken into account.

However, in our national study of type of water supply, there is some evidence of a significant association between % upland and female intestinal cancer in the weighted analysis and independant
of the social factors. This association can be accounted for by the coincidental north-west to south-east pattern in both % upland and mortality, although the factors involved in this are not known.

Although not strictly part of the gastrointestinal system, the oesophagus was included amongst the cancer sites studied. No associations were found with reuse or % upland, with the exception of a weak association between male oesophageal cancer incidence and reuse in south London, as described in Section 3.4.

7.2.3. Urinary cancers

Bladder cancer has in the past been associated with gas workers (44), rubber workers (45) and dye workers (46), and there is some evidence of an association with smoking habits (47). Page and Harris (29) showed an association between reuse of water and urinary cancer in men, and two other studies showed an association between reuse and bladder cancer, Kuzma et al (32) in men, and Salg (8) in both men and women. In London, the results for mortality and morbidity are not very consistent, but this is possibly because the mortality rates for both bladder cancer and all urinary cancer are small, and the SMRs are therefore based on small numbers of expected deaths. The results with respect to incidence are more reliable, being based on much larger numbers. There are quite large regression coefficients with reuse from both analyses on standardised hospital discharge ratios, especially for women, but it is the result for all urinary cancer incidence which provides some evidence of an association. No significant associations were found with bladder cancer or all urinary cancer and reuse or % upland in the national
7.2.4. Other health indicators

Infant mortality is a particularly responsive and sensitive index of the health status of a geographical area (48). There is evidence of a small increased risk of stillbirths associated with reuse, even after allowing for social factors and variations in borough size. Infant mortality and 'extended perinatal' mortality were not so associated.

In the national study of types of water source, the significant partial regression coefficients of % upland for stillbirths, extended perinatal and infant mortality after allowing for social factors may be explained, in the weighted analysis, by a common north-west to south-east gradient in mortality and % upland.

There was no significant association, positive or negative, between reuse and fertility ratios.

7.3. RESULTS OF HYPOTHESIS TESTING

There is some evidence of adverse health effects which are associated statistically with the use of polluted river water as a drinking source. The size of the effect increases with increasing proportions of polluted water in a borough's drinking water supply. The effect persists independently of social factors, of within-borough variations of estimated rates or ratios, and of adjustment for any spatial aggregation. These adverse health effects are stomach cancer incidence in women, all urinary cancer incidence in women, and stillbirth rate. This statistical evidence, when put with
the results of several studies in the United States, provides consistent epidemiological evidence of a small health risk associated with reused river water.

There is also some evidence of an adverse health effect associated statistically with the use of water from upland catchments. This effect is stomach cancer mortality in women. There is no corresponding evidence concerning upland water as opposed to other types of surface water in this country or the United States with which to put the evidence from this study. This finding must therefore be considered hypothesis-forming rather than hypothesis-testing.

7.4. THE LIKELY SIZE OF THE RISK

From the size of the coefficients in the multiple regression analysis we can obtain quantitative estimates of the effect on mortality (or incidence, etc.) of changing the value of one of the independent variables, keeping all the others constant. Of particular interest is the effect of changing from zero reuse to an extreme case, represented say by the River Thames, containing 14% effluent. We have concentrated on the weighted regression coefficients, although these may underestimate the size of the effect in the London boroughs since, as discussed in Sections 2.2 and 7.1.1, the smaller boroughs on the outskirts of London may have been over-penalised. Also, as discussed in Section 7.1.4, some of the water effect may have been removed in adjusting for the social factors.

For female stomach cancer incidence the weighted model
predicts an increase of 11% in changing from no reuse to that existing in the River Thames. This prediction is subject to uncertainty, and the 95% confidence limits are \(-1\frac{1}{2}\%\) and 24%. The strongest evidence from male stomach cancer comes from the national mortality study where both weighted and unweighted models predict an increase of 8% (0% to 17%).

These effects can be translated into number of cases per year in a typical borough with a total population of about 250 000. The increase in stomach cancer incidence in women aged 25 to 74 years in such a borough could be between 0 and 3 1/2 cases per year (95% confidence limits), the best estimate being 1 1/2 cases per year.

For female urinary cancer the increased incidence risk in changing from zero reuse to that existing in the River Thames is estimated to be 21% (-3% to 44%) from the weighted model. The increase in the number of cases in our typical borough could be 2 cases per year (95% confidence limits, 0 to 5 cases per year).

The increased risk of stillbirths for the same change in the reuse parameter is estimated to be 12% (95% confidence limits 1 1/2% to 23%), or in absolute terms, 14 per 10 000 births (between 1 1/2 and 26 per 10 000 births). In our typical borough this would result in 5 additional stillbirths (between 1/2 and 9) per year.

From the national study of water types the equivalent risks seemingly associated with upland supplies can be estimated in the case of an urban area switching from 0% upland to 100% upland. For female stomach cancer mortality, taking the risks after adjusting for
the NW-SE gradient (which may underestimate the risks associated with upland supplies), the estimated increase in SMR is 11% (95% confidence limits 1% to 21%). In our typical borough this represents 1 1/2 (0 to 3 1/2) cases per year.

****
8. CONCLUSIONS

There is some evidence of adverse health effects which are associated statistically both with the use of polluted river water and with the use of upland catchments as a source of drinking water. This statistical evidence when combined with the results of several studies in the United States provides consistent epidemiological evidence of a small health risk associated with reused river water, and indeed with surface water in general.

The use of data which is collected routinely for such an enquiry into the health effects associated with the reuse of water and with different types of water source has been shown to be feasible. The power of such studies to detect associations is limited because, in the case of London, there are only 29 units for the mortality analysis, and 14 units for the morbidity analysis, because of the day to day mobility of urban residents, and because of the year to year migration of residents between urban areas. The fact that the study has produced some positive evidence is very important, therefore, and demonstrates the value of retrospective population studies, at least in the first instance.

The value is enhanced by the correct application of available statistical techniques such as weighted regression, and adjustments for geographically correlated residuals, which are essential for valid interpretations from such aggregate studies.

The possible health risks associated with upland water must be considered unconfirmed until other studies by independent
researchers, if possible in other countries, have provided consistent evidence.

Although the possible health risks associated with reuse of water are not large, it would be unwise to leave the studies of reuse in Great Britain here. Aggregate population studies such as those described in this report have a number of limitations, and in general rely on data that is routinely available. Only studies on individuals can overcome these limitations, and the feasibility of such studies in the London area is currently being investigated.

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9. REFERENCES


22. WALLER, R. Personal communication.


28. BUCKATZSCH, E.J. The influence of social conditions on mortality rates. Pop. studies 1, 1947-8, p. 299


APPENDIX - TABLES OF RESULTS

In each table, a regression coefficient of 'b' indicates that if an independent (or 'X') variable changes by one unit, the dependent (or 'Y') variable will change by 'b' units.

The standard error of each regression coefficient is shown in brackets.

The probability, P, of obtaining, if there were no effect, a value of 'b' as extreme or more extreme than the value observed is greater than 0.10 in all cases except those coded as follows:

+ $P < 0.10$
* $P < 0.05$
** $P < 0.01$
*** $P < 0.001$

All dependent variables, except infant mortality, are expressed in percentage terms as a standardised mortality (or incidence, or discharge, or fertility) ratio. Infant mortality is expressed as the rate per 10 000 births.

In tables referring to the London reuse study (tables A1-A5), reuse is expressed as % dry weather effluent flow divided by mean river flow. In table A6 (national reuse study), reuse is expressed as the estimated 1951 contributing population divided by the mean river flow in thousands of cubic metres per day.
The tables are as follows:

A1 Reuse and cancer mortality in London.
A2 Reuse and cancer incidence in London.
A3 Reuse and hospital discharges (HIPE) in London.
A4 Reuse and hospital discharges (HAA) in London.
A5 Reuse and infant mortality and fertility in London.
A6 Reuse and national cancer mortality.
A7 % upland and national cancer mortality (no NW-SE factor).
A8 % upland and national cancer mortality (with NW-SE factor).
A9 % upland and national infant mortality (no NW-SE factor).
A10 % upland and national infant mortality (with NW-SE factor).
TABLE A1. Reuse and cancer mortality in the London area

29 Boroughs

<table>
<thead>
<tr>
<th>Cause</th>
<th>Reuse alone</th>
<th>Social Factors</th>
<th>% variation explained</th>
<th>Reuse after fitting social factors</th>
<th>Weighted regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastro-intestinal cancer (ICD 151-154)</td>
<td>0.94(0.41)*</td>
<td>% manual</td>
<td>64%</td>
<td>0.21(0.30)</td>
<td>% manual 73%</td>
</tr>
<tr>
<td></td>
<td>0.78(0.33)*</td>
<td>% semi or unskilled</td>
<td>19%</td>
<td>0.50(0.37)</td>
<td>% semi or unskilled 23%</td>
</tr>
<tr>
<td>Stomach cancer (ICD 151)</td>
<td>2.05(0.67)**</td>
<td>% manual</td>
<td>70%</td>
<td>0.81(0.45)+</td>
<td>% manual 74%</td>
</tr>
<tr>
<td></td>
<td>1.69(0.58)**</td>
<td>% semi or unskilled</td>
<td>74%</td>
<td>0.31(0.39)</td>
<td>% semi or unskilled 72%</td>
</tr>
<tr>
<td>Intestinal cancer (ICD 152-154)</td>
<td>-0.24(0.34)</td>
<td>% manual</td>
<td>31%</td>
<td>-0.11(0.34)</td>
<td>-0.55(0.34)</td>
</tr>
<tr>
<td></td>
<td>0.28(0.45)</td>
<td>% New Commonwealth</td>
<td>-</td>
<td>0.28(0.45)</td>
<td>0.08(0.43)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>population density 13%</td>
<td></td>
<td></td>
<td>0.56(0.44)</td>
</tr>
<tr>
<td>All urinary cancer (ICD 188-189)</td>
<td>0.20(0.49)</td>
<td>% semi or unskilled</td>
<td>11%</td>
<td>-0.29(0.54)</td>
<td>% semi or unskilled 20%</td>
</tr>
<tr>
<td></td>
<td>0.46(0.66)</td>
<td>% manufacturing industries</td>
<td>24%</td>
<td>0.04(0.61)</td>
<td>% manufacturing industries 20%</td>
</tr>
<tr>
<td>Bladder cancer (ICD 188)</td>
<td>0.34(0.70)</td>
<td>% semi or unskilled</td>
<td>32%</td>
<td>-0.88(0.66)</td>
<td>% semi or unskilled 43%</td>
</tr>
<tr>
<td></td>
<td>0.20(1.02)</td>
<td>% manufacturing industries</td>
<td>17%</td>
<td>-0.78(0.96)</td>
<td>% manufacturing industries 16%</td>
</tr>
<tr>
<td>Esophageal cancer (ICD 150)</td>
<td>2.36(1.09)*</td>
<td>% unemployment</td>
<td>44%</td>
<td>0.25(1.06)</td>
<td>% unemployment 37%</td>
</tr>
<tr>
<td></td>
<td>0.79(0.97)</td>
<td>% manufacturing industries</td>
<td>22%</td>
<td>-0.22(0.91)</td>
<td>% manufacturing industries 15%</td>
</tr>
<tr>
<td>All cancers (ICD 140-209)</td>
<td>1.35(0.36)**</td>
<td>mean socioeconomic rank</td>
<td>86%</td>
<td>0.31(0.19)</td>
<td>mean socioeconomic rank 89%</td>
</tr>
<tr>
<td></td>
<td>0.17(0.21)</td>
<td>% unemployment</td>
<td>38%</td>
<td>-0.27(0.20)</td>
<td>% unemployment 36%</td>
</tr>
<tr>
<td>Lung cancer (ICD 162)</td>
<td>1.90(0.54)**</td>
<td>% unemployment</td>
<td>85%</td>
<td>0.19(0.33)</td>
<td>mean socioeconomic rank 86%</td>
</tr>
<tr>
<td></td>
<td>0.55(0.87)</td>
<td>% lack amenities</td>
<td>85%</td>
<td>1.89(0.54)**</td>
<td>% migration 86%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% new residents</td>
<td>8%</td>
<td>-1.11(0.76)</td>
<td>% population density 39%</td>
</tr>
<tr>
<td>Bronchitis &amp; emphysema (ICD 490-492)</td>
<td>1.23(0.79)</td>
<td>% manual</td>
<td>90%</td>
<td>-0.48(0.17)+</td>
<td>% manual 89%</td>
</tr>
<tr>
<td></td>
<td>1.20(0.76)</td>
<td>% manufacturing industries</td>
<td>78%</td>
<td>-0.60(0.43)+</td>
<td>% manufacturing industries 77%</td>
</tr>
</tbody>
</table>

* A key to this table is given on page 77
<table>
<thead>
<tr>
<th>Cause</th>
<th>Reuse alone</th>
<th>Social Factors</th>
<th>% variation explained</th>
<th>Reuse after fitting social factors</th>
<th>Weighted regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal cancer</td>
<td>M 0.69(0.67)</td>
<td>% manual</td>
<td>60%</td>
<td>-0.35(0.52)</td>
<td>0.72(0.67)</td>
</tr>
<tr>
<td>(ICD 151-154)</td>
<td>F 0.86(0.39)*</td>
<td>mean socioeconomic rank</td>
<td>47%</td>
<td>0.39(0.40)</td>
<td>0.65(0.39)</td>
</tr>
<tr>
<td>Stomach cancer</td>
<td>M 2.02(1.15)</td>
<td>% manual</td>
<td>73%</td>
<td>0.11(0.81)</td>
<td>2.07(1.15)</td>
</tr>
<tr>
<td>(ICD 151)</td>
<td>F 2.51(0.73)**</td>
<td>mean socioeconomic rank</td>
<td>83%</td>
<td>1.09(0.41)*</td>
<td>2.34(0.66)**</td>
</tr>
<tr>
<td>Intestinal cancer</td>
<td>M -0.35(0.52)</td>
<td>-</td>
<td>-0.35(0.52)</td>
<td>-0.21(0.58)</td>
<td>-</td>
</tr>
<tr>
<td>(152-154)</td>
<td>F 0.17(0.38)</td>
<td>-</td>
<td>0.17(0.38)</td>
<td>-0.09(0.40)</td>
<td>-</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>M -0.31(0.52)</td>
<td>-</td>
<td>-0.31(0.52)</td>
<td>-0.15(0.58)</td>
<td>-</td>
</tr>
<tr>
<td>(ICD 153-154)</td>
<td>F 0.22(0.37)</td>
<td>-</td>
<td>0.22(0.37)</td>
<td>-0.07(0.38)</td>
<td>-</td>
</tr>
<tr>
<td>Colonic cancer</td>
<td>M -1.03(0.76)</td>
<td>-</td>
<td>-1.03(0.76)</td>
<td>-0.76(0.80)</td>
<td>-</td>
</tr>
<tr>
<td>(ICD 153)</td>
<td>F -0.18(0.53)</td>
<td>-</td>
<td>-0.18(0.53)</td>
<td>-0.55(0.55)</td>
<td>-</td>
</tr>
<tr>
<td>Rectal cancer</td>
<td>M 0.48(0.54)</td>
<td>-</td>
<td>0.48(0.54)</td>
<td>0.56(0.62)</td>
<td>-</td>
</tr>
<tr>
<td>(ICD 154)</td>
<td>F 0.93(0.51)+</td>
<td>mean socioeconomic rank</td>
<td>55%</td>
<td>0.20(0.48)</td>
<td>0.84(0.51)</td>
</tr>
<tr>
<td>All urinary cancer</td>
<td>M 1.73(0.53)**</td>
<td>% lack amenities</td>
<td>47%</td>
<td>0.97(0.83)</td>
<td>1.47(0.52)*</td>
</tr>
<tr>
<td>(ICD 188-189)</td>
<td>F 2.34(0.60)**</td>
<td>population density</td>
<td>39%</td>
<td>1.99(0.95)+</td>
<td>1.84(0.49)**</td>
</tr>
<tr>
<td>Bladder cancer</td>
<td>M 1.83(0.57)**</td>
<td>% lack amenities</td>
<td>54%</td>
<td>0.77(0.85)</td>
<td>1.58(0.57)*</td>
</tr>
<tr>
<td>(ICD 188)</td>
<td>F 1.88(0.95)+</td>
<td>-</td>
<td>1.88(0.95)+</td>
<td>1.56(0.85)+</td>
<td>-</td>
</tr>
<tr>
<td>Oesophageal cancer</td>
<td>M 1.92(0.97)+</td>
<td>-</td>
<td>1.92(0.97)+</td>
<td>1.61(0.83)+</td>
<td>-</td>
</tr>
<tr>
<td>(ICD 150)</td>
<td>F -1.37(1.23)</td>
<td>-</td>
<td>-1.37(1.23)</td>
<td>-0.75(1.21)</td>
<td>-</td>
</tr>
</tbody>
</table>

A key to this table is given on page 77
TABLE A3. Reuse and HIPE discharges in the London area
29 Boroughs

<table>
<thead>
<tr>
<th>Cause</th>
<th>Unweighted regression</th>
<th></th>
<th></th>
<th>Weighted regression</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reuse alone</td>
<td>Social Factors</td>
<td>% variation explained</td>
<td>Reuse after fitting social factors</td>
<td>Reuse alone</td>
</tr>
<tr>
<td>Gastro-intestinal cancer (ICD 151-154)</td>
<td>F 0.18(0.78)</td>
<td>% semi or unskilled 22%</td>
<td>-1.01(0.78)</td>
<td>0.06(0.78)</td>
<td>% semi or unskilled 16%</td>
</tr>
<tr>
<td>Stomach cancer (ICD 151)</td>
<td>M 1.80(1.18)</td>
<td>mean socioeconomic rank 50%</td>
<td>-0.17(0.98)</td>
<td>2.90(1.16)*</td>
<td>mean socioeconomic rank 56%</td>
</tr>
<tr>
<td></td>
<td>F 1.69(1.33)</td>
<td>% New Commonwealth 28%</td>
<td>-0.05(1.34)</td>
<td>2.42(1.34)*</td>
<td>% New Commonwealth 25%</td>
</tr>
<tr>
<td>Intestinal cancer (152-154)</td>
<td>M -0.88(0.80)</td>
<td>-</td>
<td>-0.88(0.80)</td>
<td>-1.49(0.87)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>F 0.16(0.69)</td>
<td>-</td>
<td>0.16(0.69)</td>
<td>-0.22(0.68)</td>
<td>-</td>
</tr>
<tr>
<td>All urinary cancer (ICD 188-189)</td>
<td>M 1.80(1.12)</td>
<td>% unemployment 43%</td>
<td>-0.49(1.07)</td>
<td>1.75(1.12)</td>
<td>% unemployment 41%</td>
</tr>
<tr>
<td></td>
<td>F 3.12(1.23)*</td>
<td>% unemployment 39%</td>
<td>1.02(1.28)</td>
<td>3.13(1.26)*</td>
<td>% unemployment 38%</td>
</tr>
<tr>
<td>Bladder cancer (ICD 188)</td>
<td>M 1.93(1.19)</td>
<td>% unemployment 42%</td>
<td>-0.45(1.14)</td>
<td>1.93(1.18)</td>
<td>% unemployment 40%</td>
</tr>
<tr>
<td></td>
<td>F 3.58(1.27)*</td>
<td>% unemployment 35%</td>
<td>1.58(1.37)</td>
<td>3.52(1.29)**</td>
<td>% unemployment 35%</td>
</tr>
<tr>
<td>Oesophageal cancer (ICD 150)</td>
<td>M -3.32(1.80)+</td>
<td>-</td>
<td>-3.32(1.80)+</td>
<td>-1.24(1.91)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>F -6.17(2.06)**</td>
<td>-</td>
<td>-6.17(2.06)**</td>
<td>-4.70(2.17)*</td>
<td>-</td>
</tr>
</tbody>
</table>

A key to this table is given on page 77
**TABLE A4. Reuse and HAA discharges in the London area**

**14 Boroughs**

<table>
<thead>
<tr>
<th>Cause</th>
<th>Reuse alone</th>
<th>Social Factors</th>
<th>% variation explained</th>
<th>Reuse after fitting social factors</th>
<th>Weighted regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Unweighted regression</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastro-intestinal cancer</td>
<td>1.37(0.76)</td>
<td>% manual</td>
<td>28%</td>
<td>0.78(0.85)</td>
<td>1.28(0.76)</td>
</tr>
<tr>
<td>(ICD 151-154)</td>
<td>F 0.14(0.80)</td>
<td>% manufacturing industries</td>
<td>44%</td>
<td>0.15(0.62)</td>
<td>0.06(0.78)</td>
</tr>
<tr>
<td>Stomach cancer</td>
<td>2.14(1.23)</td>
<td>% manual</td>
<td>49%</td>
<td>0.59(1.18)</td>
<td>2.18(1.23)</td>
</tr>
<tr>
<td>(ICD 151)</td>
<td>F 1.65(1.43)</td>
<td>% manual</td>
<td>38%</td>
<td>0.02(1.43)</td>
<td>1.52(1.42)</td>
</tr>
<tr>
<td>Intestinal cancer</td>
<td>0.89(0.63)</td>
<td>% manufacturing industries</td>
<td>45%</td>
<td>0.89(0.63)</td>
<td>0.64(0.64)</td>
</tr>
<tr>
<td>(ICD 152-154)</td>
<td>F -0.34(0.81)</td>
<td>% manufacturing industries</td>
<td>45%</td>
<td>-0.33(0.63)</td>
<td>-0.42(0.80)</td>
</tr>
<tr>
<td>All urinary cancer</td>
<td>3.27(1.52)*</td>
<td>% unemployment</td>
<td>41%</td>
<td>1.08(1.93)</td>
<td>3.26(1.52)*</td>
</tr>
<tr>
<td>(ICD 188-189)</td>
<td>F 5.07(1.70)**</td>
<td>% unemployment</td>
<td>42%</td>
<td>3.06(2.25)</td>
<td>5.07(1.69)**</td>
</tr>
<tr>
<td>Bladder cancer</td>
<td>3.42(1.58)*</td>
<td>% unemployment</td>
<td>41%</td>
<td>1.13(2.00)</td>
<td>3.41(1.58)*</td>
</tr>
<tr>
<td>(ICD 188)</td>
<td>F 5.20(1.83)*</td>
<td>% unemployment</td>
<td>39%</td>
<td>3.19(2.44)</td>
<td>5.20(1.82)*</td>
</tr>
<tr>
<td>Oesophageal cancer</td>
<td>-0.24(1.38)</td>
<td>% manufacturing industries</td>
<td>26%</td>
<td>-0.22(1.24)</td>
<td>-0.40(1.37)</td>
</tr>
<tr>
<td>(ICD 150)</td>
<td>F 0.30(1.60)</td>
<td>% manufacturing industries</td>
<td>42%</td>
<td>0.33(1.28)</td>
<td>0.54(1.50)</td>
</tr>
</tbody>
</table>

A key to this table is given on page 77
## TABLE A5. Reuse, infant mortality and fertility in the London area

### 27 or 29 Boroughs

<table>
<thead>
<tr>
<th></th>
<th>Reuse alone</th>
<th>Social Factors</th>
<th>% variation explained</th>
<th>Reuse after fitting social factors</th>
<th>Reuse alone</th>
<th>Social Factors</th>
<th>% variation explained</th>
<th>Reuse after fitting social factors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infant mortality</strong> (29 boroughs)</td>
<td>1.98(1.04)</td>
<td>% unemployment</td>
<td>76%</td>
<td>-0.53(0.64)</td>
<td>2.10(1.03)*</td>
<td>% unemployment</td>
<td>73%</td>
<td>-0.04(0.67)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% New Commonwealth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Extended perinatal mortality</strong> (27 boroughs)</td>
<td>3.21(1.04)**</td>
<td>parity</td>
<td>66%</td>
<td>1.50(0.78)</td>
<td>3.16(1.06)**</td>
<td>parity</td>
<td>64%</td>
<td>1.30(0.81)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% unemployment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Stillbirths</strong> (27 boroughs)</td>
<td>2.05(0.60)**</td>
<td>parity</td>
<td>52%</td>
<td>1.38(0.46)**</td>
<td>1.98(0.61)**</td>
<td>parity</td>
<td>57%</td>
<td>1.00(0.43)*</td>
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<td><strong>FERTILITY RATES:</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Live births (29 boroughs)</td>
<td>0.15(0.54)</td>
<td>% manual</td>
<td>79%</td>
<td>-0.17(0.31)</td>
<td>0.16(0.54)</td>
<td>% manual</td>
<td>77%</td>
<td>-0.18(0.31)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% unemployment</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All births (27 boroughs)</td>
<td>0.04(0.65)</td>
<td>% manual</td>
<td>81%</td>
<td>-0.43(0.33)</td>
<td>0.04(0.65)</td>
<td>% manual</td>
<td>80%</td>
<td>-0.44(0.33)</td>
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<tr>
<td></td>
<td></td>
<td>% unemployment</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

A key to this table is given on page 77
<table>
<thead>
<tr>
<th>Cause</th>
<th>Reuse alone</th>
<th>Social factors</th>
<th>% variation explained</th>
<th>Reuse after fitting social factors</th>
<th>Reuse alone</th>
<th>Social factors</th>
<th>% variation explained</th>
<th>Reuse after fitting social factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastro-intestinal</td>
<td>M -0.003(0.009)</td>
<td>% manufacturing industries</td>
<td>41%</td>
<td>-0.001(0.008)</td>
<td>M 0.003(0.007)</td>
<td>% new residents</td>
<td>41%</td>
<td>-0.004(0.008)</td>
</tr>
<tr>
<td>cancer (ICD 151-154)</td>
<td>F -0.003(0.009)</td>
<td>% manual</td>
<td>23%</td>
<td>0.005(0.008)</td>
<td>F 0.000(0.007)</td>
<td>% manual</td>
<td>25%</td>
<td>0.002(0.005)</td>
</tr>
<tr>
<td>Stomach cancer</td>
<td>M 0.011(0.012)</td>
<td>% New Commonwealth</td>
<td>39%</td>
<td>0.020(0.012)</td>
<td>M 0.015(0.011)</td>
<td>% New Commonwealth</td>
<td>41%</td>
<td>0.020(0.010)</td>
</tr>
<tr>
<td>(ICD 151)</td>
<td>F 0.005(0.015)</td>
<td>% manufacturing</td>
<td>26%</td>
<td>0.017(0.013)</td>
<td>F 0.014(0.012)</td>
<td>% manufacturing</td>
<td>33%</td>
<td>0.007(0.010)</td>
</tr>
<tr>
<td>Intestinal cancer</td>
<td>M -0.018(0.010)</td>
<td>% overcrowding</td>
<td>22%</td>
<td>-0.007(0.011)</td>
<td>M -0.010(0.008)</td>
<td>% overcrowding</td>
<td>14%</td>
<td>-0.010(0.009)</td>
</tr>
<tr>
<td>(ICD 152-154)</td>
<td>F -0.008(0.009)</td>
<td>% employment</td>
<td>11%</td>
<td>0.012(0.010)</td>
<td>F -0.003(0.006)</td>
<td>% employment</td>
<td>10%</td>
<td>0.005(0.008)</td>
</tr>
<tr>
<td>All urinary cancer</td>
<td>M 0.006(0.011)</td>
<td>% overcrowding</td>
<td>9%</td>
<td>-0.003(0.012)</td>
<td>M 0.017(0.008)</td>
<td>% overcrowding</td>
<td>7%</td>
<td>0.007(0.009)</td>
</tr>
<tr>
<td>(ICD 188-189)</td>
<td>F 0.022(0.019)</td>
<td>% new residents</td>
<td>7%</td>
<td>0.006(0.019)</td>
<td>F 0.023(0.015)</td>
<td>% new residents</td>
<td>4%</td>
<td>0.025(0.015)</td>
</tr>
<tr>
<td>Bladder cancer</td>
<td>M 0.009(0.014)</td>
<td>% overcrowding</td>
<td>18%</td>
<td>-0.006(0.014)</td>
<td>M 0.022(0.010)</td>
<td>% semi or unskilled</td>
<td>19%</td>
<td>0.004(0.010)</td>
</tr>
<tr>
<td>(ICD 188)</td>
<td>F 0.030(0.024)</td>
<td>% lack inside WC</td>
<td>3%</td>
<td>0.029(0.024)</td>
<td>F 0.035(0.022)</td>
<td>% lack inside WC</td>
<td>3%</td>
<td>0.033(0.021)</td>
</tr>
<tr>
<td>Oesophageal cancer</td>
<td>M -0.012(0.018)</td>
<td>% cars per household</td>
<td>5%</td>
<td>-0.019(0.018)</td>
<td>M -0.012(0.013)</td>
<td>% cars per household</td>
<td>2%</td>
<td>-0.020(0.013)</td>
</tr>
<tr>
<td>(ICD 150)</td>
<td>F -0.032(0.027)</td>
<td>% large families</td>
<td>14%</td>
<td>-0.019(0.025)</td>
<td>F -0.003(0.022)</td>
<td>% large families</td>
<td>3%</td>
<td>0.003(0.021)</td>
</tr>
</tbody>
</table>

A key to this table is given on page 77
| Table A7. % Upland and national cancer mortality |
|---------|----------------|----------------|----------------|----------------|----------------|----------------|
|         | Unweighted regression | Weighted regression |         |         |         |         |         |
|         | Cause                  | % upland alone | Social Factors | variation explained | % upland after fitting social factors | % upland alone | Social Factors | variation explained | % upland after fitting social factors |
|         | M                      | 0.17(0.03)*** | % new residents | 43% | 0.06(0.03)* | 0.18(0.03)*** | % new residents | 47% | 0.06(0.02)* |
|         | F                      | 0.22(0.03)*** | % manual       |                  |                  | 0.22(0.03)*** | % manual       |                  |                  |
|         | Gastro-intestinal cancer (ICD 151-154) | | % new residents | 45% | 0.21(0.04)*** | 0.21(0.04)*** | % new residents | 49% | 0.05(0.03) |
|         | M                      | 0.21(0.04)*** | % manual       |                  |                  | 0.21(0.04)*** | % manual       |                  |                  |
|         | F                      | 0.30(0.05)*** | % new residents | 39% | 0.15(0.04)*** | 0.15(0.04)*** | % new residents | 46% | 0.05(0.03) |
|         | Stomach cancer (ICD 151) | | % new residents | 20% | 0.14(0.03)*** | 0.14(0.03)*** | % new residents | 23% | 0.04(0.03) |
|         | M                      | 0.14(0.03)*** | % New Commonwealth | 20% | 0.04(0.03) | 0.14(0.03)*** | % New Commonwealth | 23% | 0.04(0.03) |
|         | F                      | 0.13(0.03)*** | % large families | 12% | 0.08(0.03)* | 0.13(0.03)*** | % large families | 15% | 0.07(0.03)** |
|         | Intestinal cancer (ICD 152-154) | | % new residents | 20% | 0.04(0.03) | 0.14(0.03)*** | % new residents | 23% | 0.04(0.03) |
|         | All urinary cancer (ICD 180-189) | | % unemployment | 8% | 0.01(0.03) | 0.01(0.03) | % over crowding | 17% | -0.06(0.03) |
|         | M                      | -0.01(0.04) | % population density | 6% | -0.05(0.04) | 0.01(0.03) | % over crowding | 17% | -0.06(0.03) |
|         | F                      | 0.09(0.06) | % overcrowding | 8% | 0.01(0.06) | 0.08(0.06) | % overcrowding | 10% | -0.03(0.06) |
|         | Bladder cancer (ICD 188) | | % large families | 7% | -0.06(0.05) | -0.00(0.04) | % large families | 14% | -0.03(0.04) |
|         | M                      | -0.02(0.04) | % population density | 6% | -0.08(0.08) | 0.04(0.08) | % overcrowding | 11% | -0.10(0.08) |
|         | F                      | 0.04(0.08) | % large families | 6% | -0.08(0.08) | 0.04(0.08) | % overcrowding | 11% | -0.10(0.08) |
|         | Oesophageal cancer (ICD 150) | | % unemployment | 8% | 0.09(0.07) | 0.17(0.06)** | % unemployment | 12% | 0.06(0.06) |
|         | M                      | 0.16(0.07)* | % New Commonwealth | 8% | 0.09(0.07) | 0.17(0.06)** | % New Commonwealth | 12% | 0.06(0.06) |
|         | F                      | 0.17(0.08)* | % overcrowding | 14% | -0.07(0.09) | 0.20(0.08)* | % overcrowding | 11% | 0.01(0.08) |

A key to this table is given on page 77
### TABLE A8. % Upland and national cancer mortality, with NW-SE factor

#### 238 Urban areas

<table>
<thead>
<tr>
<th>Cause</th>
<th>% upland alone</th>
<th>Social Factors</th>
<th>% variation explained</th>
<th>% upland alone</th>
<th>Social Factors</th>
<th>% variation explained</th>
<th>% upland alone</th>
<th>Social Factors</th>
<th>% variation explained</th>
<th>% upland alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrintestinal cancer</td>
<td>0.17(0.03)***</td>
<td>% manual</td>
<td>-0.02(0.03)</td>
<td>0.18(0.03)***</td>
<td>% manual</td>
<td>-0.02(0.03)</td>
<td>0.18(0.03)***</td>
<td>% manual</td>
<td>-0.02(0.03)</td>
<td>0.18(0.03)***</td>
</tr>
<tr>
<td>(ICD 151-154)</td>
<td></td>
<td>population density</td>
<td></td>
<td>NW-SE 45°</td>
<td></td>
<td></td>
<td>NW-SE 45°</td>
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<td>NW-SE 45°</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% overcrowding</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach cancer</td>
<td>0.22(0.03)***</td>
<td>% manual</td>
<td>45%</td>
<td>0.07(0.03)*</td>
<td>0.22(0.03)***</td>
<td>% unemployment</td>
<td>40%</td>
<td>0.06(0.03)</td>
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<tr>
<td>(ICD 151)</td>
<td></td>
<td>NW-SE 45°</td>
<td></td>
<td></td>
<td></td>
<td>% manufacturing</td>
<td>industries</td>
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<tr>
<td></td>
<td></td>
<td>population density</td>
<td>50%</td>
<td>-0.00(0.04)</td>
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<tr>
<td></td>
<td></td>
<td>% lack inside WC</td>
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<td></td>
<td></td>
<td>% unemployment</td>
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<tr>
<td>Intestinal cancer</td>
<td>0.21(0.04)***</td>
<td>% manual</td>
<td>50%</td>
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<tr>
<td>(ICD 152-154)</td>
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<td>NW-SE 45°</td>
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<tr>
<td></td>
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<td>% overcrowding</td>
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<td>% higher education</td>
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</tr>
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<td></td>
<td></td>
<td>% higher education</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

A key to this table is given on page 77
### TABLE A10. % Upland and national infant mortality, with NW-SE factor

<table>
<thead>
<tr>
<th></th>
<th>Social Factors</th>
<th>Variation explained</th>
<th>% upland alone</th>
<th>% upland after fitting social factors</th>
<th>Social Factors</th>
<th>Variation explained</th>
<th>% upland alone</th>
<th>% upland after fitting social factors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infant mortality</strong></td>
<td>cars per household</td>
<td>59%</td>
<td>0.09(0.04)*</td>
<td>0.36(0.05)**</td>
<td>cars per household</td>
<td>63%</td>
<td>0.10(0.04)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% large families</td>
<td></td>
<td></td>
<td></td>
<td>% large families</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>% manufacturing industries</td>
<td></td>
<td></td>
<td></td>
<td>% New Commonwealth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>% lack inside WC</td>
<td></td>
<td></td>
<td></td>
<td>% overcrowding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>% lack amenities</td>
<td></td>
<td></td>
<td></td>
<td>% lack inside WC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Extended perinatal mortality</strong></td>
<td>cars per household</td>
<td>53%</td>
<td>0.15(0.05)**</td>
<td>0.42(0.05)**</td>
<td>cars per household</td>
<td>55%</td>
<td>0.13(0.04)**</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% large families</td>
<td></td>
<td></td>
<td></td>
<td>% large families</td>
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<td></td>
<td>% manufacturing industries</td>
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<td></td>
<td>% manufacturing industries</td>
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<tr>
<td></td>
<td>% new residents</td>
<td></td>
<td></td>
<td></td>
<td>% lack inside WC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Stillbirths</strong></td>
<td>% manual</td>
<td>39%</td>
<td>0.10(0.03)**</td>
<td>0.22(0.03)**</td>
<td>% manual</td>
<td>43%</td>
<td>0.08(0.03)**</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% large families</td>
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<td></td>
<td></td>
<td>% large families</td>
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</tr>
<tr>
<td></td>
<td>% lack inside WC</td>
<td></td>
<td></td>
<td></td>
<td>% lack inside WC</td>
<td></td>
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</tr>
</tbody>
</table>

A key to these tables is given on page 77.
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