LETTERS TO THE EDITOR

Population change and mortality in men and women

EDITOR,— Differences in mortality between areas have been found to be related to the socioeconomic conditions of the area.[1] [2] However, people also move to improve their physical and social environment, and the health status of the migrants differs considerably from that of the non-migrants.[3] Recently, Davey Smith and colleagues[4] found that mortality, measured 1991–92, was inversely related to the population growth in the two preceding decades in 292 areas in Britain. They found a negative correlation between population change and mortality both in men and women, although the correlation was somewhat stronger in men.

We investigated the association between population growth and mortality in the 16 municipalities of the county of Värmland in Sweden. The population change, as percentage increases or decreases between 1975 and 1994 was counted from the official population statistics. In Sweden, the official population statistics are based on continuous registration of births, deaths and migration. Although the population change was similar in both sexes (correlation 0.99), we calculated it separately for men and women. Mortality in 1992–96 was derived from the database administered by the Centre for Epidemiology, National Board of Health and Welfare. Age standardised total and cause specific mortalities have been calculated using weights from a Swedish standard population (1970).

The county of Värmland is an area with one of the highest mortalities from cardiovascular disease and non-insulin dependent diabetes in men and women in Sweden. The municipalities include several industrial municipalities with comparably high rates of unemployment, some rural municipalities, a few municipalities with growing populations, and the city of Karlstad, a growing centre of the county. The number of inhabitants in the different municipalities varied between 4700 and 79 000 in 1994, while 12 of the 16 municipalities had more than 10 000 inhabitants.

We found a similar inverse association between population change and mortality as Davey Smith and colleagues[4] in men but not in women (fig 1). The correlation between population change and age standardised all cause mortality in men was −0.61 (p=0.013) in men. In women, the correlation was positive but not statistically significant: 0.15 (p=0.57). Analysis of male cause specific mortality showed strongest correlations between population change and mortality from cancer (r=−0.62, p=0.011), alcohol related diseases (r=−0.56, p=0.025) and mental disorders (r=−0.50, p=0.050). Similar negative but somewhat weaker correlations were observed for mortality from cardiovascular disease, diabetes and lung cancer. In women, only mortality from diabetes was inversely related to population change (r=−0.49, p=0.055), and to a lesser degree mortality from mental disorders (r=−0.27, p=0.31). Because we only had 16 municipalities in the analysis, we
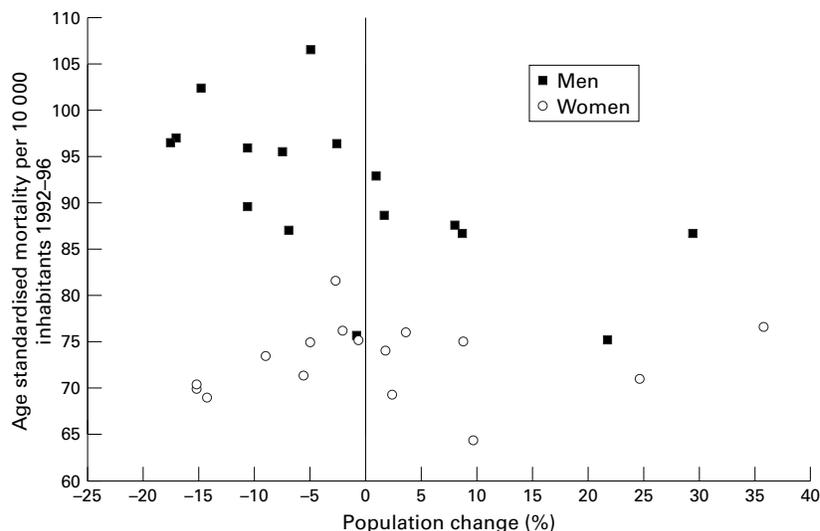

Figure 1   Mortality among men and women in the 16 municipalities of the county of Värmland, Sweden, and population change 1975–94.

repeated the analysis using non-parametric (rank) correlations. The results from the non-parametric analysis were similar to those from the parametric analysis. We also calculated the correlation between population change between 1975 and 1990 and mortality in 1988–92 and the results were consistent with those for the period 1992–96.

Population growth is closely linked to the socioeconomic conditions and deprivation of residential areas. In our study, population change was positively correlated with the proportion of inhabitants with high income (over 266 055 SEK in 1995) and proportion of inhabitants with high education (more than high school) and negatively correlated with the unemployment rate in the municipality. Therefore we calculated partial correlations between population growth and mortality controlling for these factors. The correlation between population change and all cause mortality in men was −0.41 (p=0.13) after controlling for proportion of inhabitants with high income. This indicates that about one third of the correlation between population change and mortality was explained by the proportion of inhabitants with high income. Controlling for proportion of inhabitants with high education and proportion of unemployed had a weaker effect on the association between population growth and mortality.

Why did we find the inverse association in men but not in women? It seems that, in women, different causes of mortality have different associations with population growth. Although diabetes mortality was inversely related to population growth, especially breast cancer mortality was higher in many of the growing areas (correlation between population change and breast cancer mortality 0.39, p=0.137) than in the shrinking areas. Female breast cancer mortality is known to be associated with affluency[5] and was also in our study more common in municipalities with high proportions of inhabitants with high income (r=0.45, p=0.079) and less common in municipalities with high unemployment rates (r=−0.77, p<0.001). In men, all the cause specific mortalities studied were inversely related to population growth.

This study suggests that the association between population growth and mortality differs between men and women. Men in growing, wealthy areas are better off than men

in shrinking, less affluent areas. Migration seems to strengthen the inverse association between affluency and mortality as healthier people move to more physically and socially attractive areas. This is indicated by the fact that population change was more strongly related to mortality than income or unemployment rates. The negative association between population growth and mortality does not unequivocally hold for women, among whom the association may be cause specific. Our study comprised only 16 municipalities and the findings should therefore be verified in a larger sample of areas. However, even in such a small sample of areas, the findings were consistent with previously published studies on population change and mortality in men and on socioeconomic conditions and breast cancer mortality in women.

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Non-Hodgkin's lymphoma and nitrate in drinking water

EDITOR,— We read with interest the article by Law *et al.*[1] This ecological study examined the incidence of non-Hodgkin's lymphoma (NHL) in Yorkshire and North Humberside in 1984–1993 in relation to nitrate concentrations in drinking water. Nitrate exposure was estimated for 148 water supply zones by calculating a mean of monthly means based on six

years of monitoring data (1990–1995) that largely post-dated the time period of NHL incidence. The results showed a relation between NHL incidence during 1984–1989 and nitrate concentrations in the early 1990s but not for incidence during 1990–1993.

The authors compared the distribution of their recent nitrate average with the distribution of long term average nitrate values from our population-based case-control study of NHL in the state of Nebraska, USA.[2] They also described the long term average nitrate metric we calculated as "an imprecise estimate of nitrate exposure assessed from single annual measurements for a city or town". The characterisation of our historical nitrate estimates as "imprecise" is inappropriate; rather, our nitrate metric had most elements required for an accurate estimate of historical nitrate exposure. An accurate estimate of historical nitrate requires individual level information on water source for many decades preceding cancer incidence, water consumption amount, and historical data on nitrate levels in water supplies. We had all this information, as well as individual information on potential confounders such as pesticide use and dietary intake of nitrosation inhibitors.

We collected complete residential and water source histories so that we could determine who drank community water and so that we could compute average nitrate exposure over multiple residences for an approximately 40 year period, pre-dating cancer incidence. We also obtained information on the amount of tap water intake, although incorporating information on usual consumption did not change our risk estimates. Nitrate measurement data were available for 138 Nebraska municipalities during 1947–1987. The population size of the towns in 1980 ranged from 18 to 314 000; the median size was 1300 and only two municipalities exceeded 50 000. Although measurement data before the late 1960s were sparse, most towns had multiple years of measurement data from the late 1960s to the late 1980s. In this latter period, many towns had multiple measurements within a year that we averaged to compute an annual mean. Seasonal variation in nitrate concentrations was not common because most communities used ground water from deep wells (>35 metres). The number of years with missing data was similar for cases and controls, thus misclassification of exposure would be non-differential and tend to bias the odds ratios towards the null. We calculated a long term average level for each person in the study by linking the water source history information to the historical municipal nitrate database. To reduce misclassification, we excluded people for whom we had no information on nitrate concentrations in their drinking water supplies for more than 10% of their person years after 1947. Exposure in the five years before diagnosis of cases and interview of controls was not counted in a person's average exposure level because recent exposures are unlikely to be related to risk of cancer.

Thus, the average nitrate concentrations for people in our study, calculated over approximately 35 years, are not directly comparable to the six year average population levels calculated by the authors. Furthermore, it is important to consider the calendar time period over which average nitrate concentrations are computed, because several factors affect nitrate values in community supplies, including changes in nitrogen fertilizer use over time and changes in the source of a com-

Table 1 Number of cases and controls (combined) by quartiles of their long term average nitrate concentration and quartiles of their most recent five year average nitrate concentration

Long term average nitrate quartiles (mg nitrate-N/l)	Recent (five year) average nitrate quartiles (mg nitrate-N/l)				
	Q1 (low)	Q2	Q3	Q4 (high)	Total
Q1 (low)	53	50	4	20	127
Q2	5	61	174	58	298
Q3	8	44	4	28	84
Q4 (high)	98	30	3	33	164

munity's drinking water. The residential stability of the study population has also been shown to be an important factor in the correlation between recent and long term average nitrate exposures.[3] Substantial misclassification can occur if recent measurement data are used to estimate long term average exposure. To illustrate this, we recalculated nitrate concentrations for people in our study using the last five years of nitrate measurements, data that were excluded from the original average nitrate calculation. For cases and controls, we compared quartile categories of long term average nitrate (our original metric) with the average nitrate concentrations computed using the last five years of exposure (recent five year average nitrate). We determined the per cent agreement between the exposure metrics. The results of the cross categorisation are shown in table 1; the per cent agreement was similar for cases and controls so the combined results are presented.

Only 22 per cent of people were classified into the same quartile of both exposure metrics. In our study, we observed a significantly increase risk of NHL among those in the highest quartile of long term average nitrate compared with those in the lowest quartile (odds ratio 2.0, 95% confidence intervals 1.1, 3.6). Even if we ignore the misclassification for those in the middle quartiles of long term average nitrate (382 people), the per cent agreement between the exposure metrics for those in the first and fourth quartile of long term average nitrate was only 30 per cent. Much of the misclassification was attributable to the assignment of those in the highest quartile of long term nitrate to the lowest two quartiles of recent average nitrate. These results illustrate the potential for substantial misclassification when recent data are used to estimate historical exposures.

Nitrate concentrations in water sources are influenced by agricultural, animal husbandry, and waste treatment practices, and these practices can change substantially over time. To further investigate the association between drinking water nitrate and cancer risk, well designed studies with individual information on historical nitrate exposure are needed.

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Authors' reply

EDITOR,—We strongly agree with Ward and colleagues that further investigation into the association between drinking water nitrate and cancer risk is warranted, as the evidence is equivocal. The difficulties in measuring dietary exposures are well known, and retrospective assessments of dietary, or drinking water, nitrate levels are inherently difficult to make.

Our comments on the estimate of nitrate exposure used by Ward and colleagues[1] were based on information derived from their paper. They relate to the number of nitrate measurements made and geographical delineation of the water distribution network. Their efforts to estimate an individual's exposure to nitrate over a considerable time period are to be applauded.

In the UK, nitrate concentrations in drinking water from municipal sources are tightly regulated. Every household receiving water is within a "Water Supply Zone" (WSZ).[2] This geographically delimited area has water that, at any point in time, is internally homogenous in respect to its level of nitrate. To assess the level a household receives it is simply a matter of identifying the WSZ, and using some summary of the comprehensive measurements taken throughout the year.

Furthermore, in the UK, cities and towns take water from more than one source, leading to a patchwork of nitrate concentrations at any point in time, within a single urban area. However, urban areas are split into WSZs that contain a homogenous water quality. It was not explicit in the Ward paper that this is the case within Nebraska. If there were more than a single source for a city, the assessment of nitrate concentrations from a single measurement would be less than appropriate.

We note that in the latter period of time, values were measured more frequently than once a year, we welcome this clarification. We understand that, although the values we used were accurate, they were based on a short period of time before, or around, diagnosis. However, an average nitrate value for 30–40 years would represent the persons lifetime exposure, but may not necessarily represent the time window of exposure for the initiation of cancer.

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