

# Stomach Cancer Mortality: Geographic Comparisons in the Netherlands and in Belgium

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**Abstract**—The geographic distribution of stomach cancer mortality by province in the Netherlands and Belgium, 1972-1975, is described. Areas of high risk for this disease are identified along the common border of these two countries, suggesting common etiologic factors.

## INTRODUCTION

THERE are large differences between countries in mortality due to malignancies at several sites [1]. The highest stomach cancer mortality rates are reported for Japan (58 for men and 30 for women per 100,000), while in the United States the mortality rates are relatively low (8 for men and 4 for women per 100,000). As is the case for Western Europe in general, both the Netherlands and Belgium have stomach cancer mortality rates between these two extremes (21 for men and 10 for women per 100,000). These differences in death rates between countries may be indicative of associated differences in factors related to this disease.

Variations in the regional frequency of mortality within countries may also provide information about possible etiologic associations. In the United States, a cluster of high stomach cancer mortality counties was identified [2] in the north-central region where many immigrants from north-central Europe live. There have been other reports of marked differences in the geographic distribution of cancer mortality within countries [3-5]. Although the national stomach cancer mortality rates for the Netherlands and Belgium are about the same, prominent differences in regional mortality within the countries have been observed [6, 7]. Further, an aggregation

of high stomach cancer mortality in areas adjacent to their common border suggests common cultural factors or environmental exposures which may be associated with the occurrence of stomach cancer.

## MATERIALS AND METHODS

Available data concerning the total observed number of deaths due to stomach cancer (ICD 8: 151) for men and women for the years 1972-1975 as reported on death certificates were obtained for the 11 provinces of the Netherlands and the 9 provinces of Belgium. Expected numbers of deaths due to this cause were calculated for men and women for the respective provinces.

The expected numbers of deaths per year for each province were computed as follows: mortality rates for the Netherlands (sex and 5-year age specific, 1972-1975) were multiplied by the (sex and age specific) population number (Netherlands, 1 Jan, 1974, and Belgium, 1 Jan, 1970) of the individual provinces. This gave the age-specific expected mortality. The expected number of deaths was then derived by summing the age-specific expected mortality. The ratio (O/E) of observed to expected deaths, which is often referred to as the Standardized Mortality Ratio (SMR), was then calculated. Confidence limits and tests of statistical significance were derived using a normal approximation formula for the expectation of a Poisson variable [8].

## RESULTS

In Table 1 the relationship between the stomach cancer mortality in the study area is shown for men and women. The individual O/E ratios as well as the confidence limits (95%) are shown. This data is illustrated in Fig. 1, in which the O/E ratios for stomach cancer among women in the respective provinces is plotted in relation to that for men. The individual data points are identified for the Netherlands (A-K) and for Belgium (1-9).

As illustrated in Fig. 1, there is considerable variability in stomach cancer mortality within the study area: the ratio ( $\times 100$ ) of observed to expected stomach cancer mortality ranges from 65 to 132 for men and from 65 to 169 for women.

There is a linear relationship (Pearson's  $r = 0.77$ ,  $P < 0.01$ ) between the stomach cancer mortality for men and for women by geographic region. For one province, C. Drenthe (encircled in Fig. 1), there is an apparent exception to this linear relationship in relative mortality for males as compared to females.

As shown in Fig. 2, the highest O/E ratios for men are observed for the provinces of Zeeland and Friesland in the Netherlands and for West Flanders, East Flanders and Limburg in Belgium. The areas of lowest stomach cancer

mortality for males in the Netherlands are the provinces of South Holland and Utrecht, while for Belgium the four most southern provinces show a relatively low mortality for this cause (Hainault, Liège, Luxemburg and Namur).

Figure 3 presents the distribution of stomach cancer mortality for women. As would be expected from the positive correlation of mortality by sex, there is considerable similarity in this distribution and that described for men in Fig. 2. The high stomach cancer mortality in the provinces of Zeeland, West and East Flanders in the two countries observed for men is also found here and in the adjacent provinces of North Brabant and Limburg in the Netherlands and of Antwerp and Limburg in Belgium.

This aggregation of high stomach cancer mortality areas across national boundaries may be indicative of common etiologic factors in these regions.

## DISCUSSION

The large differences in the occurrence of stomach cancer in and within different countries, and the observation [9] that migrants tend to maintain the risk of their country of origin, whereas the succeeding generations tend to assume the risk of the host country, both point

Table 1. The observed number of deaths (Obs) due to stomach cancer, the ratio of observed to expected deaths (O/E) and its 95% confidence interval for the provinces of the Netherlands and Belgium, 1972-1975

Province	Males			Females		
	Obs	O/E	(95% C.I.)	Obs	O/E	(95% C.I.)
The Netherlands						
A. Groningen	379	1.05	(0.95-1.16)	216	1.04	(0.91-1.19)
B. Friesland	452	1.23	(1.12-1.35)	229	1.10	(0.96-1.25)
C. Drenthe	239	1.04	(0.91-1.18)	159	1.69	(1.44-1.98)
D. Overijssel	529	0.98	(0.90-1.07)	335	1.13	(1.01-1.26)
E. Gelderland	779	1.04	(0.97-1.12)	472	0.93	(0.85-1.02)
F. Utrecht	351	0.79	(0.71-0.88)	240	0.82	(0.72-0.93)
G. N-Holland	1411	1.03	(0.98-1.08)	851	0.96	(0.90-1.03)
H. S.-Holland	1523	0.84	(0.80-0.88)	985	0.86	(0.81-0.92)
I. Zeeland	325	1.32	(1.18-1.47)	195	1.47	(1.27-1.70)
J. N-Brabant	919	1.06	(1.00-1.13)	594	1.25	(1.15-1.36)
K. Limburg	485	0.99	(0.90-1.08)	334	1.18	(1.06-1.32)
Belgium						
1. Antwerp	1029	1.05	(0.99-1.12)	671	1.16	(1.07-1.25)
2. Brabant	949	0.92	(0.86-0.98)	949	0.92	(0.86-0.98)
3. Hainault	695	0.76	(0.70-0.82)	634	1.01	(0.93-1.09)
4. Liège	486	0.71	(0.65-0.78)	420	0.85	(0.77-0.94)
5. Limburg	336	1.15	(1.03-1.28)	189	1.26	(1.09-1.46)
6. Luxemburg	119	0.79	(0.66-0.95)	91	0.97	(0.78-1.20)
7. Namur	164	0.65	(0.56-0.76)	114	0.65	(0.54-0.78)
8. East Flanders	1159	1.22	(1.15-1.29)	839	1.56	(1.46-1.67)
9. West Flanders	803	1.16	(1.08-1.24)	551	1.38	(1.27-1.50)

Sources: Netherlands Central Bureau of Statistics, Voorburg, the Netherlands; National Institute of Statistics, Brussels, Belgium.

to the possibility that stomach cancer may to a large extent be associated with environmental factors. A marked inverse socio-economic gradient in stomach cancer risk has been consistently reported [10], as well as suggestions that occupational exposures [11–16] may be causally related to stomach cancer mortality.

The role of diet and nutrition has been considered with regard to a possible association with several forms of cancer, including cancer of the stomach. Among the dietary factors which have been suggested to be associated with gastric cancer are higher intake of starches [17] and of salt [18], lower intake of certain

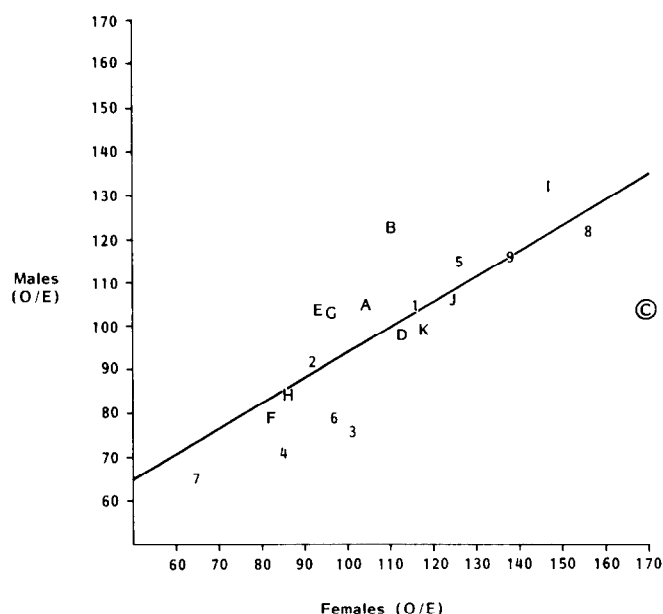


Fig. 1. The relationship between the ratios (O/E) of observed to expected number of deaths for men and women due to stomach cancer (ICD8: 151) in the Netherlands and Belgium, 1972–1975. The Netherlands: A. Groningen (\*), B. Friesland (\*), C. Drenthe (\*), D. Overijssel (\*), E. Gelderland (\*), F. Utrecht (\*), G. North Holland (\*), H. South Holland (\*), I. Zeeland (\*), J. North Brabant (\*), K. Limburg (\*). Belgium: 1. Antwerp (\*), 2. Brabant (\*), 3. Hainault (\*), 4. Liège (\*), 5. Limburg (\*), 6. Luxembourg (\*), 7. Namur (\*), 8. East Flanders (\*), 9. West Flanders (\*).

\* $P < 0.05$  (males, females), that  $O/E = 100$ .

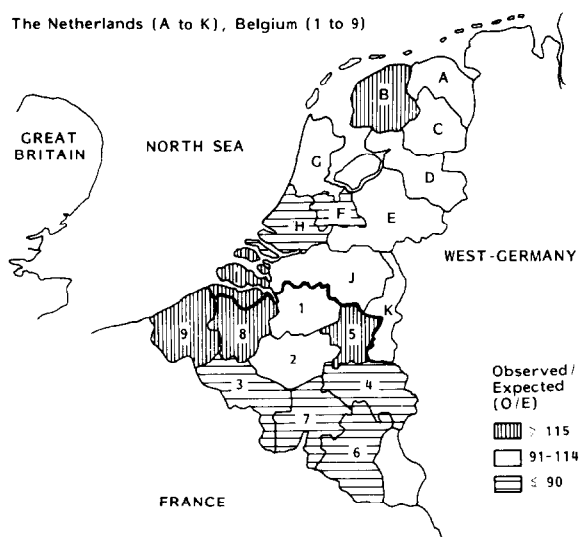


Fig. 2. Geographical distribution of the ratio (O/E) of observed to expected deaths for stomach cancer (ICD8: 151) for men in the Netherlands and Belgium, 1972–1975.

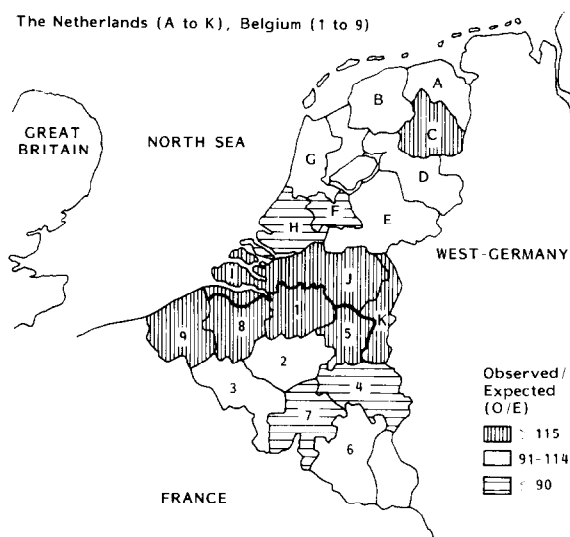


Fig. 3. Geographical distribution of the ratio (O/E) of observed to expected deaths for stomach cancer (ICD8: 151) for women in the Netherlands and Belgium, 1972–1975.

fresh produce [19] or dietary vitamin A [20], the presence of large amounts of polycyclic hydrocarbons in the diet [21] and exposure to carcinogenic nitrosamines [22].

Stomach cancer mortality has in most countries over the last several decades been markedly decreasing. In just the period 1961–1971, the age-standardized gastric cancer mortality rates for men decreased 27% in the Netherlands and 26% in Belgium [23]. Although this decrease can in part be ascribed to more effective diagnostic assessment of a previously over-rated diagnosis, there is also a discernable decrease for well-diagnosed cases [24]. The reasons for this decrease have not been well specified, although changes in living practices and, in particular, in dietary patterns are suspected of playing an important role.

The substantial geographic differences in stomach cancer mortality observed in this study could in part be due to the relative differences in the time sequence of introduction of such living practice changes in the various regions. This is not directly evident as, for the Netherlands, Tromp [25] reported a similar geographic distribution of relative stomach cancer mortality for the period 1946–1952, as reported here, although the actual mortality rates were considerably higher in that period.

In this study, the areas of high stomach cancer mortality in the two countries are predominantly in adjacent border provinces. The identification of disease risk aggregation as a result of reporting from two countries with independent disease reporting systems supports the possibility that the observed effects are, in fact, real. Although these regions have been parts of different countries for the last 150 years, the inhabitants have to a large extent a common historical and cultural background from which clues may be derived concerning the etiology of stomach cancer.

Genetic susceptibility may play a role in the etiology of stomach cancer, as suggested by Ashley and Davies [3]. Available data on blood-type among blood donors in the Netherlands and army recruits in Belgium [26] do not show any obvious relationship between blood-type and the observed disease distribution.

Meinsma [27], in 1964, reported upon the dietary patterns of stomach cancer cases and controls in areas of high and low stomach cancer mortality in the Netherlands. Using a brief dietary questionnaire, he reported that cases of gastric cancer consumed more bacon and less citrus-fruit than controls. These consumption patterns did not, however, parallel the geographic distribution of mortality. In Belgium, differences in the dietary patterns of the northern Flemish population and the southern Wallon population have been indicated by a comparative dietary survey in 1963–1964 among the inhabitants of East Flanders and of Liège, in Wallonia [28]. More fruits and less animal protein, seafood and milk were reported to be consumed in Liège than in East Flanders. Specific factors associated with stomach cancer are presently being investigated by means of a case-control study in these regions of Belgium (L. Ramioul, principal investigator).

Few studies as the one described here comparing the geographic distribution of disease within more than one country have been reported. The validity and availability of comparative data have limited such efforts. The diagnosis, reporting and classification of disease may vary between countries, making international comparisons of disease difficult. Further, cancer incidence data, which is not available for these countries, would be useful for supporting the observed mortality patterns.

In this report we had to use available estimates of the population of the Belgian provinces in 1970 for estimating expected mortality there from 1972 to 1975. This approximation does not lead to more than a marginal error. However, such data base limitations, and those of a greater magnitude, seriously hamper more extensive international studies of this type.

This report indicates the use of intra- and international mortality statistics for identifying geographic areas of excess mortality by which hypotheses concerning disease etiology can be generated. International cooperation will be needed for more extensive investigations of this type.

## REFERENCES

1. SEGI M. *Age-adjusted Death Rates for Cancer for Selected Sites in 51 Countries in 1974*. Nagoya, Japan, Segi Institute of Cancer Epidemiology, 1979.
2. HOOVER R, MASON TJ, MCKAY FW, FRAUMENI JF, JR. Cancer by county: a new resource for etiologic clues. *Science* 1975, 189, 1005–1007.
3. ASHLEY JB, DAVIES HD. Gastric cancer in Wales. *Gut* 1966, 7, 542–548.

4. GREGOR O, TOMAN R, PRUSOVA F, DRNKOVA V, PASTOROVA J. Geographical distribution of stomach cancer in Czechoslovakia. *Gut* 1969, **10**, 150–154.
5. THE EDITORIAL COMMITTEE FOR THE ATLAS OF CANCER MORTALITY IN THE PEOPLE'S REPUBLIC OF CHINA. *Atlas of Cancer Mortality in the People's Republic of China*. China Map Press, 1981.
6. HAYES RB, DE GUCHTENEIRE PFA, VAN DER KNAAP GA. *Geographic Distribution of Cancer Mortality in the Netherlands*. Rotterdam, Institute of Social Oncology, 1980.
7. RAMIOUL L, TUYNS AJ. La distribution géographique des cancer du tube digestif en Belgique. *Acta Gastroenterol Belg* 1977, **40**, 129–147.
8. LILIENFELD AM, PEDERSEN E, DOWD JE. *Cancer Epidemiology: Methods of Study*. Baltimore, MD, Johns Hopkins Press, 1967.
9. HAENSZEL W, KURIHARA M. Studies of Japanese migrants. I. Mortality from cancer and other diseases among Japanese in the United States. *J Natl Cancer Int* 1968, **40**, 43–68.
10. INTERNATIONAL UNION AGAINST CANCER. *Stomach Cancer*. Geneva, I.U.A.C., 1978, Technical Report 34.
11. STOCKS P. Cancer and bronchitis mortality in relation to atmospheric deposit and smoke. *Br Med J* 1959, **2**, 74–79.
12. BAILAR JC. Distribution of carcinoma of oesophagus, stomach and large bowel. In: BURDETTE WJ, ed. *Carcinoma of the Alimentary Tract*. Salt Lake City, University of Utah Press, 1965.
13. ARMIJO R, ORELLANA M, MEDINA E, COULSEN AH, SAYRE JW, DETELS R. Epidemiology of gastric cancer in Chile: I—Case control study. *Int J Epidemiol* 1981, **10**, 53–62.
14. ROCKETTE HE. Cause specific mortality of coal miners. *J Occup Med* 1977, **19**, 795–801.
15. MCMICHAEL MJ, ANDJELKOVIC DA, TYROLER HA. Cancer mortality among rubber workers: an epidemiologic study. *Ann NY Acad Sci* 1976, **272**, 125–137.
16. MILLER AB. Asbestos fibre dust and gastro-intestinal malignancies. Review of literature with regard to cause/effect relationship. *J Chronic Dis* 1978, **31**, 23–33.
17. MODAN B, LUBIN E, BARELL V, GREENBERG RA, MODAN M, GRAHAM S. The role of starches in the etiology of gastric cancer. *Cancer* 1974, **34**, 2087–2092.
18. JOOSSENS JV, GEBOERS J. Nutrition and gastric cancer. *Nutr Cancer* 1981, **2**, 250–261.
19. HAENSZEL W, KURIHARA M, LOCKE FB, SHIMAZU K, SEGI M. Stomach cancer in Japan. *J Natl Cancer Inst* 1976, **56**, 265–274.
20. PETO R, DOLL R, BUCKLEY JD, SPORN MB. Can dietary beta-carotene materially reduce human cancer rates? *Nature (Lond)* 1981, **290**, 201–208.
21. HAAS JF, SCHOTTENFELD D. Epidemiology of gastric cancer. In: LIPKIN M, GOOD RA, eds. *Gastrointestinal Tract Cancer*. New York, Plenum Medical Book Co., 1978.
22. HILL MJ, HAWKSWORTH G, TATTERSALL G. Bacteria, nitrosamines and cancer of the stomach. *Br J Cancer* 1973, **28**, 562–567.
23. TULINIUS H. Epidemiology of gastric cancer. *Nutr Cancer* 1979, **1**, 61–69.
24. CLEMMESSEN J. Is gastric cancer decreasing in incidence? *Acta Pathol Microbiol Scand* 1977, **65** (Suppl. 261), 65–75.
25. TROMP SW. The geographical distribution of cancer of the stomach in the Netherlands (period 1946–1952). *Br J Cancer* 1956, **10**, 265–281.
26. MOURANT AE, KOPEC AC, SOBCZAK KD. *The Distribution of the Human Blood Groups*. Oxford, Oxford University Press, 1976.
27. MEINSMA L. Voeding en kanker. *Voeding* 1964, **7**, 357–365.
28. CRESTA M, LEDERMAN S, GORNIER A, LOMBARD E, LACOURLY G. *Etude de Consommation Alimentaire de Populations de 11 Régions de la Communauté Economique Européenne en vue de la Détermination du Niveau de Contamination Radioactive*. Monographie EUR 4218F, Euratom CEA, 1969.