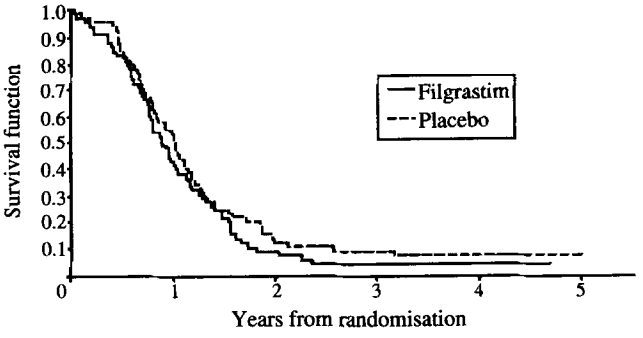

Figure 1. Overall survival.

poietic growth factors [1, 2]. This has suggested that the clinical use of such factors may result in tumour stimulation and reduced response to cytotoxic chemotherapy, and hence may adversely affect survival. A long-term follow-up has been completed on patients with small cell lung cancer (SCLC), who were randomised to receive either "r-metHuG-CSF" (Filgrastim) or placebo in a study which clearly showed that Filgrastim reduces the infectious complications of cytotoxic chemotherapy [3, 4].

Between June 1989 and April 1991, 130 patients were recruited from 13 European centres. As of 30 November 1994, disease progression and survival data were available for 129 patients (65 Filgrastim, 64 placebo). The patient that was not followed-up was randomised into the study, but received no study medication (Filgrastim or placebo) and was excluded from all study analyses. Time to disease progression was calculated by counting the number of days between the date of randomisation and first recorded date of disease progression or, in the absence of a disease progression, the date of death. The time to death was calculated as the number of days from randomisation to death. The Kaplan–Meier (KM) curves of the time to disease progression and the time to death were compared by using the log-rank test adjusting for country and disease stage (i.e. limited or extensive).

The median follow-up at this time is 1755 days (range 1306–1992). The KM median of the time to disease progression is 225 days for patients treated with Filgrastim and 198 days for patients treated with placebo ($P=0.81$). The proportion of patients surviving more than 2 years is 6/65 (9%) and 8/64 (13%) in the Filgrastim and placebo groups, respectively, and the KM median of the time to death is 323 days for patients treated with Filgrastim and 368 days for patients treated with placebo ($P=0.27$). The KM curves for the time to death are presented in Figure 1. These are the first long-term, controlled, follow-up data for SCLC patients treated with Filgrastim. In our previous publication [4], a significant but modest increase in chemotherapy dose intensity (less than 10% for all days) was noted in the Filgrastim group, and it was suggested that this increase would be insufficient to produce any enhanced antitumour effect. The data presented here support that conclusion. They also confirm preliminary conclusions derived from the original study, providing no support for the hypothesis that the use of Filgrastim in this patient population may result in tumour stimulation.

1. Dedhar S, Gaboury L, Galloway P, *et al.* Human granulocyte colony-stimulating factor, is a growth factor active on a variety of cell types of non hemopoeitic origin. *Proc Natl Acad Sci USA* 1988, **85**, 9253.
2. Berdel WE, Danhausen-Riedl S, Stenhauser G, *et al.* Various human haematopoietic growth factors (interleukin-3, GM-CSF, G-CSF) stimulate clonal growth of non-haematopoietic cells. *Blood* 1989, **73**, 80–83.
3. Green JA, Trillet V, Manegold C, *et al.* G-CSF in CAE chemotherapy in small cell lung cancer. *Proc Am Soc Clin Oncol* 1991, **10**, A832.
4. Trillet-Lenoir V, Green JA, Manegold C, *et al.* Recombinant granulocyte colony stimulating factor reduces the infectious complications of cytotoxic chemotherapy. *Eur J Cancer* 1993, **29A**, 319–324.

European Journal of Cancer Vol. 31A, No. 12, pp. 2116–2117, 1995.

0959-8049/95 $9.50 + 0.00

0959-8049(95)00465-3

Increasing Incidence of Cancer of the Sigmoid and Ascending Colon for Men in South-east Netherlands

R.A.M. Damhuis,[1,2] J.W.W. Coebergh,[1,2] W.M.M. Driessen[3] and L.H. van der Heijden[1]

[1]Comprehensive Cancer Centre South, P.O. Box 231, 5600 AE Eindhoven; [2]Comprehensive Cancer Centre, Rotterdam; [3]Department of Epidemiology and Biostatistics, Erasmus University Medical School, Rotterdam; and [4]Department of Internal Medicine, St Joseph Hospital, Veldhoven, The Netherlands

COLORECTAL CANCER is the third most prevalent cancer in Europe and its large geographical variation in incidence [1] is generally attributed to exogenous factors [2]. The uneven anatomical distribution of colorectal tumours [3] and the subsite-specific trends in incidence [4, 5] indicate that aetiological factors may not be similar throughout the large bowel. Since time trends may reflect changes in exposure to risk factors, we studied incidence patterns related to subsite, gender and age in the southeastern area of The Netherlands from 1975 to 1989, a period in which flexible endoscopy and sphincter-saving surgery for rectal cancer became more common.

Correspondence to J.W.W. Coebergh.
Revised 26 Jul. 1995; accepted 10 Aug. 1995.

Incidence data were derived from the population-based cancer registry in Eindhoven, The Netherlands. The registry covers the southeastern area of the province of North Brabant and the northern area of the province of Limburg with a population of approximately 850,000. It has been considered complete in a core area since the early 1970s. Newly diagnosed cancer patients are notified to the registry by three pathology laboratories: the Radiotherapy Department in Eindhoven, hospital discharge diagnoses from most of the 10 community hospitals in the area and reports from the surgical departments. Professional registrars collect data from clinical records within 6 months from diagnosis.

We included all newly diagnosed patients with colorectal cancer (International Classification of Disease-9) diagnosed between 1 January 1975 and 1 January 1990. Age-standardised incidence rates (per 100 000 person-years, European standard) were calculated after combining subsites (ascending 153.5, 153.4, 153.6; transverse 153.0/2, 153.7; sigmoid 153.3; rectosigmoid 154.0; rectum 154.1; other 153–154), and presented as 5 year moving averages. Linear regression analysis was performed on the annual rates. The beta coefficients were tested for significance with the T-test and are reported with 95% confidence limits (CL).

In the period 1975–1989, 2554 invasive tumours were registered in men and 2413 in women, and the number of non-invasive tumours increased from 18 in the 1975–1982 period to 31 in the 1982–1989 period. The number of carcinomas detected in polyps also increased from 9 (0.4%) to 50 (1.9%) in those periods. Eighty per cent of non-invasive lesions and carcinomatous polyps were located distal to the splenic flexure. The incidence of tumours in the distal parts of the large bowel was markedly higher in men and the male/female ratio increased from 1 for caecal cancer to 1.7 for rectal cancer. The transverse colon only comprised 15% of tumours.

For men, trend analyses revealed a marked increase in the incidence of tumours of sigmoid (beta = 0.43, CL (0.14, 0.72)) and ascending colon (beta = 0.34, CL (0.05; 0.62)) (Figure 1). A decrease in the incidence of rectal cancer (beta = −0.16, CL (−0.46; 0.15)) coincided with an increase in the incidence of rectosigmoid cancer (beta = 0.17, CL (−0.07, 0.41)), which started after 1982. For women, a similar decrease of rectal cancer (beta = −0.21, CL (−0.43, 0.02)) was accompanied by a significant increase of rectosigmoid tumours (beta = 0.22, CL (0.07, 0.36), data not shown).

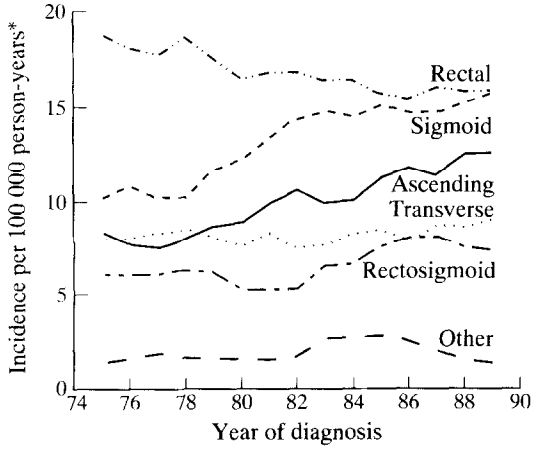

Figure 1. Trends in incidence of colorectal cancer by subsite, men 1975–1989. *Age-standardised (European standard), 5 year moving averages.

Changing trends were primarily observed in the older age groups. For men between 60 and 74 years, the incidence of cancer of the sigmoid and ascending colon increased by more than 1.5-fold and for men older than 74 years by 2.34-fold and by 1.89, respectively. This trend was not seen for the transverse colon nor for the combination of rectum and rectosigmoid. For women older than 74 years, there was a substantial increase in cancer of the transverse and descending colon; for women between 60 and 74 years, there was a moderate increase in cancer of the ascending colon. The male–female ratio increased for distal tumours in patients of 60 years and older.

In conclusion, the incidence of colorectal cancer increased steadily in elderly men but remained stable among women. Converse trends for rectal and rectosigmoid cancer were seen, probably caused by changing classification practice. The wider application of sphincter-saving surgery for distal tumours may have led to a shift from rectum to rectosigmoid. The uneven anatomical distribution of colorectal cancers and the subsite-specific trends suggest that tumour formation is primarily determined by exposure to faecal contents, and thus dependent on factors influencing transit time or composition and consistency of faeces, such as physical activity and diet. In the 1950s and 1960s, consumption of meat and vegetables increased in The Netherlands, whereas the use of milk products decreased [6]. The rising trends in elderly men, and the long latency period between cigarette smoking and the occurrence of colorectal cancer [7], would also be consistent with the increasing use of tobacco by up to 95% of adult males in the Eindhoven area since 1940 [8].

1. Jensen OM, Esteve J, Moller H, Renard H. Cancer in the European Community and its member states. *Eur J Cancer* 1990, **26**, 1167–1256.
2. Trock B, Lanza E, Greenwald P. Dietary fiber, vegetables, and colon cancer: critical review and meta-analyses of the epidemiologic evidence. *J Natl Cancer Inst* 1990, **82**, 650–661.
3. Jensen OM. Different age and sex relationship for cancer of subsites of the large bowel. *Br J Cancer* 1984, **50**, 825–829.
4. Kee F, Wilson RH, Gilliland R, Sloan JM, Rowlands BJ, Moorehead RJ. Changing site distribution of colorectal cancer. *Br Med J* 1992, **305**, 158.
5. Pillon D, Boutron MC, Arveux P, *et al.* Evolution de l'incidence du cancer colo-rectal dans le departement de la Cote-d'Or entre 1976 et 1985. *Gastroenterol Clin Biol* 1989, **13**, 860–864.
6. Cleton FJ, Coebergh JWW, eds. *Cancer in the Netherlands, Volume 1, Scenario Report.* Dordrecht, Kluwer Academic Publishers, 1988, 220.
7. Giovannucci E, Rimm EB, Stampfer MJ, *et al.* A prospective study of cigarette smoking and risk of colorectal adenoma and colorectal cancer in U.S. men. *J Natl Cancer Inst* 1994, **86**, 183–191.
8. Heijnen MLG, Nab HW, Reek J van, Heijden LH van der, Schipper R, Coebergh JWW. Striking changes in smoking behaviour and lung cancer incidence according to histomorphology in SE Netherlands. *Eur J Cancer* 1995, **31A**, 949–952.