

ABC of colorectal cancer

Epidemiology

Peter Boyle, J S Langman

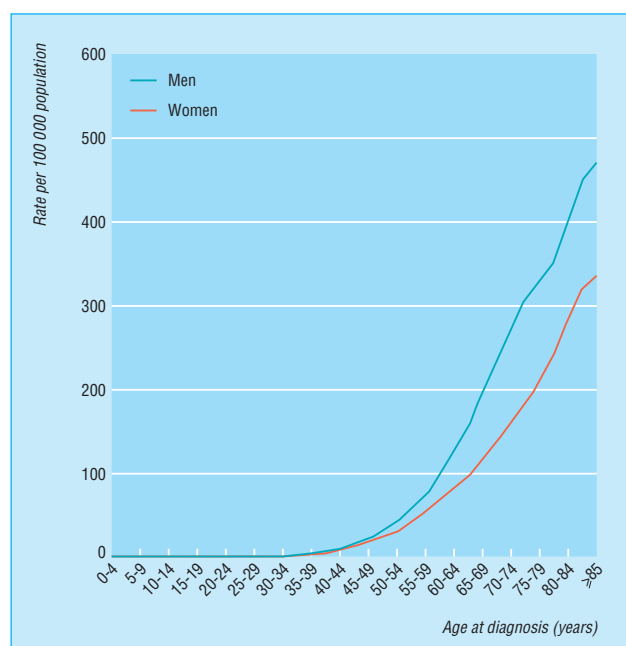
In countries with a westernised lifestyle about half of all deaths are caused by circulatory disease and a quarter by cancer. Cancer is an important problem in both public health and political terms worldwide, irrespective of a country's development. The most recent estimates of the global cancer burden suggest that there were 8.1 million new cases, excluding non-melanoma skin cancer, worldwide in 1990. About 10 million new cases are now diagnosed each year.

Colorectal cancer is the fourth commonest form of cancer occurring worldwide, with an estimated 783 000 new cases diagnosed in 1990, the most recent year for which international estimates are available. It affects men and women almost equally, with about 401 000 new cases in men annually and 381 000 in women. The number of new cases of colorectal cancer worldwide has been increasing rapidly since 1975 (when it was 500 000).

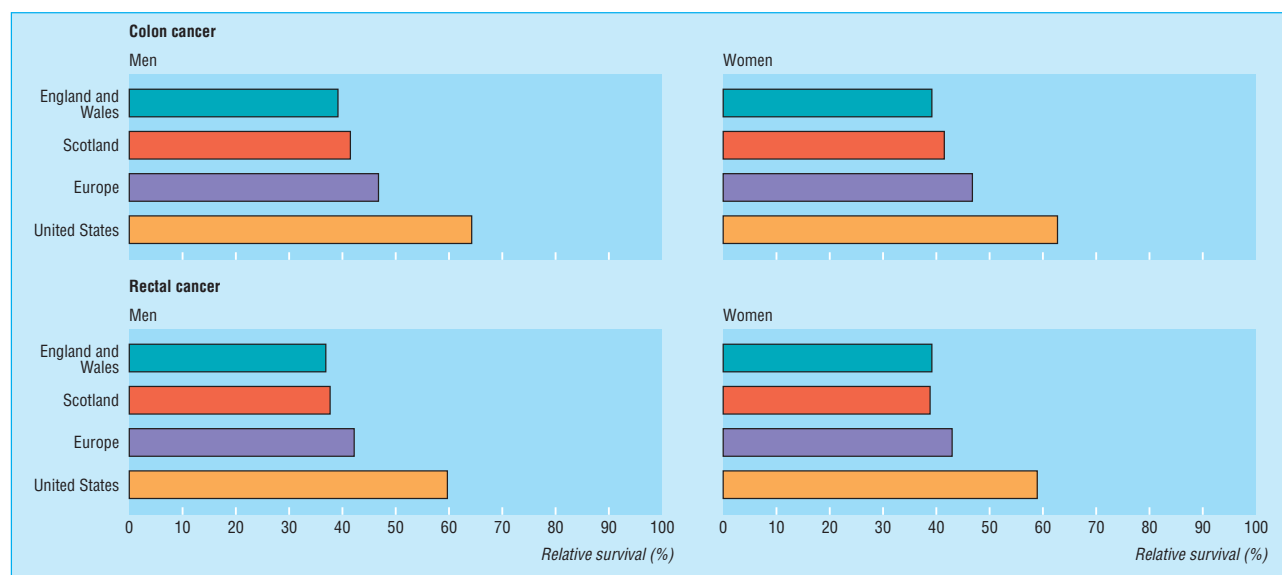
Worldwide, colorectal cancer represents 9.4% of all incident cancer in men and 10.1% in women. Colorectal cancer, however, is not equally common throughout the world. If the westernised countries (North America; those in northern, southern, and western Europe; Australasia; and New Zealand) are combined, colorectal cancer represents 12.6% of all incident cancer in westernised countries in men and 14.1% in women. Elsewhere colorectal cancer represents 7.7% and 7.9% of all incident cases in men and women respectively.

Large differences exist in survival, according to the stage of disease. It is estimated that 394 000 deaths from colorectal cancer still occur worldwide annually, and colorectal cancer is the second commonest cause of death from any cancer in men in the European Union. Substantial differences in cancer survival seem to exist between Great Britain, Europe as a whole, and the United States. This variation in survival is not easily explained but could be related to stage of disease at presentation or treatment delivery, or both of these.

The numbers of new cases of colorectal cancer worldwide has increased rapidly since 1975



Estimated incidence of colorectal cancer in United Kingdom, by age and sex, 1995



International comparison of five year relative survival for colon and rectal cancer in adults aged 15-99 at diagnosis (based on Coleman et al, *Cancer survival trends in England and Wales, 1971-1975*; Berrino et al, *Survival of cancer patients in Europe: the EURO-CARE-2 study*; and Surveillance Epidemiology and End Results (SEER) programme, National Cancer Institute, 1998)

Survival and deprivation

The relation between poverty and ill health has been researched for more than 100 years. In Scotland, since the 1851 census, all cause occupational mortality has been routinely reported, and since 1911, inequalities in health, as shown by mortality, have been examined in decennial reports classified by social class (based on occupation) and by occupational group alone.

No single, generally agreed definition of deprivation exists. Deprivation is a concept that overlaps but is not synonymous with poverty. Absolute poverty can be defined as the absence of the minimum resources for physical survival, whereas relative poverty relates to the standards of living in a particular society. Deprivation includes material, social, and multiple deprivation. In Scotland the Carstairs and Morris index of deprivation was derived from 1981 census data with the postcode sector as the basic geographical unit (covering a population of about 5000). This index describes a deprivation category on a scale of 1 (least deprived) to 7 (most deprived) for each household address in Scotland.

The incidence of colorectal cancer is higher in men than women among each of the seven deprivation categories in Scotland, although incidence varies little with deprivation category. Survival, however, clearly improves with decreasing deprivation. At each milestone, there is a notable gradient in survival, with the most affluent doing best and the least affluent doing worst. The reasons that such variations exist are unclear and highlight an important priority for research.

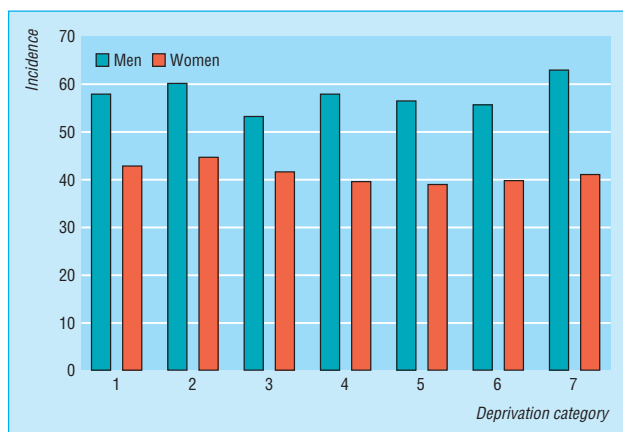
Descriptive epidemiology

Different populations worldwide experience different levels of colorectal cancer, and these levels change with time. Populations living in one community whose lifestyles differ from those of others in the same community also experience different levels of colorectal cancer. Groups of migrants quickly lose the risk associated with their original home community and acquire the patterns of the new community, often starting within one generation of arrival.

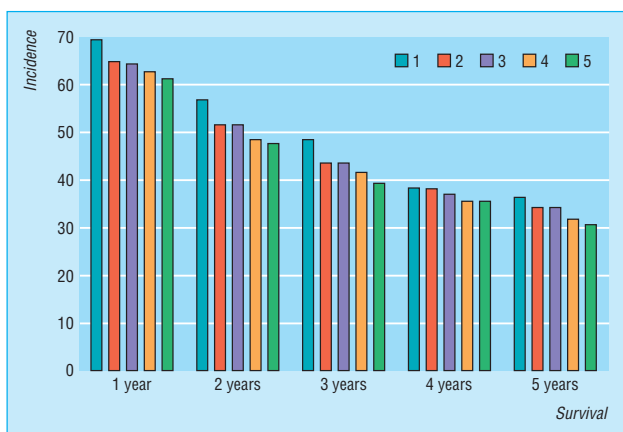
Ethnic and racial differences in colorectal cancer, as well as studies on migrants, suggest that environmental factors play a major part in the aetiology of the disease. In Israel male Jews born in Europe or the United States are at higher risk of colon cancer than those born in Africa or Asia. Risk in the offspring of Japanese populations who have migrated to the United States has changed—incidence now approaches or surpasses that in white people in the same population and is three or four times higher than among the Japanese in Japan.

For reasons such as these, colorectal cancer is widely believed to be an environmental disease, with “environmental” defined broadly to include a wide range of ill defined cultural, social, and lifestyle practices. As much as 70-80% of colorectal cancers may owe their appearance to such factors; this clearly identifies colorectal cancer as one of the major neoplasms in which causes may be rapidly identified, and a large portion of the disease is theoretically avoidable.

The move from theoretically avoidable causes to implementation of preventive strategies depends on the identification of risk factors, exposures that have been associated with an increased (or decreased) risk of colorectal cancer, and the smaller subset of risk determinants, whose alteration would lead directly to a reduction in risk. From analytical epidemiology some clear ideas have now emerged about measures for reducing the risk of colorectal cancer.



Incidence according to deprivation category in Scotland, 1998 (1=least deprived, 7=most deprived)



Survival according to deprivation category in Scotland, 1998 (1=least deprived, 5=most deprived)

Highest incidence of colorectal cancer in men worldwide around 1990

Registry	Age standardised incidence per 100 000
US (Hawaii: Japanese), 1988-92	53.48
New Zealand (non-Maori), 1988-92	51.30
Japan (Hiroshima), 1986-90	50.99
France (Haut-Rhin), 1988-92	49.90
Italy (Trieste), 1989-92	49.37
France (Bas-Rhin), 1988-92	49.24
Canada (Yukon), 1983-92	48.98
US (Detroit: black), 1988-92	48.32
Czech Republic, 1988-92	48.23
US (Los Angeles: black), 1988-92	47.89
Canada (Nova Scotia), 1988-92	47.84
Canada (Newfoundland), 1988-92	47.29
Australia (New South Wales), 1988-92	46.92
US (San Francisco: black), 1988-92	46.82
Israel (Jews born in America or Europe), 1988-92	46.79

Data taken from Parkin et al, eds (*Cancer incidence in five continents*. Vol 7. IARC Scientific Publications, 1997:120)

Dietary and nutritional practices

Evidence from epidemiological studies seems to show consistently that intake of dietary fat and meat is positively related to risk of colorectal cancer. This evidence is obtained from ecological studies, animal experiments, and case-control and cohort studies.

In 1990 Willett et al published the results from the US nurses health study involving follow up of 88 751 women aged 34-59 years who were without cancer or inflammatory bowel disease at recruitment. After adjustment for total energy intake, consumption of animal fat was found to be associated with increased risk of colon cancer. The trend in risk was highly significant ($P = 0.01$), with the relative risk in the highest compared with the lowest quintile being 1.89 (95% confidence interval 1.13 to 3.15). No association was found with vegetable fat. The relative risk in women who ate beef, pork, or lamb as a main dish every day was 2.49 (1.24 to 5.03) compared with women reporting consumption less than once a month. The authors suggested that their data supported the hypothesis that a high intake of animal fat increases the risk of colon cancer, and they supported existing recommendations to substitute fish and chicken for meats high in fat.

Intake of vegetables, fruit, and fibre

Dietary fibre has been proposed as accounting for the differences in the rates of colorectal cancer between Africa and westernised countries—on the basis that increased intake of dietary fibre may increase faecal bulk and reduce transit time. Various other factors, related to risk of colorectal cancer, are now thought to contribute to explaining these differences.

Fibre has many components, each of which has specific physiological functions. The components are most commonly grouped into insoluble, non-degradable constituents (mainly found in cereal fibre) and soluble, degradable constituents, such as pectin and plant gums (mainly found in fruits and vegetables). Epidemiological studies have reported differences in the effect of these components. Many studies, however, found no protective effect of fibre in cereals but have consistently found a protective effect of fibre in vegetables and perhaps fruits. This might reflect an association with other components of fruits and vegetables, with fibre intake acting merely as an indicator of consumption.

Physical activity, body mass index, and energy intake

Evidence from epidemiological studies is strong that men with high occupational or recreational physical activity seem to have a decreased risk of colon cancer. Such evidence comes from follow up studies of cohorts who are physically active or who have physically demanding jobs, as well as from case-control studies that have assessed physical activity by, for example, measurement of resting heart rate or questionnaire. The association remains even after potential confounding factors, such as diet and body mass index, are controlled for.

The available data, however, show no consistent association between obesity and risk of colorectal cancer (analysis and interpretation of this factor is difficult in retrospective studies, where weight loss may be a sign of the disease), although evidence now suggests an association between obesity and adenomas. This increased risk associated with energy intake does not seem to be the result merely of overeating; it may reflect differences in metabolic efficiency. If the possibility that the association with energy intake is a methodological artefact is excluded (as such a consistent finding is unlikely to emerge from such a variety of study designs in diverse population groups), it would imply that individuals who use energy more efficiently may be at a lower risk of colorectal cancer.



Intake of dietary fat and meat may increase risk of colorectal cancer



Fruits are a good source of fibre and may protect against cancer

Physical activity and colorectal cancer

- Giovannucci et al examined the role of physical activity, body mass index, and the pattern of adipose distribution in the risk of colorectal adenomas
- In the nurses health study, 13 057 female nurses, aged 40-65 years in 1986, had an endoscopy during 1986-92. During this period, adenoma of the distal colorectum was newly diagnosed in 439 nurses
- After age, prior endoscopy, parental history of colorectal cancer, smoking, aspirin use, and dietary intake were controlled for, physical activity was associated inversely with the risk of large adenomas (≥ 1 cm) in the distal colon (relative risk 0.57 (95% confidence interval 0.30 to 1.08)) when high and low quintiles of average weekly energy expenditure from leisure activities were compared
- Much of this benefit came from activities of moderate intensity, such as brisk walking

Hormone replacement therapy

Increasing evidence supports an (originally unexpected) association between hormone replacement therapy and a reduced risk of colorectal cancer.

Of 19 published studies of hormonal replacement therapy and risk of colorectal cancer, 10 support an inverse association and a further five show a significant reduction in risk. The risk seems lowest among long term users. Although some contradictions still exist in the available literature, hormone replacement therapy seems likely to reduce the risk of colorectal cancer in women. The risk seems to halve with 5-10 years' use. The role of unopposed versus combination hormone replacement therapy needs further research.

Whether this association is causal or is associated with some selection factor that directs women to using hormone replacement therapy is, however, not known. This question is important; if the link is indeed causal, women who are at high risk of colorectal cancer could be offered the therapy to lower their risk.

Control of colorectal cancer

Prospects for preventing death from colorectal cancer are now more promising than even 10 years ago. To achieve this goal public health decisions have to be taken, and part of this decision process involves deciding at which point enough epidemiological evidence is available to change focus comfortably from information generation to health actions.

To turn research findings into public health strategies for controlling the incidence of and mortality from colorectal cancer requires a profound change of mentality in the epidemiological community. It is easy to say that more studies are needed, but they would be unlikely to alter existing conclusions. Moreover, the implementation of strategies to control cancer must be considered separately from research into the control of cancer.

One consequence of epidemiological research into the contribution of lifestyle factors to cancer risk has been to blame the individual who develops cancer. Smoking, alcohol, dietary imprudence, and exposure to sunlight tend to assign responsibility to the individual. The individual is often not principally responsible for decisions about factors that influence his or her risk of cancer, and society—including government and industry—could do more to discourage lifestyles associated with cancer risk. Government legislation, including taxation policy and other actions, could have profound effects on smoking habits, for example.

The goal of all cancer research and treatment is to prevent people dying from the disease. Knowledge has been accruing rapidly about actions and interventions that could lead to a reduction in death from colorectal cancer by reducing the risk of developing the disease, identifying the disease at a stage when it is more curable, or improving the outcome of treatment.

The two graphs showing incidence of colorectal cancer in the United Kingdom and an international comparison of five year relative survival for colon and rectal cancer are adapted with permission from the Cancer Research Campaign (*CRC CancerStats: Large Bowel—UK*; factsheet, November 1999). The graphs of incidence and survival according to deprivation category are adapted from McLaren G et al (*Deprivation and health in Scotland*. ISD Scotland Publications, 1998). The photograph of meat is published with permission from Tim Hall/CEPHAS.

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How individuals can reduce their risk of colorectal cancer

- Increase intake of vegetables and fruits (eat five servings of fruits and vegetables each day); replace snacks such as chocolate, biscuits, and crisps with an apple, orange, or other fruit or vegetable
- Reduce intake of calories (animal fats in particular); often replace beef, lamb, and pork with fish and poultry
- Increase physical activity—by activities of moderate intensity, such as brisk walking
- Participate in population screening programmes; when these are not in place, strongly consider having a colonoscopy with polyp removal once between ages 50 and 59
- Consult a doctor as soon as possible if a noticeable and unexplained change in bowel habits occurs, blood is present in the stool, colicky pain occurs in the abdomen, or a sensation of incomplete evacuation after defecation recurs

Further reading

- Boyle P. Progress in preventing death from colorectal cancer [editorial]. *Br J Cancer* 1995;72:528-30.
- Berrino F, Capocaccia R, Estève J, Gatta G, Hakulinen T, Micheli A, et al, eds. *Survival of cancer patients in Europe: the EURO-CARE-2 study*. Lyons: International Agency for Research on Cancer, 1999. (Scientific publication No 151.)
- Coleman MP, Babb P, Damiecki P, Grosclaude P, Honjo S, Jones J, et al. Cancer survival trends in England and Wales, 1971-1995: deprivation and NHS region. London: Stationery Office, 1999.
- Giovannucci E, Colditz GA, Stampfer MJ, Willett WC. Physical activity, obesity and risk of colorectal cancer in women (United States). *Cancer Causes Control* 1996;7:253-63.
- McLaren G, Bain M. *Deprivation and health in Scotland: insights from NHS data*. Edinburgh: ISD Scotland, 1998.
- MacLennan SC, MacLennan AH, Ryan P. Colorectal cancer and oestrogen replacement therapy: a meta-analysis of epidemiological studies. *Med J Aust* 1991;162:491-3.
- Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of 25 major cancers in 1990. *Int J Cancer* 1999;80:827-41.
- Shephard RJ. Exercise in the prevention and treatment of cancer—an update. *Sports Med* 1993;15:258-80.
- Willett WC. The search for the causes of breast and colon cancer. *Nature* 1989;338:389-94.
- Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Speizer FE. Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. *N Engl J Med* 1990;323:1664-72.

Peter Boyle is director of the division of epidemiology and biostatistics at the European Institute, Milan, and honorary professor of cancer epidemiology at the University of Birmingham; Michael J S Langman is professor of medicine at the University of Birmingham.

The ABC of colorectal cancer is edited by D J Kerr, professor at the Institute for Cancer Studies, University of Birmingham; Annie Young, research fellow at the School of Health Sciences, University of Birmingham; and F D Richard Hobbs, professor in the department of primary care and general practice, University of Birmingham. The series will be published as a book by the end of 2000.