Epidemiology of Colorectal Cancer: Incidence, Survival, and Risk Factors

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Florence Canouï-Poitrine, Claudia Martinez-Tapia, Lydia Guittet, and Anne-Marie Bouvier

2.1 Introduction

Colorectal cancer is still a major challenge in oncology. Population-based studies, which accurately record all cases diagnosed in a well-defined population and thus provide unbiased measurements, are the best way to assess changes in colorectal cancer frequency or survival. Worldwide incidence data are available from cancer registries, in particular through the successive volumes of Cancer Incidence in Five Continents covering registration up to 2012 [1–3]. For meaningful survival

F. Canouï-Poitrine (✉)
Public Health Department, University Henri-Mondor Hospital, Créteil, France

Paris Est Creteil University (UPEC), A-TVB DHU, CEpiA (Clinical Epidemiology And Ageing) Unit EA4393, Créteil, France
e-mail: florence.canoui-poitrine@aphp.fr

C. Martinez-Tapia
Paris Est Creteil University (UPEC), A-TVB DHU, CEpiA (Clinical Epidemiology And Ageing) Unit EA4393, Créteil, France
e-mail: claudia.tapia@aphp.fr

L. Guittet
U1086 INSERM-UCBN, ANTICIPE, Caen, France

University Hospital of Caen, Caen, France
e-mail: guittet-l@chu-caen.fr

A.-M. Bouvier
Digestive Cancer Registry of Burgundy, Dijon, France

EPICAD INSERM LNC-UMR 1231, Dijon, France

University Bourgogne Franche-Comté, Dijon, France

Dijon University Hospital, Dijon, France
e-mail: anne-marie.bouvier@u-bourgogne.fr

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comparisons between countries or time periods, net survival is used. Net survival from cancer is the survival that would be observed if cancer were the only cause of death. This major epidemiological indicator allows thus comparisons without interference from other causes of death. Reliable survival rates are regularly published through international (CONCORD) [4–6] and European (EUROCARE) [7, 8] programs and using the French population-based cancer registries network (FRANCIM) [9–11] data. The aim of the present study was to provide updated temporal trends in colorectal cancer incidence and prognosis over the past decades.

2.2 Incidence

Last available worldwide data showed that colorectal cancer was the third most common cancer in men (746,000 cases, 10.0% of the total) and the second in women (614,000 cases, 9.2% of the total) in 2012 [12]. Differences in the incidence of colorectal cancers over the world are striking, with a tenfold variation between highest and lowest area, and geographical patterns are very similar in men and women (Fig. 2.1). Historically, the highest incidence rates have been reported in more developed countries. North America; Australia; New Zealand; Western Europe, including France; and Japan were considered high-risk incidence countries. Colorectal cancer was scarce in South America, China, or Africa. Other countries, mainly Northern, Southern, and Eastern Europe, were considered as middle-risk area. Starting from the mid-1990s, incidence rates declined for both sexes (Fig. 2.2) in the high-risk countries whereas slightly increased in most middle-risk ones (Denmark, Italy, Spain, or the Netherlands) and remained relatively stable in

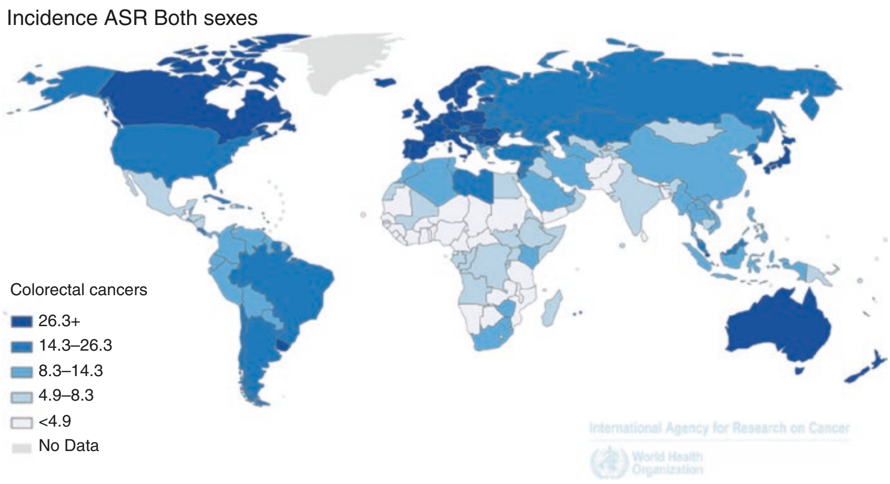

Fig. 2.1 Worldwide colorectal cancer incidence—*GLOBOCAN 2012, International Agency for Research on Cancer IARC*

Switzerland and the UK. In contrast, increasing trends have been seen in developing countries. In the last worldwide published monography covering the 2008–2012 time period, European countries exhibited similar incidence rates as the USA and North America, whereas Eastern Europe and Japan had the highest rates. In France, incidence slightly decreased from the early 2000s with a mean annual decreased of −0.3% in men and in women between 2005 and 2012. The cumulative risk decreased from 2.0% for men born around 1920 to 0.9% for those born around 1950, a more than twofold increase. The corresponding values in women were 0.1% and 0.2%.

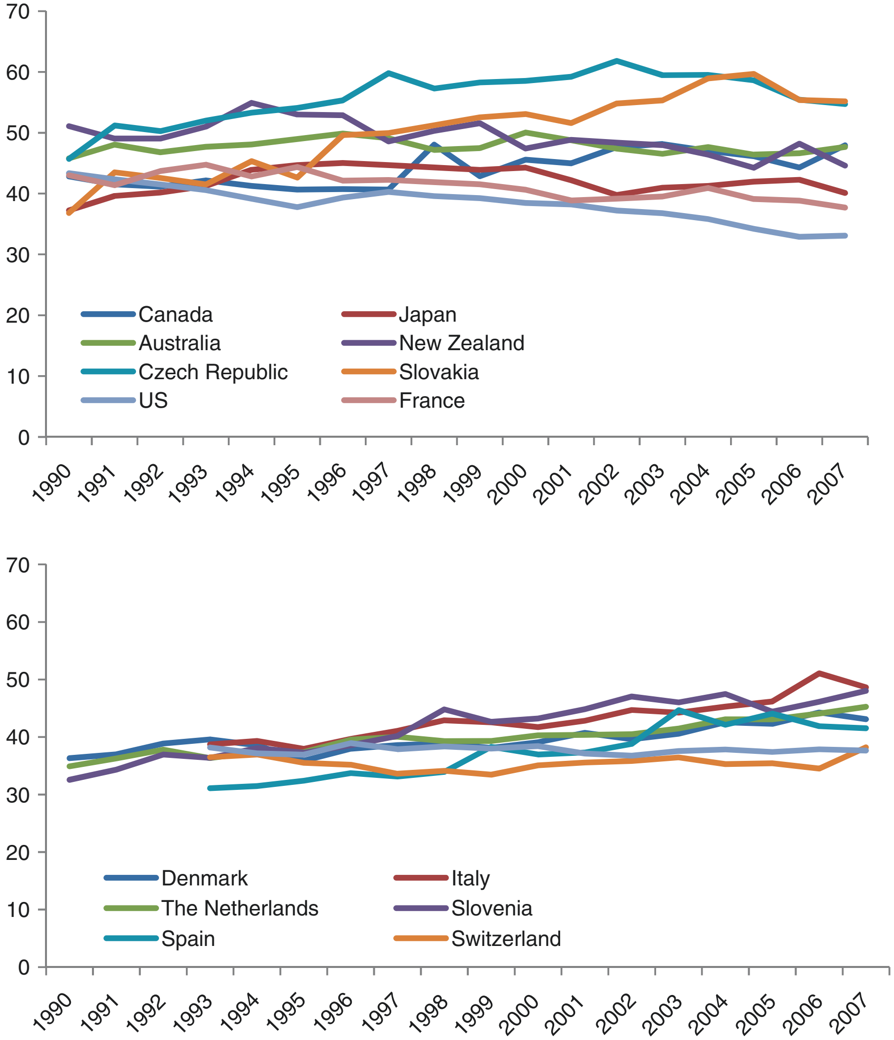

Fig. 2.2 Time trends in incidence of colorectal cancer *(International Agency for Research on Cancer (IARC). Cancer Incidence in Five Continents monographies)*

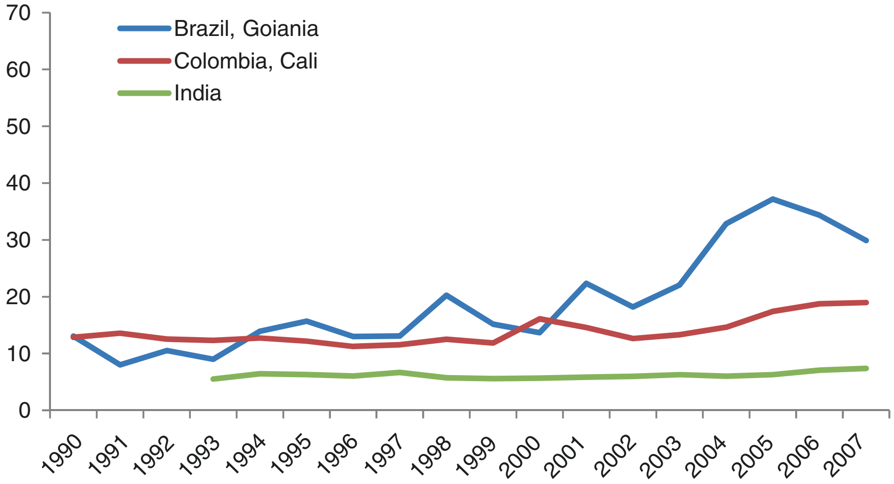

Fig. 2.2 (continued)

Estimated world standardized incidence rates in 2015 are 37.0 per 100,000 inhabitants in men 23.6 per 100,000 in women. Through the GLOBOCAN database, the effects of demographic changes on the expected number of new cancer cases in different regions can be estimated (Fig. 2.3). Overall, nearly 1,700,000 new cases are predicted worldwide in 2020.

In contrast to this overall decreasing trend, the incidence of colorectal cancer has appeared to be increasing in male and female young adults under age 50 years in the USA, Canada, Australia, and New Zealand [13–16]. This trend is not described in European data. Reasons for explaining this trend are unclear or speculative. The measure of the role of established risk factors such as smoking, sedentary lifestyle, and diet in this population required dedicated epidemiologic research.

2.3 Survival

Results from the 65 countries involved in the CONCORD program comparing data from population-based registries show wide variations in survival from colorectal cancer (Fig. 2.4). For patients diagnosed with colon or rectal cancer during 2010–2014, 5-year net survival was higher than 60% in Australia, Canada, the USA, Japan, and New Zealand. In Europe, survival was as high in Northern (Denmark, Finland, Iceland, Ireland, Norway, Sweden, the UK), Southern (Italy, Portugal, Slovenia, Spain), and Western countries (Belgium, France, Germany, the Netherlands, Switzerland). For colon cancer, survival ranged from 50% to 60% in Central and South America, in China, and in Eastern Europe such as Estonia, Lithuania, the Czech Republic, Poland, and Slovakia. Survival was less than 50% in Colombia and India. For rectal cancer, survival ranged from 50% to 60% in Central

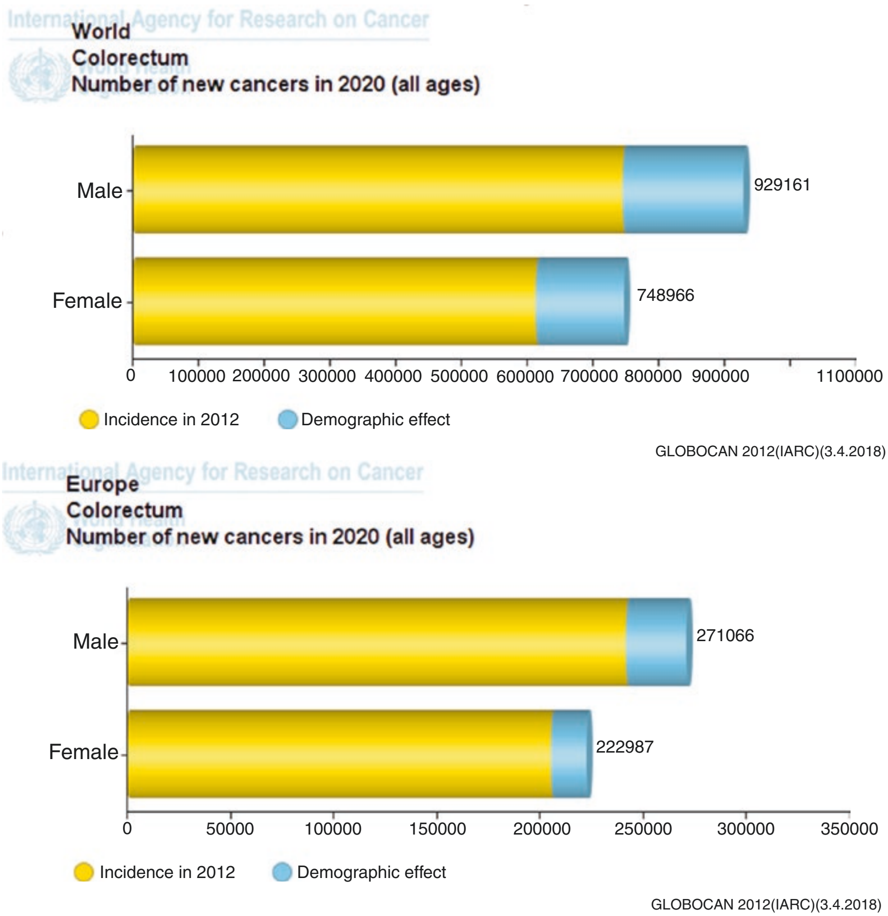

Fig. 2.3 Expected changes in incidence of colorectal cancer between 2012 and 2020, due to demographic changes in Europe and in the World. *GLOBOCAN 2012, International Agency for Research on Cancer IARC. Numbers are computed using age-specific rates and corresponding populations for ten age-groups*

and South America, in China, in Estonia, and in the Czech Republic and was less than 50% in Slovakia, Poland, Croatia, and India.

Through the CONCORD program, a high-resolution study was set up among colorectal cancer cases diagnosed during 1996–1998, in order to explain the difference in 5-year net survival observed between the USA and Europe [4]. Age-standardized survival was quite similar in the USA and Northern and Western Europe (around 54–58%) while lowest in Southern Europe (49%) and in Eastern Europe (42%). The transatlantic difference in survival was attributed to an earlier stage at diagnosis, a higher frequency of surgery, and use of adjuvant treatments in the USA.

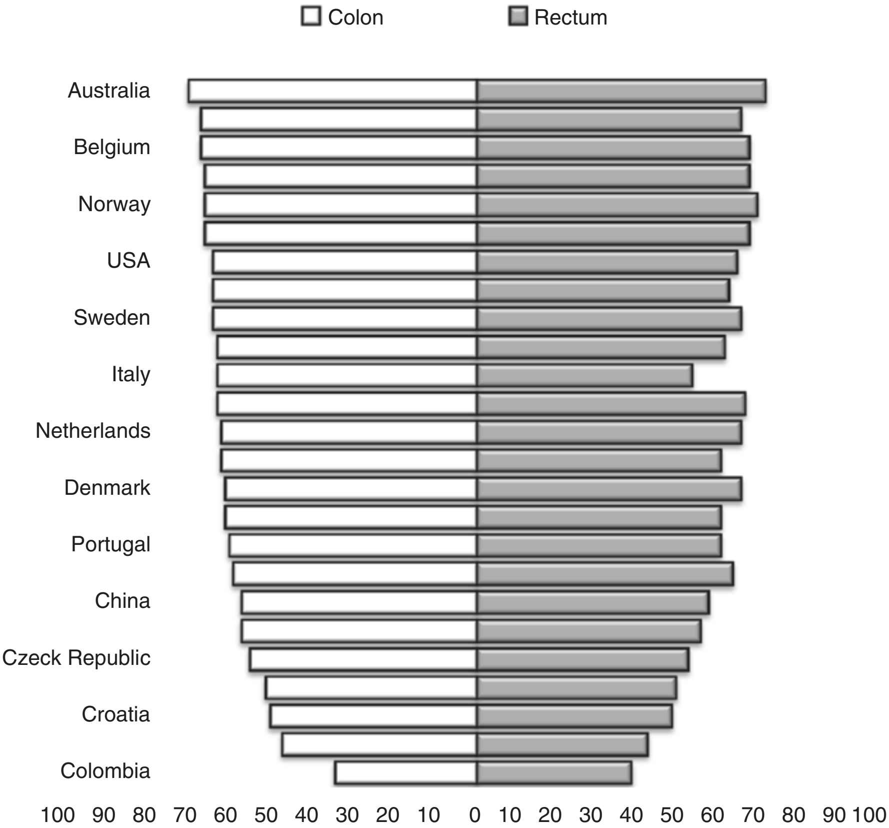

Fig. 2.4 Five-year net survival of colorectal cancer. *Cancer survival 2000–2014, CONCORD-3 program*

Taking into account bowel location, European mean age-standardized 5-year relative survival was 57% after colon cancer and 56% after rectal cancer [8]. There were negligible differences between the sexes for colon cancer, but survival was higher for women than for men for rectal cancer. In all European regions, survival was best for patients aged 15–44 years, roughly constant for those aged 45–64 years, and decreased thereafter for colon cancer, whereas there were smooth age differences up to 74 years with a substantial drop thereafter in rectal cancer.

According to time period, survival varied little between 1995 and 1999 and 2000–2014 [6]. For colon cancer, it mostly flatted, with an increase less than 10% in Canada, Australia, Japan, Estonia, Finland, Lithuania, Sweden, Italy, France, and the Netherlands. It was more than 10% in China, Denmark, Norway, the UK, Portugal, Slovenia, Spain, the Czech Republic, Poland, and Switzerland. For rectal cancer, time trend did not vary in Japan, France, Italy, and New Zealand, whereas it was more marked, with a 10–20% increase in Australia, Canada, Denmark, Estonia, the UK, Portugal, Spain, the Czech Republic, Poland, the Netherlands, and Switzerland. Increase in 5-year relative survival was about 20% or more in China and Slovenia.

2.4 Risk Factors for Colorectal Cancer

Three risk's levels are identified for colorectal cancer according to personal or familial past history:

– *Individuals with middle risk*: men and women aged 50 and more. More than 90% of colorectal cancer cases are diagnosed after this age [17]. The median age at diagnosis for colon cancer, 69 in men and 73 in women, is older than that of rectal cancer, which is 63 in men and 65 in women [18].
– *Individuals with high risk*:
  1. First-degree relatives of patients with common colorectal cancer or with a large adenoma (>1 cm) have an increased risk of colorectal cancer when occurred before 60 years, or two first-degree relatives of patients with common colorectal cancer or with a large adenoma (>1 cm) have an increased risk of colorectal cancer irrespective of age.
  2. Personal past history of colorectal cancer or large adenoma.
  3. Personal history of chronic gastrointestinal inflammatory bowel disease (ulcerative colitis and Crohn's disease).
– *Individuals with very high risk*: familial adenomatosis polyposis and hereditary nonpolyposis colorectal cancer (Lynch syndrome).

2.4.1 Environmental Risk Factors

Based on solid evidence from the published literature, these factors include excessive alcohol intake, smoking, and excess body weight. A sedentary behavior has been also associated with an increased risk of colorectal cancer [19, 20]. Conversely, high levels of physical activity are associated with a lower risk of colon cancer with a reported risk reduction of approximately 25% [21]. Such a relationship has not been established for rectal cancer [21]. Other modifiable risk factors that have been convincingly associated with higher colorectal cancer risk are the consumption of red and processed meat [22]. The findings for some risk factors suggest sex differences and/or sub-site variations. Additionally, some studies show a dose-response association. Table 2.1 summarizes the results of each environmental risk factor mentioned above from recent and large meta-analyses.

Table 2.1 Environmental and lifestyle risk factors for colorectal cancer

Risk factor	Meta-analyses	No. of studies	Study population	Measure	Relative risk (RR) or hazard ratio (HR) [95% CI]
Overweight/ obesity	Xue et al. [23]	CRC: 12 CC: 17 RC: 13	Systematic review of prospective cohort studies from databases inception to April 2015 (the USA, Asia, Europe, and Australia) CRC, 3,574,422 participants; follow-up, 5.5–49 years, 15,958 cases CC, 5,731,240 participants; follow-up, 5.5–23 years, 14,637 cases RC, 5,500,069 participants; follow-up, 5.5–23 years, 8000 cases	Body mass index (BMI): obesity (BMI ≥ 30) vs. normal (18 < BMI < 25)	RRs or CRC: – Among males: 1.38 [1.32–1.44] – Among females: 1.17 [1.06–1.30] RRs for CC: – Among males: 1.48 [1.40–1.57] – Among females: 1.12 [1.01–1.25] RRs for RC: – Among males: 1.25 [1.17–1.35] – Among females: 1.05 [0.99–1.12]
Tobacco (smoking)	Cheng J et al. [24]	24	Systematic review of prospective studies from databases MEDLINE (from 1966) and EMBASE (from 1974) through April 2013 14,186 colon cases; 6814 rectal cases (the USA, Europe, Canada, and Asia)	Smoking status Daily cigarette consumption Pack-years (p-y) Duration (years)	Summary RRs for current vs. never smokers: – CC: 1.09 [1.01–1.18] – RC: 1.24 [1.16–1.39] Summary RRs for former vs. never smokers: – CC: 1.16 [1.11–1.28] – RC: 1.20 [1.11–1.30] RR for an increase of 10 cigarettes/day – CC: 1.05 [1.02–1.09] – RC: 1.11 [1.02–1.21] RR for every additional 10 p-y: – CC: 1.08 [1.04–1.11] – RC: 1.10 [1.01–1.20] RR for an increase of 10 years: – CC: 1.02 [1.00–1.04] – RC: 1.06 [1.03–1.10]

Alcohol intake	Bagnardi V et al. [25]	66	Systematic review using MEDLINE, ISI Web of Science and EMBASE databases before September 2012 41,715 CRC cases (North America, Europe, Asia, other areas)	Grams (g) per day (1 drink = 12.5 g)	Pooled RRs compared with nondrinkers: – Light drinkers (12.5 g/d): 0.99 [0.95–1.04] – Moderate drinkers (12.6–50 g/d): 1.17 [1.11–1.24] – Heavy drinkers (>50 g/d): 1.44 [1.25–1.65]
Sedentary behavior	Ma P et al. [20]	28	Systematic review from PubMed and EMBASE databases through February 2017 4,784,339 participants with 46,071 CRC cases (North America, Europe, Asia, and Australia)	Prolonged television viewing time per day (12 studies) Prolonged total sitting time per day (6 studies)	Pooled RR compared with the lowest time: – CC: 1.23 [1.08–1.39] – RC: 1.15 [1.07–1.23] Summary RR for an increase of 2 h per day: 1.07 [1.05–1.10] Pooled RR compared with the lowest time: – CC: 1.03 [1.01–1.06] – RC: 1.42 [1.04–1.79] Summary RR for an increase of 2 h per day: 1.04 [1.01–1.06]
	Cong YJ et al. [19]	23	Systematic review from PubMed, EMBASE, and Google Scholar databases through May 2013 4,324,756 participants with 27,231 CC cases and 13,813 RC cases (North America, Europe, Australia, Asia)	Sedentary behavior (sedentary work, total sitting time, TV viewing time)	Pooled RRs for sedentary vs. non-sedentary behavior: – CC: 1.30 [1.22–1.39] – RC: 1.05 [0.98–1.13]

(continued)

Table 2.1 (continued)

Processed meat	Zhao Z et al. [26]	34	Systematic review using PubMed and EMBASE databases from inception through September 2016 1,892,692 participants and 35,165 CRC cases (America, Europe, Asia, and Australia)	Highest vs. lowest consumption (12 cohort studies) grams per day (g/d) (8 cohort studies)	Pooled RRs: – CRC: 1.15 [1.07–1.24] – CC: 1.21 [1.13–1.31] – RC: 1.17 [0.99–1.38] –>10 studies Pooled RRs for 50 g/d increase: – CRC: 1.22 [1.12–1.33] – CC: 1.23 [1.11–1.37] – RC: 1.22 [0.99–1.28] –>7 studies
Red Meat	Zhao Z et al. [26]	34	Systematic review using PubMed and EMBASE databases from inception through September 2016 1,892,692 participants and 35,165 CRC cases (America, Europe, Asia, and Australia)	Highest vs. lowest consumption (15 cohort studies) Grams per day (g/d) (9 cohort studies)	Pooled RRs: – CRC: 1.12 [1.03–1.21] – CC: 1.12 [1.04–1.20] –>11 studies – RC: 1.12 [0.89–1.40] –> 8 studies Pooled RRs for 100 g/d increase: – CRC: 1.16 [1.05–1.29] – CC: 1.10 [0.96–1.26] –> 8 studies – RC: 1.22 [1.01–1.47] –> 6 studies

CRC colorectal cancer, *CC* colon cancer, *RC* rectal cancer, *RR* relative risk, *HR* hazard ratio, *95% CI* 95% confidence interval, *BMI* body mass index, *p-y* pack-years, *g/d* grams per day

2.4.2 Personal or Familial History of Adenoma or Colorectal Cancer

Results from population-based studies and meta-analyses showed that the risk of developing colorectal cancer is about two times higher in persons with at least one affected first-degree relative than in those without family history. The risk of colorectal cancer is more than threefold higher among persons with a first-degree relative diagnosed under age 50 (pooled relative risk (RR) from meta-analysis = 3.55; 95% confidence interval = 1.84–6.83) and between two- and threefold higher if a first-degree relative is diagnosed under the age of 60 (RR range = 1.81–3.30). The risk of colorectal cancer associated with having a first-degree relative with an adenoma is less than 2 (RR range = 1.3–51.99). The risk of colorectal cancer is higher if the adenoma was 'large' (>10 mm; RR = 1.68; 1.29–2.18) or 'advanced' (with villous histology; RR = 3.90; 0.89–17.01) and if the first-degree relative is diagnosed with an adenoma under age 60 (RR range: 1.41–1.54) [27].

2.4.3 Inflammatory Bowel Diseases: Ulcerative Colitis and Crohn's Disease

Several meta-analyses of population-based studies quantified the over-risk of colorectal cancer associated with ulcerative colitis and Crohn's disease (RR from 1.7 to 21.6). The variation of over-risk is attributable to the age of onset of the disease, extent of the disease (pancolitis is associated with a 10–15-fold excess risk), intensity of inflammation, concomitant primary sclerosing management, and familial history of colorectal cancer. The incidence of colorectal cancer, in this population with inflammatory bowel diseases, is from 0.5 to 12.4/100,000 persons-years between 0 and 10 years of follow-up, from 1.4 to 11.5 between 10 and 20 years, and between 2.4 and 44.9 after 20 years [28].

2.4.4 Genetic Mutation

High-risk mutations in known colorectal cancer susceptibility genes are involved in 5–10% of colorectal cancer cases [29]. Two dominantly inheritant syndromes are described: the familial adenomatosis polyposis (APC adenomatous polyposis coli gene; <1% of colorectal cancer cases) and the hereditary nonpolyposis colorectal cancer (Lynch syndrome with several mutations in mismatch repair genes; roughly 5% of colorectal cancer cases). In both of these syndromes, the mean age of onset of colorectal cancer is much smaller (less than 50 years old) than in sporadic colorectal cancers, and extracolonic malignancies are also observed. The prevalence of Lynch syndrome varies according to studies. Recently, using data from the international Colon Cancer Family Registry, the prevalence of Lynch syndrome was estimated at 1 in 279 of the population [30]. The overall hazard ratio for colorectal cancer in carriers of Lynch syndrome decreased with each additional decade of life, from 135 (95%CI, 112–165) for men and 99 (95%CI, 79–125) for women when in their 30s to 4.0 (95%CI, 2.8–5.7), respectively, when in their 70s [31].

2.5 Emergency Presentation with Colorectal Cancer: Frequency and Risk Factors

Studies examining risk factors and circumstances surrounding emergency colorectal cancer diagnosis are limited. Incidence of obstructing and perforated colorectal cancers is variously estimated in the literature, from 8% to 40% due to varying definition, from sub-occlusion to the necessity of emergency surgery. Using a strict definition of obstruction through population-based studies, approximately, 10% will occur in an emergency context because of obstruction, and less than 5% because of perforation [32–34].

Two large database studies [34, 35] have found that patients with advanced age (adjusted odds ratios, $aOR_{\text{per 10 years increment}}$ = 1.19; 95% confidence interval, 1.16–1.22 [34], and $aOR_{\text{80 years vs. 70 years}}$ = 1.49; 1.47–1.52 [35]), women (aOR = 1.08; 1.01–1.14 and 1.12; 1.08–1.16, respectively), and patients with lower income ($aOR_{\text{lowest vs. highest}}$ = 1.28; 1.18–1.39) [34] or higher socioeconomic deprivation ($aOR_{\text{most vs. least deprived}}$ = 1.54; 1.45–1.64) [35] and comorbidities are significantly associated with emergency presentation. In the Canadian population-based study, which included 41,356 patients (7739 emergency presentations), Rabeneck et al. [34] reported that lack of a regular source of a family physician (aOR = 1.43; 1.30–1.54) and not having a previous bowel evaluation (aOR = 1.45; 1.33–1.59) were additionally associated with colorectal cancer emergencies and consistent with other studies [36–38]. In their large study of over 90,000 patients, Wallace and colleagues found that ethnicity had an impact on the risk of an emergency admission for colorectal cancer, with higher risk for nonwhite patients (aOR = 1.13; 1.02–1.24) [35]. *The most recent systematic review by Mitchell et al.* [39] identified 19 studies that considered factors associated with diagnosis of colorectal cancer in the context of an emergency presentation and found older age to be a strong significant factor in the majority of the studies analyzed, with aOR varying from 1.19 to 5.85. Results for the other risk factors were less conclusive. Evidence regarding symptoms before emergency cancer diagnosis is still limited. Abdominal pain, constipation, weight loss, and diarrhea are the preceding symptoms more generally associated with an increased risk of emergency presentation [39–42].

2.6 Conclusion

Colorectal cancer is the third most common cancer in men and the second in women worldwide (2012). Starting from the mid-1990s, incidence rates decline for both sexes in the high-risk countries (mostly developed countries) whereas increase in most middle-risk ones (mostly developing countries). Five-year net colorectal cancer survival varies from 35% to 75%. Survival varies little between 1995 and 1999 and

2000–2014. The main risk factors for colorectal cancer are environmental factors (obesity, tobacco use, alcohol intake, sedentary behavior, and consumption of red and processed meat), inflammatory bowel disease (ulcerative colitis and Crohn's disease), family or personal history of colorectal cancer or large adenoma, and inherited genetic factors (familial adenomatosis polyposis and hereditary nonpolyposis colorectal cancer). Colorectal cancer diagnosis occurs in an emergency context in about 10% because of obstruction and less than 5% because of perforation particularly in older patients, women, and patients with socioeconomic deprivation and comorbidities.

References

1. Foman D, Bray F, Brewster D, Gombe Mbalawa C, Kholer B, Pinreros M, et al. Cancer incidence in five continents, vol. X. Lyon: International Agency for Research on Cancer; 2013.
2. Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, et al. Cancer incidence in five continents, vol. IX. Lyon: IARC; 2007.
3. Bray F, Colombet M, Mery L, Piñero M, Znaor A, Zanetti R, et al. Cancer incidence in five continents, vol. XI. Lyon: International Agency for Research on Cancer; 2017.
4. Allemani C, Rachet B, Weir HK, Richardson LC, Lepage C, Faivre J, et al. Colorectal cancer survival in the USA and Europe: a CONCORD high-resolution study. BMJ Open. 2013;3(9):e003055. https://doi.org/10.1136/bmjopen-2013-003055.
5. Allemani C, Weir HK, Carreira H, Harewood R, Spika D, Wang XS, et al. Global surveillance of cancer survival 1995-2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet. 2015;385(9972):977–1010. https://doi.org/10.1016/S0140-6736(14)62038-9.
6. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Niksic M, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet. 2018;391(10125):1023–75. https://doi.org/10.1016/S0140-6736(17)33326-3.
7. Holleczek B, Rossi S, Domenic A, Innos K, Minicozzi P, Francisci S, et al. On-going improvement and persistent differences in the survival for patients with colon and rectum cancer across Europe 1999-2007 - results from the EUROCARE-5 study. Eur J Cancer. 2015;51(15):2158–68. https://doi.org/10.1016/j.ejca.2015.07.024.
8. De Angelis R, Sant M, Coleman MP, Francisci S, Baili P, Pierannunzio D, et al. Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE--5-a population-based study. Lancet Oncol. 2014;15(1):23–34. https://doi.org/10.1016/S1470-2045(13)70546-1.
9. Cowppli-Bony A, Uhry Z, Remontet L, Voirin N, Guizard AV, Tretarre B, et al. Survival of solid cancer patients in France, 1989-2013: a population-based study. Eur J Cancer Prev. 2017;26(6):461–8. https://doi.org/10.1097/CEJ.0000000000000372.
10. Cowppli-Bony A, Uhry Z, Remontet L, Guizard AV, Voirin N, Monnereau A, et al. Survie des personnes atteintes de cancer en France métropolitaine 1989-2013. Partie 1 Tumeurs solides. Saint Maurice: Institut de veille sanitaire; 2016.
11. Binder-Foucard F, Bossard N, Delafosse P, Belot A, Woronoff AS, Remontet L, et al. Cancer incidence and mortality in France over the 1980-2012 period: solid tumors. Revue d'epidemiologie et de sante publique. 2014;62(2):95–108. https://doi.org/10.1016/j.respe.2013.11.073.
12. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. GLOBOCAN 2012 v1.0. Cancer incidence and mortality worldwide: IARC CancerBase. Lyon: International Agency for Research on Cancer; 2013. (extracted in 2017).
13. Troeung L, Sodhi-Berry N, Martini A, Malacova E, Ee H, O'Leary P, et al. Increasing incidence of colorectal cancer in adolescents and young adults aged 15-39 years in Western

Australia 1982-2007: examination of colonoscopy history. Front Public Health. 2017;5:179. https://doi.org/10.3389/fpubh.2017.00179.
14. Siegel RL, Jemal A, Ward EM. Increase in incidence of colorectal cancer among young men and women in the United States. Cancer Epidemiol Biomarkers Prev. 2009;18(6):1695–8. https://doi.org/10.1158/1055-9965.EPI-09-0186.
15. Brenner DR, Ruan Y, Shaw E, De P, Heitman SJ, Hilsden RJ. Increasing colorectal cancer incidence trends among younger adults in Canada. Prev Med. 2017;105:345–9. https://doi.org/10.1016/j.ypmed.2017.10.007.
16. O'Connell JB, Maggard MA, Liu JH, Etzioni DA, Livingston EH, Ko CY. Rates of colon and rectal cancers are increasing in young adults. Am Surg. 2003;69(10):866–72.
17. Colorectal Cancer Prevention (PDQ(R)): Health Professional Version. PDQ cancer information summaries. Bethesda, MD: National Cancer Institute; 2018.
18. Howlader N, Noone A, Krapcho M, Garshell J, Neyman N, Altekruse S, et al. SEER Cancer statistics review, 1975-2010. [Based on the November 2012 SEER data submission, posted to the SEER web site, April 2013.]. Bethesda, MD: National Cancer Institute; 2013. p. 9.
19. Cong YJ, Gan Y, Sun HL, Deng J, Cao SY, Xu X, et al. Association of sedentary behaviour with colon and rectal cancer: a meta-analysis of observational studies. Br J Cancer. 2014;110(3):817–26. https://doi.org/10.1038/bjc.2013.709.
20. Ma P, Yao Y, Sun W, Dai S, Zhou C. Daily sedentary time and its association with risk for colorectal cancer in adults: a dose-response meta-analysis of prospective cohort studies. Medicine (Baltimore). 2017;96(22):e7049. https://doi.org/10.1097/MD.0000000000007049.
21. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492–505. https://doi.org/10.1097/CEJ.0b013e328360f434.
22. Lippi G, Mattiuzzi C, Cervellin G. Meat consumption and cancer risk: a critical review of published meta-analyses. Crit Rev Oncol Hematol. 2016;97:1–14. https://doi.org/10.1016/j.critrevonc.2015.11.008.
23. Xue K, Li FF, Chen YW, Zhou YH, He J. Body mass index and the risk of cancer in women compared with men: a meta-analysis of prospective cohort studies. Eur J Cancer Prev. 2017;26(1):94–105. https://doi.org/10.1097/CEJ.0000000000000231.
24. Cheng J, Chen Y, Wang X, Wang J, Yan Z, Gong G, et al. Meta-analysis of prospective cohort studies of cigarette smoking and the incidence of colon and rectal cancers. Eur J Cancer Prev. 2015;24(1):6–15. https://doi.org/10.1097/CEJ.0000000000000011.
25. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. Br J Cancer. 2015;112(3):580–93. https://doi.org/10.1038/bjc.2014.579.
26. Zhao Z, Feng Q, Yin Z, Shuang J, Bai B, Yu P, et al. Red and processed meat consumption and colorectal cancer risk: a systematic review and meta-analysis. Oncotarget. 2017;8(47):83306–14. https://doi.org/10.18632/oncotarget.20667.
27. Lowery JT, Ahnen DJ, Schroy PC III, Hampel H, Baxter N, Boland CR, et al. Understanding the contribution of family history to colorectal cancer risk and its clinical implications: a state-of-the-science review. Cancer Am Cancer Soc. 2016;122(17):2633–45. https://doi.org/10.1002/cncr.30080.
28. Adami HO, Bretthauer M, Emilsson L, Hernan MA, Kalager M, Ludvigsson JF, et al. The continuing uncertainty about cancer risk in inflammatory bowel disease. Gut. 2016;65(6):889–93. https://doi.org/10.1136/gutjnl-2015-311003.
29. Lorans M, Dow E, Macrae FA, Winship IM, Buchanan DD. Update on hereditary colorectal cancer: improving the clinical utility of multigene panel testing. Clin Colorectal Cancer. 2018;17:e293. https://doi.org/10.1016/j.clcc.2018.01.001.
30. Win AK, Jenkins MA, Dowty JG, Antoniou AC, Lee A, Giles GG, et al. Prevalence and penetrance of major genes and polygenes for colorectal cancer. Cancer Epidemiol Biomarkers Prev. 2017;26(3):404–12. https://doi.org/10.1158/1055-9965.EPI-16-0693.

31. Jenkins MA, Dowty JG, Ait Ouakrim D, Mathews JD, Hopper JL, Drouet Y, et al. Short-term risk of colorectal cancer in individuals with lynch syndrome: a meta-analysis. J Clin Oncol. 2015;33(4):326–31. https://doi.org/10.1200/JCO.2014.55.8536.
32. Cheynel N, Cortet M, Lepage C, Benoit L, Faivre J, Bouvier AM. Trends in frequency and management of obstructing colorectal cancers in a well-defined population. Dis Colon Rectum. 2007;50(10):1568–75. https://doi.org/10.1007/s10350-007-9007-4.
33. Cheynel N, Cortet M, Lepage C, Ortega-Debalon P, Faivre J, Bouvier AM. Incidence, patterns of failure, and prognosis of perforated colorectal cancers in a well-defined population. Dis Colon Rectum. 2009;52(3):406–11. https://doi.org/10.1007/DCR.0b013e318197e351.
34. Rabeneck L, Paszat LF, Li C. Risk factors for obstruction, perforation, or emergency admission at presentation in patients with colorectal cancer: a population-based study. Am J Gastroenterol. 2006;101(5):1098–103. https://doi.org/10.1111/j.1572-0241.2006.00488.x.
35. Wallace D, Walker K, Kuryba A, Finan P, Scott N, van der Meulen J. Identifying patients at risk of emergency admission for colorectal cancer. Br J Cancer. 2014;111(3):577–80. https://doi.org/10.1038/bjc.2014.300.
36. Murchie P, Smith SM, Yule MS, Adam R, Turner ME, Lee AJ, et al. Does emergency presentation of cancer represent poor performance in primary care? Insights from a novel analysis of linked primary and secondary care data. Br J Cancer. 2017;116(9):1148–58. https://doi.org/10.1038/bjc.2017.71.
37. Sikka V, Ornato JP. Cancer diagnosis and outcomes in Michigan EDs vs other settings. Am J Emerg Med. 2012;30(2):283–92. https://doi.org/10.1016/j.ajem.2010.11.029.
38. Comber H, Sharp L, de Camargo Cancela M, Haase T, Johnson H, Pratschke J. Causes and outcomes of emergency presentation of rectal cancer. Int J Cancer. 2016;139(5):1031–9. https://doi.org/10.1002/ijc.30149.
39. Mitchell ED, Pickwell-Smith B, Macleod U. Risk factors for emergency presentation with lung and colorectal cancers: a systematic review. BMJ Open. 2015;5(4):e006965. https://doi.org/10.1136/bmjopen-2014-006965.
40. Sheringham JR, Georghiou T, Chitnis XA, Bardsley M. Comparing primary and secondary health-care use between diagnostic routes before a colorectal cancer diagnosis: cohort study using linked data. Br J Cancer. 2014;111(8):1490–9. https://doi.org/10.1038/bjc.2014.424.
41. Cleary J, Peters TJ, Sharp D, Hamilton W. Clinical features of colorectal cancer before emergency presentation: a population-based case-control study. Fam Pract. 2007;24(1):3–6. https://doi.org/10.1093/fampra/cml059.
42. Renzi C, Lyratzopoulos G, Card T, Chu TPC, Macleod U, Rachet B. Do colorectal cancer patients diagnosed as an emergency differ from non-emergency patients in their consultation patterns and symptoms? A longitudinal data-linkage study in England. Br J Cancer. 2016;115(7):866–75. https://doi.org/10.1038/bjc.2016.250.