

2020



Roadmap for the Prevention and Treatment of Colorectal Cancer in Europe



DIGESTIVE CANCERS
EUROPE

Executive Summary and Recommendations ●

Every year, around **500,000 new cases** of colorectal cancer (CRC) are diagnosed in Europe, and around **250,000 of those patients die**. That is 50%. Interestingly enough, in the largest and more specialised cancer centers, the probability of survival up to 5-years is 85%. The logical question arises: why are not all patients treated with the same care? Why are these differences arising within the same country, where all patients can benefit from the same system? The potential upside of applying best practices everywhere is huge, even without further technological innovation.

The total cost of colorectal cancer in the European Union is estimated at 19 billion euros annually.

So one would expect the stakes – *both human and financial* – to be sufficiently high, to collect information, think and act. With this roadmap we are starting on these reflections.

More than 55% of new colorectal cancer cases could be prevented by better lifestyle choices. Thanks to good national colorectal cancer screening programmes, some countries manage to significantly increase early stage diagnoses, resulting in much better overall survival and even a reduction in incidence. In Europe, the probability of survival up to 5 years of patients diagnosed with colorectal cancer and treated in the best hospitals is 85%. We observe a lack of patient information and support, whether psychological, nutritional or in terms of physical revalidation. We also observe a lack of support and efforts to help people to go back to work and to provide a good context for survivors to continue their lives in the most positive way possible.

Despite all the knowledge, technology and information that is available, we notice that data are lacking or that best practices are not being applied.

Every type of cancer is different and requires adapted approaches. It is insufficient to just have a 'national cancer plan'.

Considering the size and the burden of each cancer, each requires specific, detailed and monitored plans, allocated budgets, with full provision of the latest and real-time input and outcomes data.

Recommendations for Member State governments to increase colorectal cancer survival and quality of life:



- 1 Invest more in prevention and citizen education on lifestyle choices and risk of disease
- 2 Significantly increase the colorectal cancer screening efforts. They have demonstrated to save lives and money
- 3 Reduce the number of treatment centers to specialised Comprehensive Cancer Networks, allowing all patients to have access to the best possible cancer care in which multi-disciplinary teams deliver high quality treatment and supportive care for better outcomes including quality of life
- 4 Ensure that no public money is given to any healthcare stakeholder without the full demonstration of outcomes for every patient they treated, together with public availability and transparency of these data
- 5 Invest in access to new medicines, both originators and generics, and do not use delaying tactics for fiscal reasons. Patients should not be the victim of delays in market access
- 6 Have a systematic health economic analysis of financial inputs and outcomes so that the most rational choices can be made on where tax-payers' money is invested with best effect
- 7 Support and fund patient organisations dedicated to a cancer type, so that patients can achieve the full support needed throughout the patient journey
- 8 Empower patient organisations, and accredit them if need be, to become the custodian of the patient journey at national level, so they can organise the optimal patient pathways in collaboration with all other stakeholders
- 9 Invest in research in proportion to the burden of the disease and prioritise research based on patient insights
- 10 Invest in health systems research to reach optimal knowledge of best outcomes and their causes

Recommendations for hospitals



- 1 Apply all the international guidelines for cancer care in a systematic way, including the European Cancer Organisation's Essential Requirements for Quality Colorectal Cancer Care
- 2 Hospitals that do not meet the requirements should associate themselves with a specialised cancer center or stop treating colorectal cancer patients
- 3 Hospitals should refer patients to dedicated patient organisations immediately after diagnosis
- 4 Hospitals should have systems of Shared Decision-Making so that patients can be fully informed on the disease, its treatment and consequences and share their expectations and context
- 5 Ensure that patients have access to all the best information on nutrition, physical activity, psychological support and set up information sessions with patient organisations and specialised partners

Recommendations for patient organisations



- 1 Work with hospitals to create the best possible services for patients after diagnosis
- 2 Become the custodian of the patient journey, advocating from prevention to end of life to improve every step of the way, working to advocate for the use of best practices and a coherent colorectal cancer health policy
- 3 Act as the driving force to bring together all key stakeholders to capture insights and action steps to develop and implement national colorectal cancer plans
- 4 Capture the collective intelligence of all your members to give information and provide insights on how colorectal cancer treatment can be improved



Introduction

Despite the huge annual burden of colorectal cancer in Europe, both human and financial, there are no overarching plans to improve the situation. Efforts are being made, on a technological and organisational level, but these efforts are often the result of initiatives by public health agencies, hospitals and companies. There is no big picture vision of how outcomes can be improved for even more citizens and patients, and this at a lesser cost, if all efforts are bundled and part of a coherent whole.

Despite the burden of colorectal cancer in Europe, such a Roadmap still does not exist and it is very much needed. The report or roadmap that we present here looks at all the aspects related to the management of the illness, and not only at the clinical aspects of treating the disease. Today - and this is true for almost all diseases - public policy is focused on managing provider budgets (hospitals, physicians, nurses, technology, ...), leaving the healthcare providers to sort out the treatment pathway. This often means that investments are not made to achieve the best possible result for a specific disease, and that patients are treated sub-optimally and that taxpayers' money is being wasted.

In an ideal environment of rational disease management, policy decisions are made based on last-year's statistics on patient population and segmentation, treatment outcomes, patient satisfaction, best practices and total costs, including the treatment and the socio-economic costs. Up-to-date statistics about the state of health of citizens and patients are hard to find, and often outdated, and it is even rarer to have long term objectives by disease area to have a sense of direction and purpose.

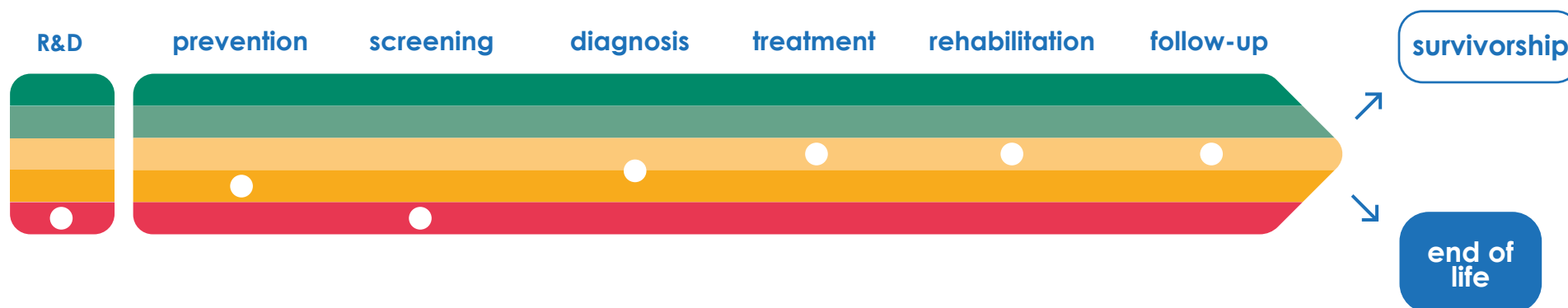
Our goal and commitment are clear: we want to save 250,000 lives of colorectal cancer patients in Europe by 2028. This can only be done with the right investments and by applying best practices.

This Roadmap has the ambition to bring these elements together to move in this direction.

The framework

The patient journey from prevention to 5-year survival or end of life

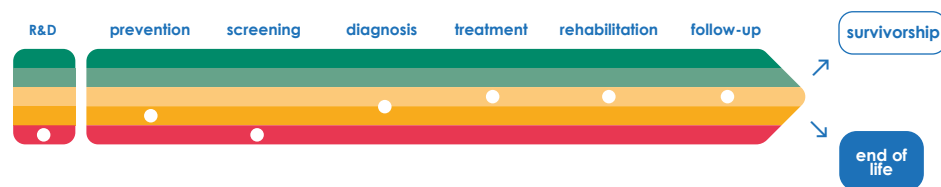
Figure 1: The Patient Pathway



We will use the patient journey from prevention to the end of the journey, either a cure and a return to normal life, or an untimely death. The latter also deserves attention to address how patients are supported during the most difficult moments. We will look at the available data for every step of the patient's journey, and try to identify which health approach works best, based on current technology and insights, and what information is lacking to make the correct decisions.

We will see that no single country has the best possible approach today, but we hope to identify the best practices, so that policy-makers in every European country can make the correct choices of what needs to be included in future national colorectal cancer plans.

Moving forward, we will use this patient journey (Figure 1) with a qualifying colour coding to illustrate the current status today, with red indicating a negative situation and green the best possible situation. The white dot identifies where we stand today, based on country averages and qualitative evaluation. Around this clinical journey, a full treatment plan should be established, including psychosocial and rehabilitation care, survivorship issues, and a survivorship care plan.



For every step we will identify best practices, suggest policy or medical practice recommendations, and then try to evaluate how many lives could potentially be saved by the application of current best practices.

Disease-specific patient organisations such as Digestive Cancers Europe and its members help patients navigate the healthcare system, and coach them for all the medical and non-medical aspects of their disease. As a result, the entire patient journey can become more effective and efficient.

In order to better understand patient needs and experience, we conducted a survey among metastatic colorectal cancer patients in Europe. More than 800 patients completed the questionnaire, and some of the findings will be used in this publication. The full report of the survey is published separately¹.

¹ Understanding the Experience and Needs of Patients with Metastatic Colorectal Cancer – Results of a European Patient Survey, Digestive Cancers Europe, 2020 - <https://www.digestivecancers.eu/wp-content/uploads/2020/09/mCRCsurvey-FINAL.pdf>

The current status

Incidence, survival, prevalence and mortality

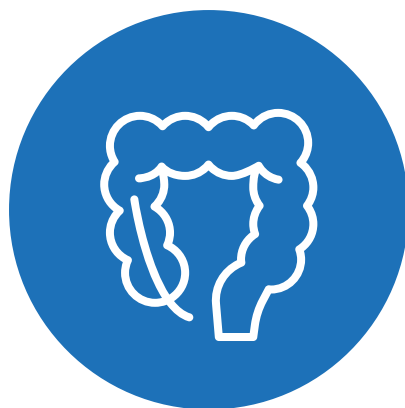


Table 1: Incidence and mortality of colorectal cancer in Europe

	annual number of cases	annual number of deaths	number of survivors
colon	344,974	169,573	
rectum	195,992	89,319	
TOTAL	540,966	258,892	1,629,437

In Europe, every year, 344,974 citizens² get diagnosed with colon cancer and 195,992 with rectal cancer. Around 170,000 colon cancer patients and 90,000 rectal cancer patients die every year. There are about 1,6 million colorectal cancer survivors in Europe, of which 950,000 live in the European Union³.

The incidence of colorectal cancer is increasing in most countries, with the exception of Switzerland, France, Austria, Germany and the Czech Republic, where the numbers are decreasing or stagnating⁴.

When we look at the incidence, calculated as the number of new cases per year per 100,000 inhabitants of the country, Europe scores very high compared to other regions in the world⁵.

² Globocan, figures 2020, WHO Europe region

³ Globocan, figures 2020, WHO Europe region

⁴ Martin Wong, et al. Differences in Incidence and Mortality Trends of Colorectal Cancer Worldwide Based on Sex, Age, and Anatomic Location, in: "Clinical Gastroenterology and Hepatology, February 2020

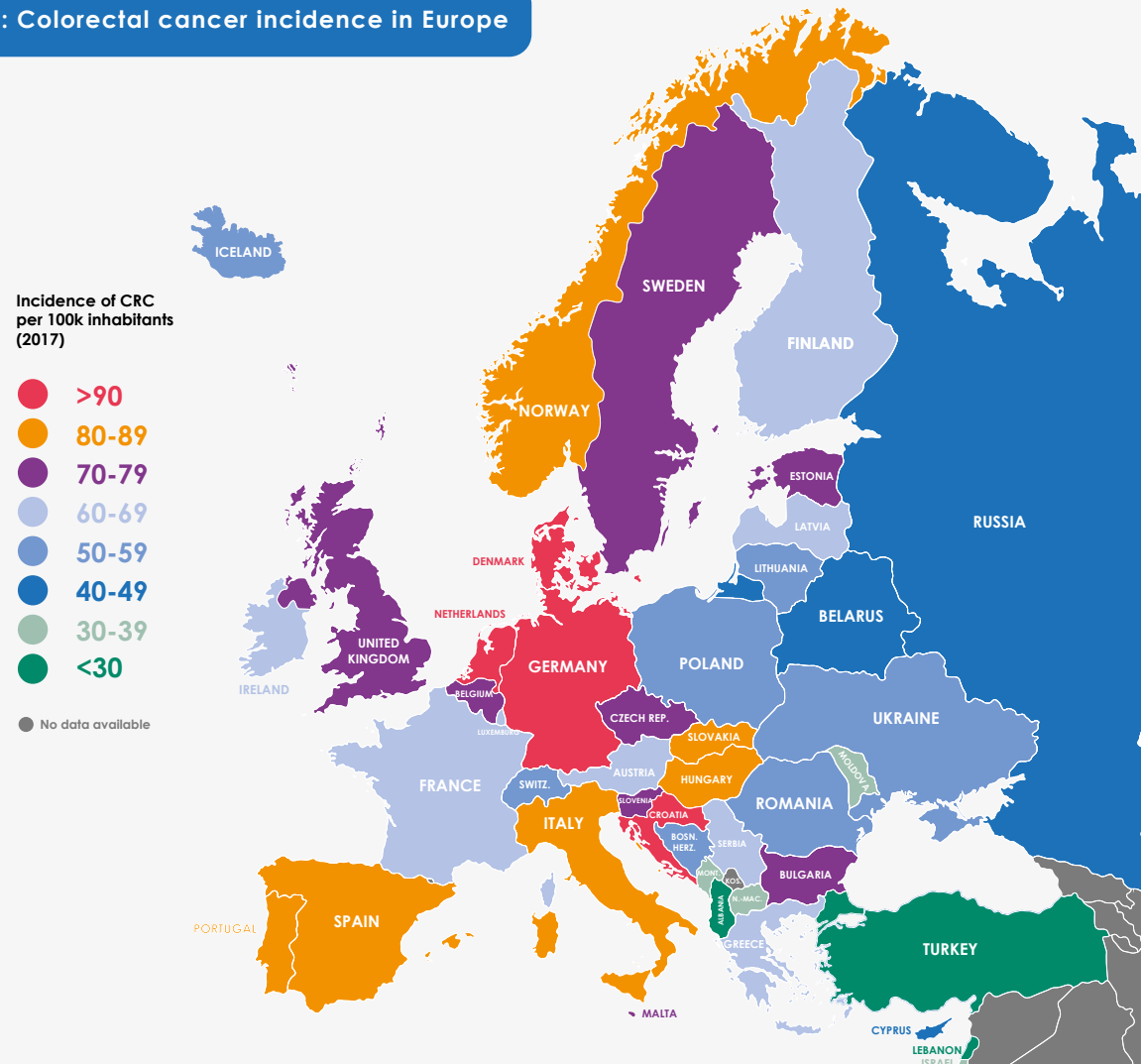
⁵ Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.1, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2014. Available from: <http://globocan.iarc.fr>.



There is a clear link between colorectal cancer and lifestyle, with a higher incidence in the more affluent countries. In Europe, the highest incidence of colorectal cancer is to be found in the Netherlands, followed by Germany, Denmark and Croatia.

The countries in Europe with the lowest incidence are Turkey and Albania⁶.

Figure 2: Colorectal cancer incidence in Europe

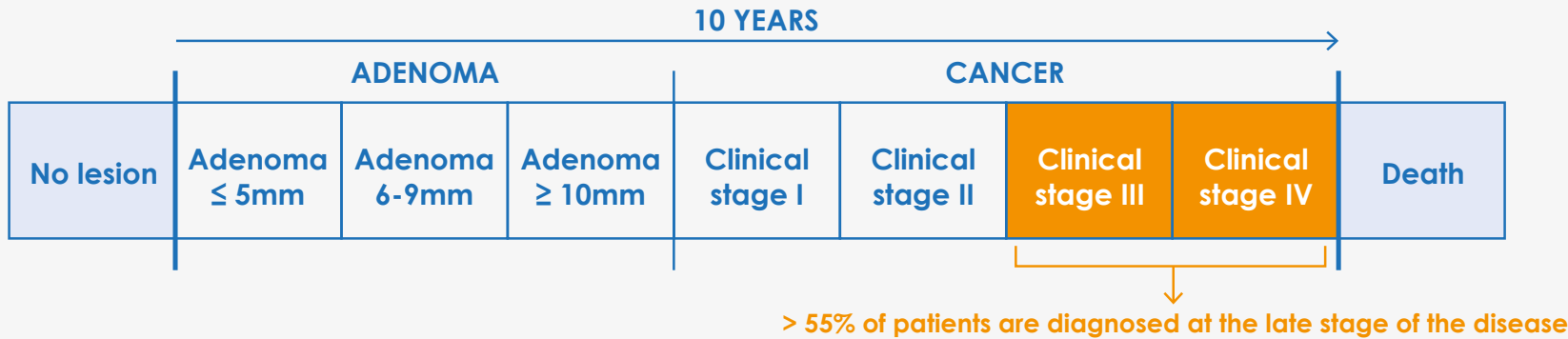


⁶ Institute for Health Metrics & Evaluation, data 2017, consulted 2019

5-Year Survival by stage of the disease

Colorectal cancer shows slow progress from initial adenomas to the cancerous stage. This timeframe may be longer than 10 years, sometimes even as long as 20 years.

Figure 3: Time sequence for the development of a colorectal tumour



Despite this long and slow polyp and tumour growth, 55% of patients are diagnosed in the clinical stages III and IV⁷.

The statistics in the following table show the difference in overall 5-year survival by stage of

the disease, and the average treatment cost by stage of the disease. The chance of survival is significantly higher in stage I, and the treatment cost around ten times lower⁸. Despite this, the majority of patients are still diagnosed in late stages.

It is therefore obvious that early detection is absolutely essential to increase the chance of survival and to reduce costs to the healthcare system. We refer to our White Paper on Colorectal Cancer Screening for more details⁹.

⁷ The statistics are derived from several studies at national level: Figures from the US and the UK come to comparable results : American Cancer Society: Survival Rates for Colorectal Cancer, by Stage, 2018 and Bowel Cancer UK, Figures 2006. Source: **Cancer.net** , Cancer Burden In Belgium 2003-2014, Belgian Cancer Registry 2014 , Feller, A., Schmidlin, K., Bordonj, A., Bouchardy, C., Bulliard, J., Camey, B., Oris, M. (2018). Socioeconomic and demographic inequalities in stage at diagnosis and survival among colorectal cancer patients: evidence from a Swiss population based study. Cancer Medicine, 7(4), 1498–1510. <http://doi.org/10.1002/cam4.1385>, Manuel Zorzi et alii: Characteristics of the colorectal cancers diagnosed in the early 2000s in Italy. Epidemiology & Prevention, 2015

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⁹ Digestive Cancers Europe: White Paper on Colorectal Cancer Screening in Europe, 2019

Table 2: Survival, diagnoses and cost by stage of colorectal cancer

	stage I	stage II	stage III	stage IV
Chance of survival	90%	75%	70%	10%
Patients diagnosed per stage	13%	31%	32%	24%
ESTIMATED TREATMENT COST	€ 4,000	€ 25,000	€ 30,000	€ 40,000

In a recent study for Europe, these figures were corroborated: the age-standardised 5-year survival in stage I is around 90% versus around 10% in the metastatic stage IV. Around 13% of colon cancer patients are diagnosed in stage I and 19% for rectal cancer patients. Around 22% are diagnosed in Stage IV for colon and 19% for rectal cancer¹⁰, demonstrating again that a lot of value can be generated by earlier diagnosis.

We commissioned a study with the Institute of Health Economics¹¹ to quantify the burden of colorectal cancer in economic terms.

The total cost of colorectal cancer in Europe is estimated at 19 billion euro, of which 9.8 billion is direct healthcare costs, 3.1 billion euro in informal care and 7.1 billion euro in indirect costs (premature mortality costs and labour productivity loss). Despite the burden of the disease, there are barely any figures available at national level to verify investments versus outcomes. Considering the amount of citizens affected and the money involved, this shows how much more progress can be made to obtain systems efficiency.

A recent study on the health economic burden of colorectal cancer came with even higher potential benefits, when all costs are taken into consideration: "If all EU27+UK countries could achieve the midpoint between the minimum European guideline rate and the Basque screening participation levels, aggregate annual direct savings would reach €405 million (0.027% of the aggregate health expenditure), ranging between €274.3 and €535.4 million (0.018% to 0.035% of aggregate health expenditure). These participation rates would also reduce CRC deaths by between 10,000 and 20,000 and be associated with an additional 171,000 to 331,000 QALYs per year through morbidity and premature mortality avoided. Using a willingness-to-pay of €30,000 per QALY, this implies an additional indirect efficiency gain of between €5.1 and €9.9 billion"¹².

10 Minicozzi et al: "Is low survival for cancer in Eastern Europe due principally to late stage at diagnosis?", in: European Journal of Cancer, 2018

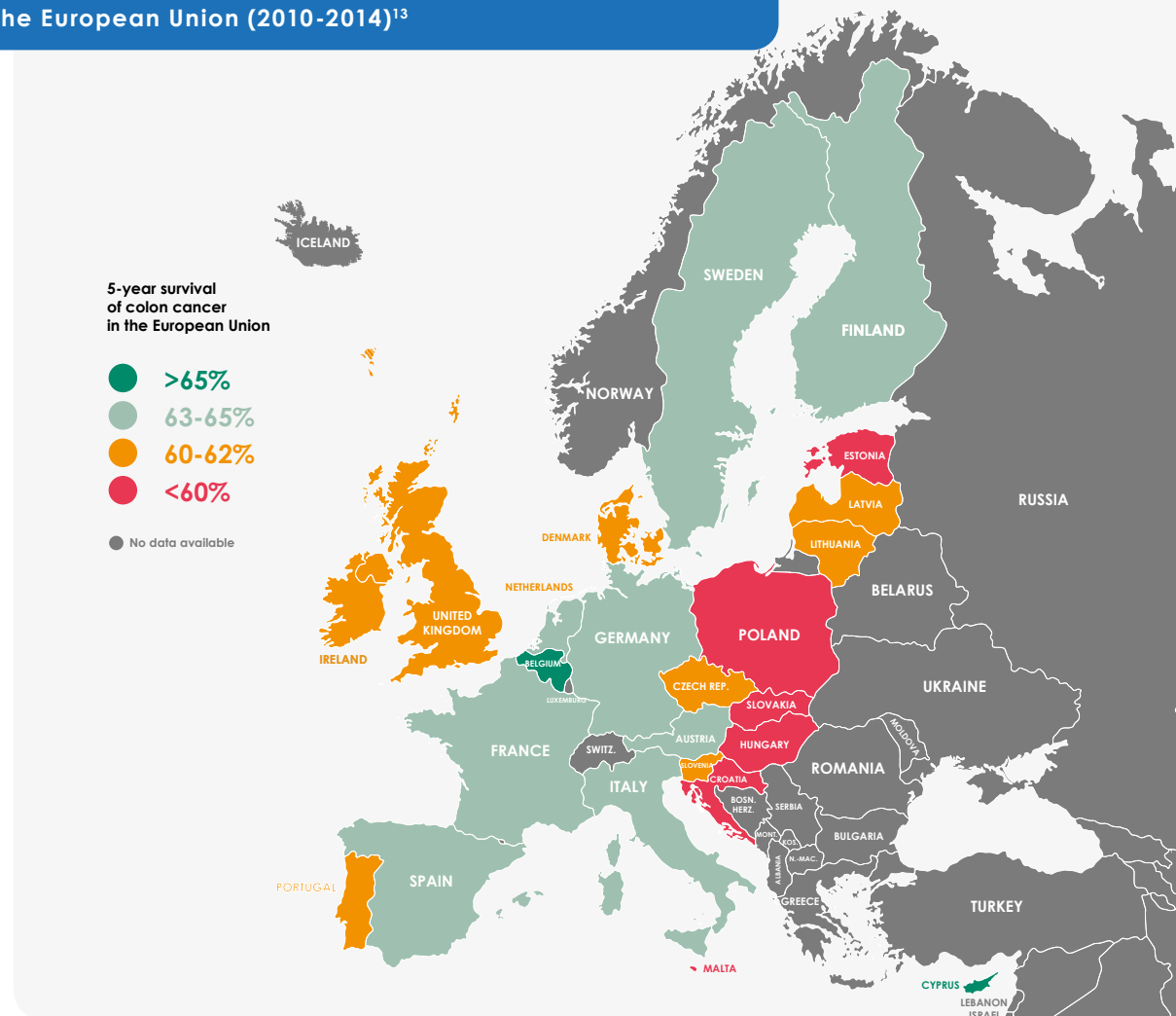
11 Hofmarcher, T., Lindgren, P. (2020) The Cost of Cancers of the Digestive System in Europe. IHE Report 2020:6. IHE: Lund, Sweden.

12 Office of Health Economics, Opportunities to Increase Efficiency In Healthcare, October 2020

The probability for cancer patients to survive their cancer for at least 5 years after diagnosis, is around 67 to 68% in the best performing countries, which is a slow advance compared to the beginning of the century, when the best survival in any country was around 64%. In the majority of European countries, including in some of the richest, survival is around 60%, which shows that there is still significant room for improvement. Interestingly enough, the countries with the highest survival, such as Belgium, do not even have the highest screening percentages, which implies that even there significant improvement can be made. Better screening, better GP education and better health literacy among patients can all contribute to better results.



Figure 4: 5-year net survival for colon cancer in the European Union (2010-2014)¹³



¹³ CONCORD Programme for the global surveillance of cancer survival (Allemani C et al.; Lancet 2018)

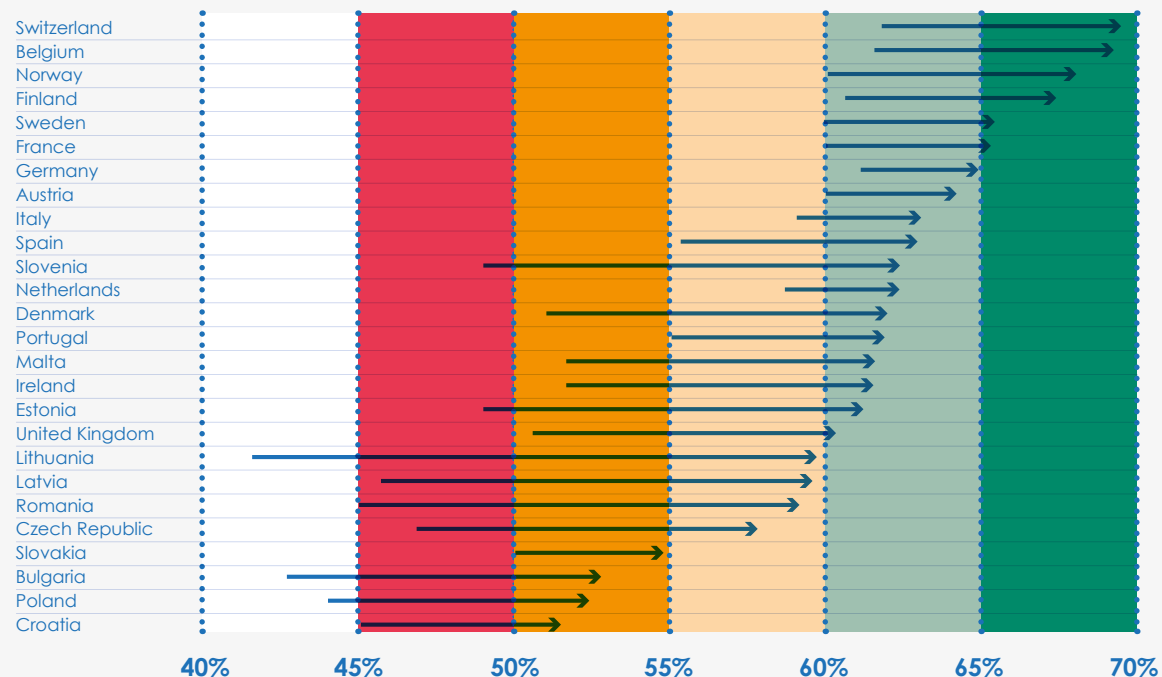
On the positive side, survival has improved over the years in every country in Europe. Based on the data from the CONCORD programme for global surveillance of cancer survival trends, we can see a marked evolution of population-based 5-year age-standardised net survival for colon cancer¹⁴ in all countries in Europe between 2000-2004 and 2010-2014, with Slovenia and Lithuania clearly making the most substantial progress. Slovenia has outperformed the Netherlands, and Lithuania has caught up with the United Kingdom. The graph also shows clearly how much better the system can become if the best practices of Switzerland and Belgium are applied.

In sum, despite the increase of colorectal cancer incidence in most European countries, the mortality is decreasing and the 5-year survival increasing, showing that progress is being made. Much more progress could be made by the systematic implementation of national colorectal cancer screening programmes: many lives can be saved together with a lot of economic benefits for the countries. One last aspect that requires attention is the lack of recent data on a disease with this level of impact on society. Every country should be able to provide annual statistics with yearly follow-up of patients diagnosed with cancer.

Cancer registries should be funded in proportion to the huge cost of cancer to society. Without recent data, it is very difficult to develop cancer policies that are based on the correct facts.

The European Union should also guarantee that GDPR is correctly interpreted and used, because it is often used as a pretext for not collecting patient data.

Figure 5: Progress of colon cancer 5-year population-based survival between 2000-2004 and 2010-2014



¹⁴ Results are published also for rectal cancer, but they are not included here: the trend is the same.

Prevention

The current situation

The risk factors for colorectal cancer are largely known:

- **Age:** colorectal cancer is more frequent among people older than 50 years. For colon cancer, the average age at the time of diagnosis for men is 68 and for women is 72. For rectal cancer, it is age 63 for both men and women¹⁵. In recent years, the number of younger people diagnosed with colorectal cancer is increasing.
- **A family history of colorectal cancer.** Citizens with a family history of colorectal cancer should have a colonoscopy already ten years before the age at which the family member was diagnosed. Today, around 15% of all colorectal cancers can be traced to a family history (first degree relative) of cancer, and of those, around 3% have an identified genetic cause.
- Other determining factors include **nutrition** (consumption of processed meat), alcohol consumption, smoking, lack of physical activity and obesity. According to IARC, 55% of colorectum cancers could be prevented by better lifestyle choices¹⁶.

It is clear that age and hereditary factors cannot be changed by prevention, but this still leaves a big potential upside for prevention campaigns to citizens.

Table 3 gives a good overview of the protective and risk factors, together with the robustness of the current scientific evidence¹⁷.

¹⁵ Cancer.net – website consulted 2020

¹⁶ IARC – Cancer Prevention Europe website

¹⁷ World Cancer Research Fund, 2017



Table 3: Diet, nutrition, physical activity and colorectal cancer (2017)

		Decreases risk	Increases risk
STRONG EVIDENCE	Convincing	Physical activity	Processed meat Alcoholic drinks Body fatness Adult attained height
	Probable	Wholegrains Foods containing dietary fibre Dairy products Calcium supplements	Red meat
LIMITED EVIDENCE	Limited - suggestive	Foods containing vitamin C Fish Vitamin D Multivitamin supplements	Low intakes of non-starchy vegetables Low intakes of fruits Foods containing haem iron
	Limited - no conclusion	Cereals (grains) and their products; potatoes; animal fat; poultry; shellfish and other seafood; fatty acid composition; cholesterol; dietary n-3 fatty acid from fish; legumes; garlic; non-dairy sources of calcium; foods containing added sugars; sugar (sucrose); coffee; tea; caffeine; carbohydrate; total fat; starch; glycaemic load; glycaemic index; folate; vitamin A; vitamin B6; vitamin E; selenium; low fat; methionine; beta-carotene; alpha-carotene; lycopene; retinol; energy intake; meal frequency; dietary pattern	
STRONG EVIDENCE	Substantial effect on risk unlikely		

The healthy lifestyle recommendations are known by everyone, but despite all the information campaigns to the general public about healthy eating, not smoking, the importance of physical activity and the moderate consumption of alcohol, only a minority of citizens actually apply all the recommendations. According to a study in the United States, this is only 3% of the population.

Knowledge about the subject is an insufficient driver for behavioural change. Human behaviour is driven by social, psychological and biological needs, such as indulging in the pleasure of the moment instead of considering distant risks. Many studies have been conducted on what will change healthy lifestyles. The conclusion is that positive encouragement works better than negatives such as risk emphasis or shaming. Positive external factors ('hedonia' in the literature) such as weight loss, looking good or acceptance by others will also have less effect than internal drivers ('eudaimonia') such as greater self-acceptance, higher quality relationships, being in charge of your life, owning your own opinions even when others oppose them, personal growth, and having a strong intrinsic sense of purpose¹⁸.

¹⁸ Bujacz A, Vittersø J, Huta V, Kaczmarek LD. Measuring hedonia and eudaimonia as motives for activities: cross-national investigation through traditional and Bayesian structural equation modeling. *Front Psychol.* 2014;5:984. Published 2014 Sep 8. doi:10.3389/fpsyg.2014.00984

Colorectal cancer increasingly occurs among younger people, possibly due to lifestyle choices such as nutrition, physical inactivity and alcohol consumption. This may require the adaptation of clinical guidelines, GP education and screening choices.

Recommendation

All education programmes should emphasise the importance of a healthy lifestyle, including diet and encourage young people to be physically active. This should be extended to all employers who should offer their employees the opportunity for physical activity and healthy food habits in the workplace (including the availability of fruit instead of vending machines with snacks).



Screening

The current situation

We refer to our other publications: the White Paper on Colorectal Cancer Screening in Europe¹⁹, and the Roadmap for Colorectal Cancer Screening in Europe²⁰, which were both published in 2019, and give an outline and recommendations of the current situation, the ideal situation and how to get there, both from a policy perspective (White Paper) and an organisational perspective (Roadmap). To summarise: screening for colorectal cancer is not only the most effective type of cancer screening, when organised correctly, it may save significant amounts of lives and save money to the healthcare system.

In 2003 the European Ministers of Health in the EU committed²¹ to screen all citizens of 50 to 74 years old in their countries, using the latest screening technology. A European Commission report²² sets a 65% participation rate as desirable for the defined target population.

Today, only a few countries in the European Union have actually achieved this: Slovenia, the Netherlands, Denmark and Lithuania. Despite this commitment, today only 14% of EU citizens between 50 and 74 year old have the opportunity to participate in a formal population-based colorectal cancer screening programme. Having a programme is not sufficient, it also has to meet quality criteria in terms of awareness creation, repeat messages, and sensitivity to tone and style that will enhance citizen participation.

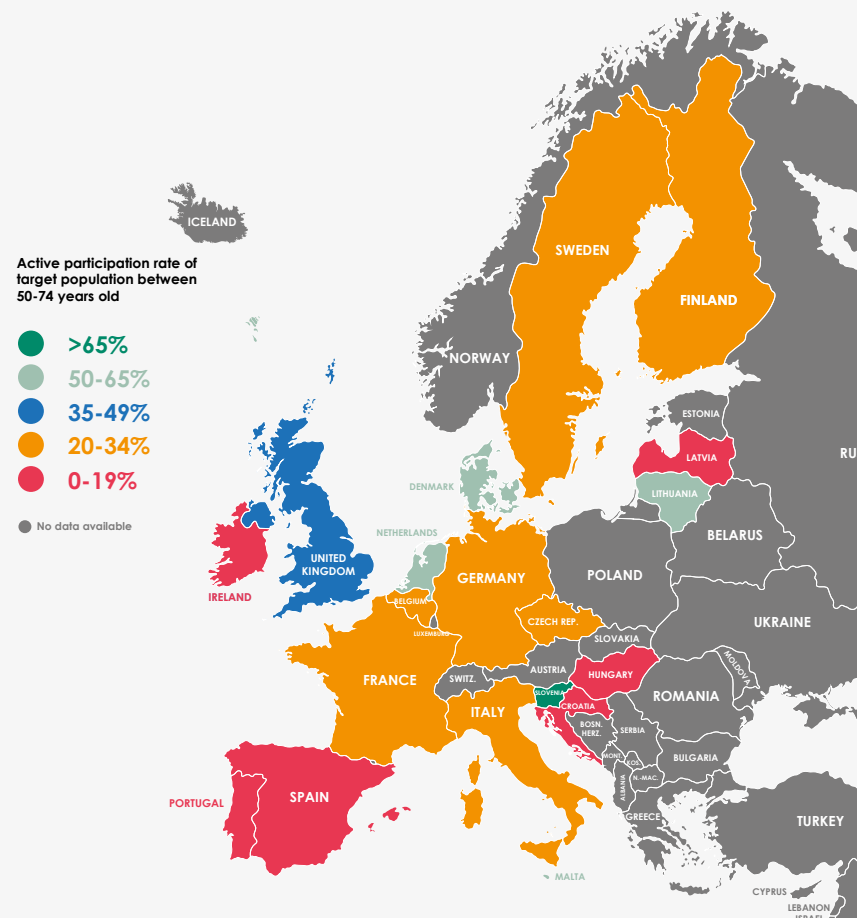
¹⁹ Digestive Cancers Europe: White Paper on Colorectal Cancer Screening in Europe, 2019

²⁰ Digestive Cancers Europe: Roadmap for Colorectal Cancer Screening in Europe, 2019

²¹ European Council Recommendations on Cancer Screening, December 2, 2003

²² European Commission Guidelines For Quality Assurance in Colorectal Cancer Screening and Diagnosis, 2020

Figure 6: Active participation rate of citizens aged 50-74 years in colorectal cancer screening programmes



Best practice

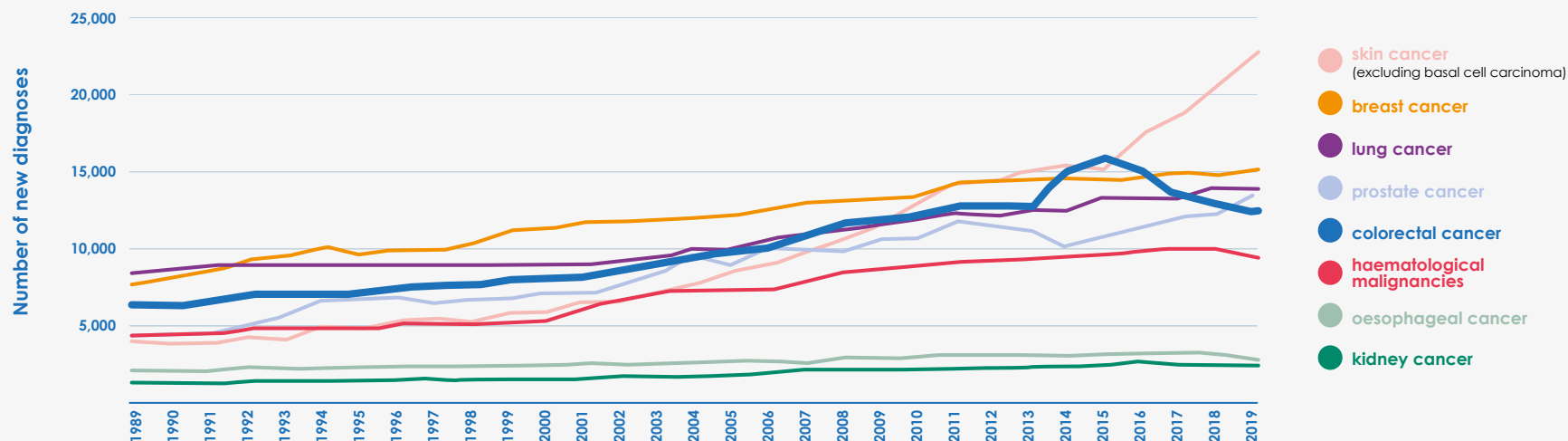
The advantage of population-based screening is that a simple test can be done at home. The test identifies whether or not the citizen may have colorectal cancer. People with a positive test are then invited for a colonoscopy which gives the actual diagnosis. Some countries, such as the Netherlands, have a very high participation rate of 70%, despite the country only screening citizens between 55 and 74 years old. The results have been remarkable, with 48% of patients now diagnosed at Stage I, as compared to 15%

without screening²³. Another good example is the Basque region in Spain, where a very high participation rate of 75% is achieved, and 92% of all patients with a positive test also adhere to colonoscopy. Slovenia reaches 62% within the full target group across the country, also resulting in 48% of the patients now being diagnosed at Stage I²⁴.

The success of the Netherlands, Slovenia and the Basque region is the result of intensive preparation and collaboration among all stakeholders, and of continued political support to make it happen.

The figure below shows the increase of all cancer cases in the Netherlands between 1989 and 2019. The purple line shows the effect of the implementation of the national screening programme for colorectal cancer. It leads to a sharp increase in the first years, but then because of early detection of polyps, the actual incidence declines. A similar picture is seen in Slovenia, where the incidence also decreased.

Figure 7: Evolution of the number of new diagnoses per year (incidence) in the Netherlands



²³ Integraal Kankercentrum Nederland, March 2018

²⁴ Slovenian National Colorectal Cancer Screening Programme, Ljubljana, 2018

The patient voice

Only 5% of patients were diagnosed through a formal screening programme, and 19% through emergency hospitalisation²⁵.

Recommendation

Our recommendation is simple: every country should invest more in population-based screening as of the age of 50, with a solid collaboration among all partners (screening agencies, hospitals, laboratories, diagnostic companies, general practitioners, citizen groups and patient organisations).

We also recommend to have a more sustained effort among all the national and regional screening agencies to share best practices and results. An initiative such as EU-TOPIA which brings together the screening agencies of different member states to share ideas, is one that deserves follow-up and expansion.

Expected outcome

If all countries in the European Union had the same results as the Netherlands, the potential upside for citizens would be significant, as well as the cost-savings that would be generated. Shifting the distribution of all European patients diagnosed at stage I from the current 15% to a higher percentage of 48% as in the Netherlands, would raise the number of citizens with an expected overall survival of 90%.

It would make sense to calculate this potential upside in terms of Years of Life Gained and the savings in medical costs.

The role of patient organisations

The role of patient organisations is critical in formal screening programmes. Patient organisations know what information citizens need to make the right choice to participate in screening, they understand the barriers to screening. They can offer testimony about the importance of early detection. They have the networks and the communication channels to advocate for better screening and higher participation rates. They are often the only ones acting to raise awareness about the issue.

It is no surprise that both in the Netherlands and Slovenia, patient organisations were part of the official process to set up the colorectal cancer screening programmes.



²⁵ Understanding the Experience and Needs of Patients with Metastatic Colorectal Cancer – Results of a European Patient Survey, Digestive Cancers Europe, 2020 - <https://www.digestivecancers.eu/wp-content/uploads/2020/09/mCRCsurvey-FINAL.pdf>

Diagnosis

The current situation

It may take at least ten years for a precancerous adenoma to evolve into a late stage tumour. And it is often in the latter situation that the symptoms become undeniable: blood in the stool, pain in the abdomen, loss of weight and energy. But even then, the symptoms may be mistaken for other diseases, such as hemorrhoids, appendicitis, and many more. Many colorectal cancer patients have gone back and forth between different treatments and visits to specialists before the actual diagnosis was made. This makes population-based screening all the more important and relevant.

In the past decade, several new technologies have entered the market that allow for improved screening and better diagnosis. These technologies have also been demonstrated to be cost-effective and even cost-saving with sufficient participation rates.

The most used screening tests are the Fecal Immunological Test (FIT) and the Fecal Occult Blood Test (FOBT). FIT is currently the most advanced and easiest to use for citizens.

It allows for one test sample to identify blood in the stool. FOBT is still used, but requires three times two samples, making the threshold for participation higher. Some countries opt to screen with sigmoidoscopy (lower part of the large intestine) or colonoscopy (full intestine) by inserting a flexible tube with camera. This method is not recommended as a screening tool: it is expensive and does not lead to the expected participation rates of the target population.

Citizens with positive screening tests with FIT and FOBT will be invited for a colonoscopy or sigmoidoscopy to confirm the diagnosis.

There is ample scientific evidence that screening and colonoscopy reduce mortality of colorectal cancer patients²⁶.

Apart from formal screening, there appears to be a lack of awareness or sense of urgency among GPs to identify colorectal cancer. All GPs should be encouraged to ask for the family history of their patients for colorectal cancer (or other cancers for that matter), as part of a standard questionnaire, which will allow them to inform

patients at risk about the possibility to get tested. The same holds true for patients who are at risk: citizens older than 50 who are obese, are or were smokers, with a daily intake of alcohol and with little physical activity. GPs should provide information to the patient about the option to get tested.

In the future, liquid biopsies will become available, which will facilitate the diagnosis and hopefully lower the threshold for participation in screening programmes.

As part of the diagnosis, genetic and molecular tests can determine the exact nature of the tumour, allowing for a more accurate decision on the treatment.

Patients with a family history of Familial Adenomatous Polyposis or Lynch Syndrome should be tested at an earlier age – mid-teens and mid-twenties respectively - to decide about a monitoring programme, and to decide on whether or not prophylactic surgery or other interventions are needed.

²⁶ International Agency for Research on Cancer - The IARC Perspective on Colorectal Cancer Screening, New England Journal of Medicine, 2018

The patient voice

Around 24% of patients wait more than three months before contacting a clinician once they have identified symptoms. Once a clinician is contacted, 71% of respondents say they are diagnosed within a month²⁷.

25% of patients were misdiagnosed and 33% of patients felt the process was either not very satisfying or were not satisfied at all with the process of establishing the CRC diagnosis.

Recommendations

Today, the time between reporting the first symptoms and the actual diagnosis is four months. It would be advisable for general practitioners to understand the symptoms of colorectal cancer. For patients living with sometimes painful symptoms for months without clarity on the cause or the possible treatment is a burden. It seems essential that all GPs know all the risk factors of the patient (including family history of colorectal cancer and lifestyle choices) in order to be able to assess the risk.

Expected outcomes

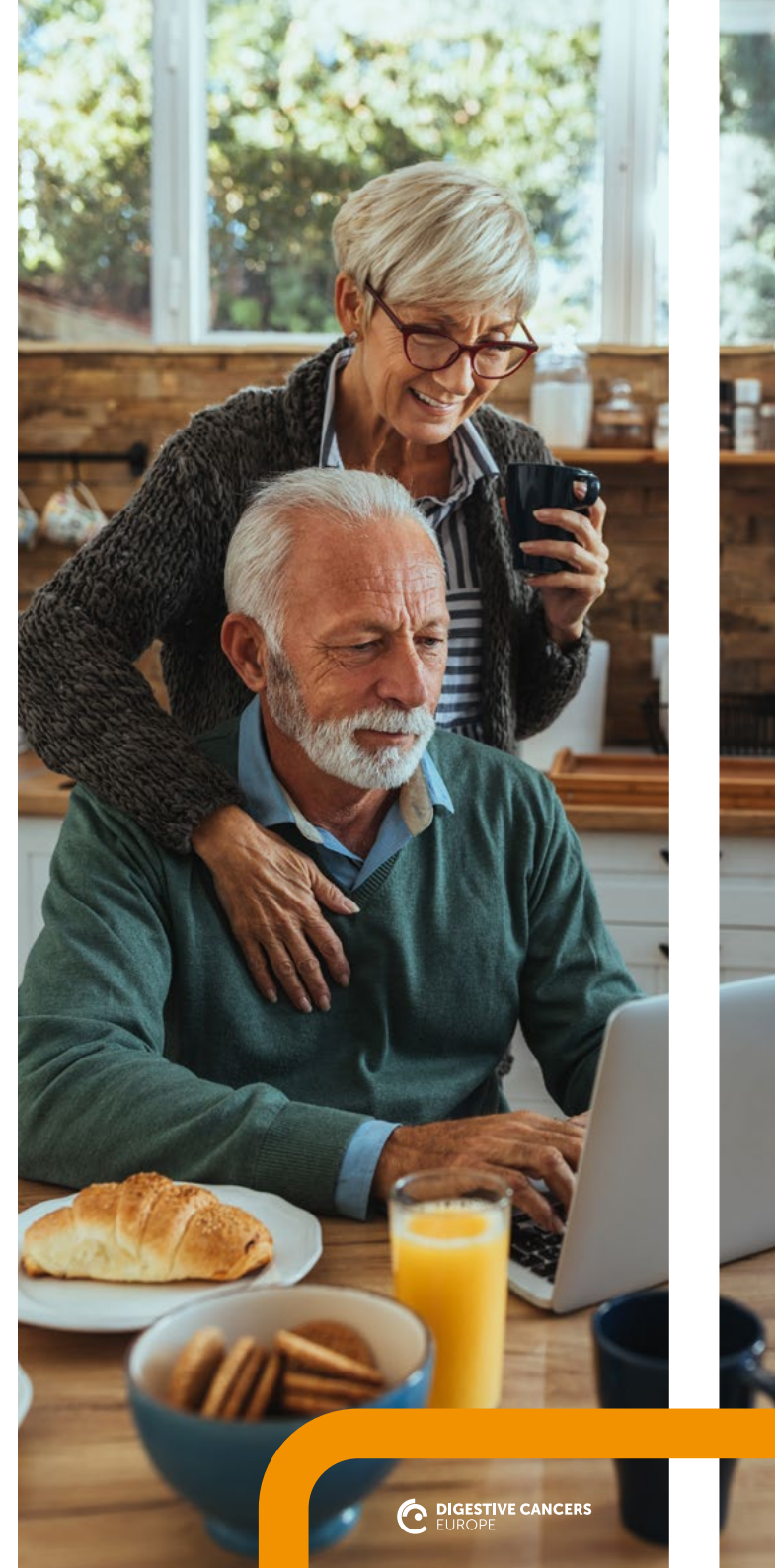
Considering the slow evolution of colorectal cancer, the few months earlier detection will not make a huge difference in terms of population-based outcomes, but it makes a big difference for the individual patient who is kept in discomfort and uncertainty for many months, including the cost of consultations, misdiagnosis and hence also the use of wrong treatments.

The role of patient organisations

Patient organisations help spread the word about the importance of detecting symptoms and reporting them to the GP. Patient organisations participate in education and health literacy campaigns to increase disease awareness and inform citizens on the possibility of getting screened.



²⁷ Understanding the Experience and Needs of Patients with Metastatic Colorectal Cancer – Results of a European Patient Survey, Digestive Cancers Europe, 2020 - <https://www.digestivecancers.eu/wp-content/uploads/2020/09/mCRCsurvey-FINAL.pdf>



The treatment decision: medical and non-medical

The current situation

Once diagnosed, the patient should be able to choose where, when and how to be treated. The patient has a voice, and should be empowered to actively participate in the process.

The European Cancer Organisation developed the European Code Of Cancer Practice²⁸ with a summary of 'Cancer Patient's Rights' on the following core topics:

- 1 Equal access
- 2 Information
- 3 Quality of Care, Expertise and Best Outcomes
- 4 Specialised Multidisciplinary Care
- 5 Shared Decision-Making
- 6 Research & Innovation
- 7 Quality of Life
- 8 Integrated Supportive and Palliative Care
- 9 Survivorship and Rehabilitation
- 10 Reintegration

We refer to this document to understand the full rights of the patient.

The choice of hospital

It is clear from hospital outcomes data that there is a clear-cut association between mortality at one month after surgery and the level of expertise of the hospital in terms of number of patients treated (low and high case load hospitals). A recent report from Germany²⁹ showed that patients with colorectal cancer have a greater chance of survival if they are operated in hospitals with a high case load because complications that can happen after surgery can be better managed in such hospitals³⁰.

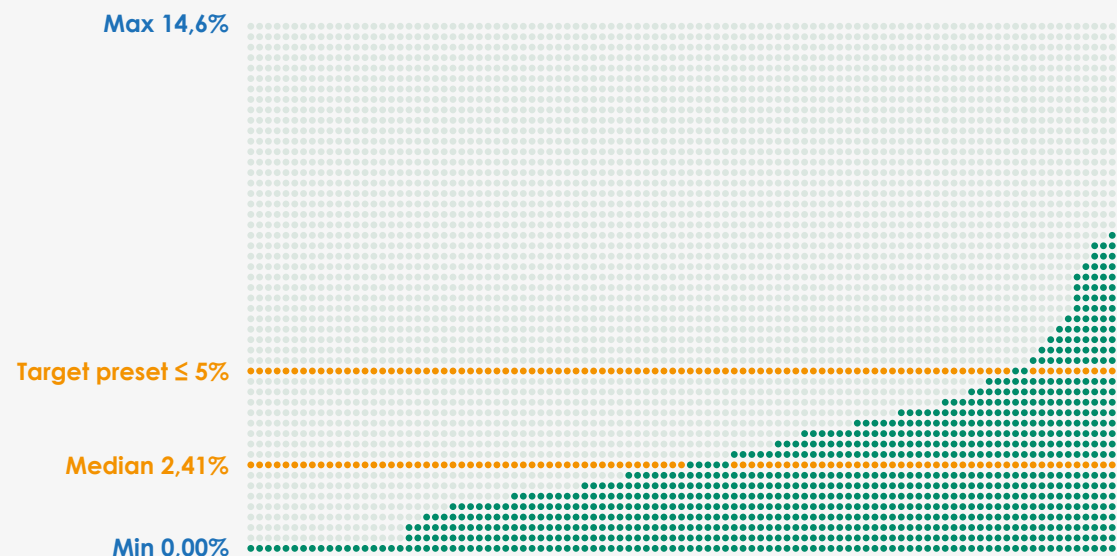


²⁸ The European Code of Cancer Practice, European Cancer Organisation, 2020 - <https://www.europeancancer.org/2-standard/66-european-code-of-cancer-practice>

²⁹ German Cancer Society, Annual Report 2018 of the Certified Colorectal Cancer Centres (CRCCs)

³⁰ Diers J, Wagner J, Baum P, et al. Nationwide in-hospital mortality rate following rectal resection for rectal cancer according to annual hospital volume in Germany. BJS Open. 2020;4(2):310-319

Figure 8: Post-operative mortality of colorectal cancer patients one month after surgery (total of 283 hospitals)



In Belgium, the Netherlands and Sweden, hospital outcomes data are available (albeit not published on an annual basis), which show that patients have a significant higher risk to die in the low volume hospitals compared with high volume ones, with a factor of 10³¹, 13³² and 20³³ respectively.

To note is, unsurprisingly many low volume hospitals do not even have patient statistics. Similar results were found in Switzerland³⁴.

Moreover a study in the UK demonstrated better results for CRC patients in hospitals where clinical trials have been conducted³⁵.

Data from Belgium show that the larger and specialised cancer centres have 5-year survival data of 85% for all colorectal cancer patients (age and stage-adjusted) compared to 60% of other hospitals in the same country. The big difference in outcomes is the result of expertise and specialisation, with all other factors being equal. It is obvious that a cancer centre that treats hundreds of patients with the same condition every year will obtain better results than hospitals that treat a dozen patients with that same condition.

That is why we strongly advocate that all hospitals should be transparent about mortality and survival, and that hospitals that do not reach the threshold of 100 colorectal cancer patients per year should not be allowed to treat them. This is in line with the European Cancer Organisation's Essential Requirements for Quality Colorectal Cancer Care³⁶.



31 Flanders Ministry of Health - www.zorgkwaliteit.be

32 Dutch Ministry of Health - zorgkiezer.nl

33 Institute for Clinical Health Outcomes Measurement (ICHOM)

34 Freya Trautmann et al. "Evidence-based quality standards improve prognosis in colon cancer care", European Journal of Surgical Oncology, May 2018

35 Downing A, Morris EJ, Corrigan N, et al High hospital research participation and improved colorectal cancer survival outcomes: a population-based study, in Gut 2017;66:89-96

36 ECCO Essential Requirements for Quality Cancer Care: Colorectal Cancer. A critical review, in: Critical Reviews in Oncology/Hematology Volume 110, February 2017, Pages 81-93

'Shared Decision-Making'

Once the diagnosis has been established, the patient should be referred to the relevant patient organisation. The patient will be assisted by the experts of the association to better understand the disease and how to manage his or her life around the disease. This also includes the non-medical aspects. Patients who are coached by patient organisations are assumed to have better outcomes, because of better health literacy, less social isolation, better control over the organisation of practical things such as transport, home support, home nursing support, psychological and emotional support, although this has never been measured.

In the last decade, the concept of 'Shared Decision-Making' has been introduced. It is a process that helps the medical team understand the context and expectations of the patient, while at the same time introducing the different treatment options and long term consequences. Studies have demonstrated that Shared Decision-Making leads to higher patient satisfaction and less 'decision regret'³⁷.

The treatment decision should be prepared by the multi-disciplinary oncology team at the hospital. They will evaluate the case of the patient

and come with a recommended approach for treatment. The patient should be informed on the actual diagnosis and about the treatment options, and their consequences, both short-term and long-term.

There is a need to train clinicians in better communication skills. Scientific evidence documents the importance of good doctor-patient communication for the patient to adhere to the treatment and to play an active role in trying to achieve the best outcomes. It has been proposed by consecutive European Initiatives such as the European Partnership for Action Against Cancer (EPAAC) and Cancer Control (CANCON), and it is now also recommended by the ASCO and ESMO Guidelines.

It is important that the patient is fully informed, and that he or she can also ask the relevant questions about the treatment, but also about the capacity and the expertise of the treatment center to deal with the complexity of the diagnosis. The patient has the right to choose where to be treated and by whom as well as having the right to a second opinion.

Patients do not live on their own. The spouse/partner or family should be invited to be part of the discussion, and be equally informed.

The diagnosis will have a deep impact on the patient's life: professionally, financially, mentally. It will require a lot of paperwork with employers, insurance companies, the ministry of health, home nursing organisations, and carers. It requires counsel on the mental aspects of the disease, on nutrition, on physical activity, on social interaction. The disease and its treatment may have lasting physical consequences, such as the use of a stoma pouch, incontinence, sexual dysfunction, sensory neuropathy, or more temporary effects such as low energy levels, fatigue or memory loss.

The European Commission's 'Innovative Partnership for Action Against Cancer' (iPAAC) has taken up the initiative to design a standard for the treatment of colorectal cancer patients in Comprehensive Cancer Networks. This treatment pathway includes the importance of Shared Decision-Making and for the role of patient organisations.



37 Søndergaard SR, Madsen PH, Hilberg O, Jensen KM, Olling K, Steffensen KD. A prospective cohort study of shared decision making in lung cancer diagnostics: Impact of using a patient decision aid. *Patient Educ Couns*. 2019;102(11):1961-1968. doi:10.1016/j.pec.2019.05.018

The patient voice

We refer to the All.can survey among cancer patients. It demonstrates that almost half of respondents (47%) did not feel sufficiently involved in deciding which treatment option was best for them³⁸.

Because managing an illness is much more than its clinical aspects, it is critical that newly diagnosed patients are brought in contact with patients who have already gone through the patient journey, so that they can anticipate what awaits them and how to deal with the disease, its treatment and possible consequences. In the same survey by All.can, 41% of respondents say they were not given information at the hospital about available peer-support groups.

In our own survey³⁹, 84% of patients named their oncologist to be the most valuable contact for medical information, and 36% of patients felt they should be spoken to in a language they understand to improve their relationship with their Healthcare Team.

Recommendation

We refer to the “ESMO consensus guidelines for the management of patients with metastatic colorectal cancer”⁴⁰ for the clinical aspects of the diagnosis and the subsequent treatment, the “ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up of Rectal Cancer”⁴¹ and the “ESMO Consensus Guidelines for management of patients with colon and rectal cancer. A personalized approach to clinical decision making”⁴². It is essential that patients are provided with the full picture of their diagnosis, treatment options and long-term consequences of both the disease and the treatment. Patients should be referred to the relevant patient organisations from the start.

Hospitals and patient organisations can organise patient information sessions to help patients address the non-medical aspects of the disease.

³⁸ All.can: Patient insights on cancer care: opportunities for improving efficiency, 2019-
<https://www.all-can.org/what-we-do/research/patient-survey/>

³⁹ Understanding the Experience and Needs of Patients with Metastatic Colorectal Cancer – Results of a European Patient Survey, Digestive Cancers Europe, 2020 -
<https://www.digestivecancers.eu/wp-content/uploads/2020/09/mCRCsurvey-FINAL.pdf>

⁴⁰ ESMO consensus guidelines for the management of patients with metastatic colorectal cancer, Annals of Oncology, 2016

⁴¹ ESMO Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up, Annals of Oncology, 2019

⁴² ESMO Consensus Guidelines for management of patients with colon and rectal cancer. A personalized approach to clinical decision making, Annals of Oncology, 2012



Psychosocial oncology care

contributes to better clinical outcomes and patients' well-being

Cancer and its treatments⁴³ have a significant impact on the quality of life of patients and their families and carers. Once the diagnosis has been given, the emotional impact on a patient and his or her family is strong. Children or parents need to be informed, friends and family, employers and colleagues. The diagnosis is disruptive to a patient's life. Everything changes, all perspectives, all plans. It weighs on self-image and relational aspects. It has often financial consequences that make the situation even worse.

A substantial number of cancer patients and survivors experience high levels of cancer-related distress (30-45%)^{1,2}, and may develop more serious mental health problems such as adjustment disorders, anxiety disorders and depression³⁻⁵. These conditions negatively impact on clinical outcomes such as treatment compliance, survival and quality of life and require specialised psychosocial care⁶. Psychosocial problems also affect

the patient's family with a resultant increase in the emotional distress among the patient's caregivers that may continue into the bereavement period with greater risk of complicated or traumatic grief among relatives⁷. Patients' and their family supportive care needs must be central component of quality comprehensive cancer care⁸.

The speciality of psycho-oncology addresses a range of psychosocial, behavioural, spiritual and existential dimensions that the patient and family face throughout the cancer care continuum. Therefore a primary goal is that all cancer patients and their families receive optimal psychosocial care at all stages of the disease and through survivorship⁹.

Despite the major implications of psychosocial morbidity for patients' clinical outcomes and well-being, psychosocial issues in cancer are still all too often dismissed or underestimated, and not yet regularly offered to cancer patients^{10,11}.

The significance of the psychosocial aspects of cancer and its treatment is growing in importance owing to the trend for increasing survival from cancer that has resulted in growing numbers of people that are cured from or living with cancer for many years in several countries of the European region.

In 2014, the International Psycho-Oncology Society (IPOS) (www.ipos-society.org) proposed a new international standard of quality cancer care¹² endorsed by the UICC and 75 other international organisations and scientific societies related to cancer treatment and care, which states:

- Psychosocial cancer care should be recognised as a universal human right;
- Quality cancer care must integrate the psychosocial domain into routine care;
- **Distress** should be measured as the **6th Vital Sign** after temperature, blood pressure, pulse, respiratory rate and pain^{13,14}.



43 Travado L, & Dalmas M. Psychosocial Oncology Care. (35-39). In European Guide for Quality National Cancer Control Programmes. Tif Albreht, Jose M. Martin-Moreno, Marjetka Jelenc, Lydia Gorgojo, Meggan Harris (Eds). National Institute of Public Health, Ljubljana, Slovenia, 2015.

Screening for Distress, 6th Vital Sign and assessment of psychosocial needs

Methods for assessing distress and psychological morbidity in cancer patients are often not routinely employed in cancer settings. Addressing the often-neglected aspects of patients' and families' psychosocial needs should be routine in clinical practice. There is evidence this has positive benefits for patients' clinical outcomes¹⁸ and can be used as an endpoint of cancer care, as a useful indicator of the quality of performance of the services.

Easy-to-use methods for screening for distress (e.g., NCCN Distress Thermometer) have been developed, tested, and validated in many European countries and worldwide¹⁹. Integration of psychosocial care professionals in cancer care (multidisciplinary teams) is important for proper identification, and treatment of patients' psychosocial needs, or referral to more specialised services according to their needs such as psycho-oncology care.

Evidence-based psychosocial interventions

Psycho-oncology interventions have proved to be effective in preventing and reducing severe distress and psychological morbidity and in improving patients' clinical outcomes including quality of life and survival²⁰⁻²². A wide range of psycho-oncology approaches and treatments such as educational and psychological support interventions, counselling, coping skills and psychotherapy (individual, group or family) can be employed.

It is recommended that psycho-oncology services be located in national cancer care facilities. The allocation of specialised healthcare professionals in psycho-oncology for these services and a budget for its sustainability will be the best way to ensure service provision and quality of services.

In a recent review of the literature⁴⁴ various psychosocial interventions for patients with colorectal cancer, including educational interventions, cognitive-behavioural therapy, relaxation training and supportive group therapy were found to reduce colorectal patients' length of hospital stay,

days to stoma proficiency and hospital anxiety and depression, and to improve patients' quality of life.

The Australian Cancer Council has developed Guidelines for psycho-social care that could be used more widely around the world⁴⁵.

The voice of the patient

Around 26% of patients believe there should be psychologists to help them during their colorectal cancer treatment, which is currently not available⁴⁶.



44 Hoon LS, Chi Sally CW, Hong-Gu H. Effect of psychosocial interventions on outcomes of patients with colorectal cancer: a review of the literature. *Eur J Oncol Nurs*. 2013;17(6):883-891. doi:10.1016/j.ejon.2013.05.001

45 https://wiki.cancer.org.au/australia/Guidelines:Colorectal_cancer/Psychosocial_care

46 Understanding the Experience and Needs of Patients with Metastatic Colorectal Cancer – Results of a European Patient Survey, Digestive Cancers Europe, 2020 - <https://www.digestivecancers.eu/wp-content/uploads/2020/09/mCRCsurvey-FINAL.pdf>

The current situation

Surgery is the primary treatment for colorectal cancer patients. When diagnosed at early stage (I and II), surgical treatment aiming to remove the involved segment of bowel together with its lymphatic drainage represents the gold standard without the need of other oncologic therapy. Unfortunately, as we have seen, most patients (about two third) are diagnosed in advanced stage when the tumor has already involved regional lymph nodes (stage III) or metastatised to other organs. Advanced surgery alone is not sufficient and other therapies – chemo and radiotherapy – are necessary for adequate treatment⁴⁷.

In colon cancer, but even more so in rectal cancer, precision surgery is of the essence, because of the longer term consequences on the quality of life for patients, including the use of a stoma bag or also the risks of incontinence.

It is well recognized that a minimally invasive technique (i.e. laparoscopic or robotic approach) can be safely carried out for colorectal cancer offering the patients a lot of advantages compared to the conventional open surgery approach in terms of postoperative recovery and long-term quality of life⁴⁸.

As for any technical intervention the importance of having the right equipment and the right experienced surgeon is crucial especially when surgery is performed by a minimally invasive approach. The rate of minimally invasive surgery for colorectal cancer is currently higher than 50% in Korea, the Netherlands, the UK and Australia. The remaining European countries present high variations, ranging from 7 to 35%⁴⁹.

The type and the nature of the surgery also differs by country. A recent study shows that the lower overall survival of colorectal cancer in Denmark and the UK as compared to Norway and Sweden may be attributable to the type of surgery and the age at which resection is still conducted, with Norway and Sweden also conducting more surgery on patients older than 75 years of age⁵⁰.



47 Siegel RL, Miller KD, Goding Sauer A, Fedewa SA, Butterly LF, Anderson JC, Cercek A, Smith RA, Jemal A. Colorectal cancer statistics, 2020. CA Cancer J Clin. 2020 Mar 5;Van Cutsem E, Cervantes A, Nordlinger B, Arnold D; ESMO Guidelines Working Group. Metastatic colorectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2014 Sep;25 Suppl 3:iii1-9

48 Clinical Outcomes of Surgical Therapy Study Group. A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med 2004; 350: 2050–2059.28. Hewett PJ, Allardycce RA, Bagshaw PF et al. Short-term outcomes of the Australasian randomized clinical study comparing laparoscopic and conventional open surgical treatments for colon cancer: the ALCCaS trial. Ann Surg 2008; 248:728–738

49 Lorenzon L, Biondi A, Carus T, et al. Achieving high quality standards in laparoscopic colon resection for cancer: A Delphi consensus-based position paper. Eur J Surg Oncol. 2018 Apr;44(4):469-483

50 Sara Benítez Majano et al. Surgical treatment and survival from colorectal cancer in Denmark, England, Norway, and Sweden: a population-based study, The Lancet, January 2019

Best practice

The best practice hospitals typically treat hundreds of patients annually and have 5-year overall survival of 85%, despite having the highest number of patients. These hospitals have multi-disciplinary teams, highly-specialised surgeons, better technology, and of course more experience and expertise in the management of complex patients. Many studies confirmed clearly the presence of a volume-outcome relationship in colorectal cancer surgery, based on hospital and surgeon case volume and specialisation⁵¹.

Best practice hospitals also follow what happens with their patients during hospital stays. They organise exit interviews to understand and improve all aspects of the patient experience in the hospital, and they organise focus group sessions with patients to brainstorm. We also welcome the Italian approach to benchmark hospitals for their performance in order to apply best practices to improve overall patient outcomes.

Recommendations

Patients should have freedom of choice in their treatment, and that includes the hospital where they will have their surgery. Therefore hospitals and treating physicians have to be transparent about their expertise and the number of patients they treat annually.

All hospitals in Europe should report their data, so that patients and referring GPs can make informed choices.

Policy-makers have to ensure that patients with complex diseases are only treated in hospitals with the right expertise.

This includes the application of the European Cancer Organisation's Essential Requirements for Quality Cancer Care in Colorectal Cancer: "Based on the existing evidence, the European Cancer Organisation's expert group recommends that for a hospital to be considered as a colorectal cancer centre it should manage at least 100 new CRC cases a year"⁵².

In this respect, we already welcome the example given by the Belgian government for oesophageal and pancreatic cancer, where complex surgery can only be conducted in specialised hospitals. This approach should be expanded across Europe and include colorectal and gastric cancers.

51 Archampong D, Borowski D, Wille-Jørgensen P, Iversen LH. Workload and surgeon's specialty for outcome after colorectal cancer surgery. Cochrane Database Syst Rev. 2012 Mar 14;(3):CD005391 - Huo YR, Phan K, Morris DL, Liauw W. Systematic review and a meta-analysis of hospital and surgeon volume/outcome relationships in colorectal cancer surgery. J Gastrointest Oncol. 2017 Jun;8(3):534-546

52 Beets et al: "ECCO Essential Requirements for Quality Cancer Care: Colorectal Cancer", Critical Reviews in Oncology/Hematology 110 (2017) 81-93

Expected outcomes

Today, colorectal cancer overall survival after 5 years is around 60%. The best hospitals reach a 5 year survival of 85% among their patients. The impact of treating patients in expert centers is obvious. Again, this has not yet been calculated at a population level, but the result is possibly very significant.

The role of patient organisations

Patient organisations are critical in this respect. They can educate individual patients in asking the right questions to their treating physicians, so that they can make informed choices about where best to be operated.

Furthermore, patient organisations can work with the hospitals to educate and inform newly diagnosed patients about their treatment pathway, about the practical and non-medical aspects of treatment. Patients who are coached in this way have better outcomes than patients without support.



Radiotherapy

Radiation therapy⁵³ is a treatment using high-energy rays (such as x-rays) or particles to destroy cancer cells. It is part of standard management for rectal cancer, but rarely used for colon cancer. For some colon and rectal cancers, treating with chemotherapy at the same time can make radiation therapy work better. Using these 2 treatments together is called chemoradiation.

For **rectal cancer**, radiation therapy is used either before and/or after surgery, often along with chemotherapy, to help keep the cancer from coming back. Many doctors now favor giving radiation therapy before surgery, as it may make it easier to remove the cancer, especially if the cancer's size and/or location might make surgery difficult. This is called neoadjuvant treatment. Giving chemoradiation before surgery can also help lower the chances of damaging the sphincter muscles in the rectum when surgery is done. In either case, nearby lymph nodes are usually treated too. We refer to the ESMO Guidelines on Rectal Cancer for more information⁵⁴.

With pre-operative radiotherapy, better results are obtained for locoregional control and less acute toxicity. After the use of radiotherapy, a 'watch and wait' strategy can be adopted to evaluate the outcome of the treatment.

Most countries apply preoperative radiotherapy or chemoradiotherapy for defined subgroups of patients.

Recommendation

Preoperative radiotherapy or chemoradiotherapy is part of the routine management of rectal cancers. National guidelines differ, but it is generally used for locally advanced cancers with high risk of local recurrence.

As for surgery, radiotherapy needs to be conducted in specialised cancer centers.



⁵³ American Cancer Society, 2020

⁵⁴ R. Glynn-Jones et al. Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up, Annals of Oncology, 2017

Oncology drugs



The current situation

Pharmaceutical treatment can be used either prior to surgery (neo-adjuvant) or after surgery (adjuvant). Or both.
In some cases no surgery is required, only pharmaceutical treatment.

The current standard of care in chemotherapy are the combination treatments Folfiri (leucovorin calcium + fluorouracil + irinotecan hydrochloride) or Folfex (leucovorin calcium + fluorouracil + oxaliplatin) in combination with Anti-EGFR (epidermal growth factor receptor) therapies or anti-VEGF (Anti-vascular endothelial growth factor) therapies.

With the better understanding of our genetic system, new drugs have become available that target specific mutations of the disease.

Since the year 2000, eleven new pharmaceutical treatments have been approved to treat colorectal cancer (see table on next page), offering additional opportunities to the few existing treatments. Most new pharmaceuticals are used for metastatic patients for whom limited treatment options remain available. With proper health education, screening and early diagnosis, the use of many of these drugs would not even be needed. For the individual patients they can make a significant difference, in terms of overall survival and quality of life.

The estimated cost per capita in Europe for pharmaceutical treatment for colorectal cancer patients is 2.28 billion euro in 2018, or 5 euro/inhabitant⁵⁵.



⁵⁵ The Cost of Cancers of the Digestive System in Europe, Swedish Institute of Health Economics, 2020

Generic name	Brand name	Indication
Capecitabine	Xeloda*	Adjuvant stage III or First line metastatic
Bevacizumab	Avastin/Mvasi/Zirabev	In combination for metastatic patients
Irinotecan Hydrochloride	Camptosar	Metastatic cancer or recurred cancer
Cetuximab	Erbitux	EGFR Protein or wild-type KRAS mutation. Metastatic combination therapy or for non-responders with other treatments
Ramucirumab	Cyramza	Metastasised in combination with Folfiri
Oxaliplatin	Eloxatin	Advanced colorectal, adjuvant
Fluorouracil (5-FU)	Efudex	Injection
Leucovorin Calcium	Fusilev	Palliative treatment in advanced stage
Ipilimumab	Yervoy	Used with nivolumab to treat metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) cancer that got worse after treatment with a fluoropyrimidine, oxaliplatin, and irinotecan hydrochloride.
Pembrolizumab	Keytruda	treat metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) cancer that got worse after treatment with a fluoropyrimidine, oxaliplatin, and irinotecan hydrochloride
Trifluridine and Tipiracil Hydrochloride	Lonsurf	metastasized (spread to other parts of the body). It is used in adults who have already been treated with a fluoropyrimidine, oxaliplatin, irinotecan hydrochloride, and a VEGF inhibitor.
Nivolumab	Opdivo	It is used alone or with ipilimumab to treat metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) cancer that got worse after treatment with a fluoropyrimidine, oxaliplatin, and irinotecan hydrochloride.
Panitumumab	Vectibix	Wild Type RAS, in combination with Folfax or alone
Ramucirumab	Cyramza	Metastatic. It is used with FOLFIRI in patients whose disease has gotten worse during or after treatment with bevacizumab, oxaliplatin, and a fluoropyrimidine.
Regorafenib	Stivarga	Metastatic. It is used in patients who have not gotten better with other treatments.
Ziv-Aflibercept	Zaltrap	To be used with Folfiri in metastasised tumours. It is used in patients whose disease has not gotten better with other chemotherapy.

* there are other generic drugs

** there are other biosimilar drugs

The current standard of care has become a generic treatment, and several new biosimilars have been approved for colorectal cancer by the European Medicines Agency, and they will be available in 2022 once the current originator loses its exclusivity.

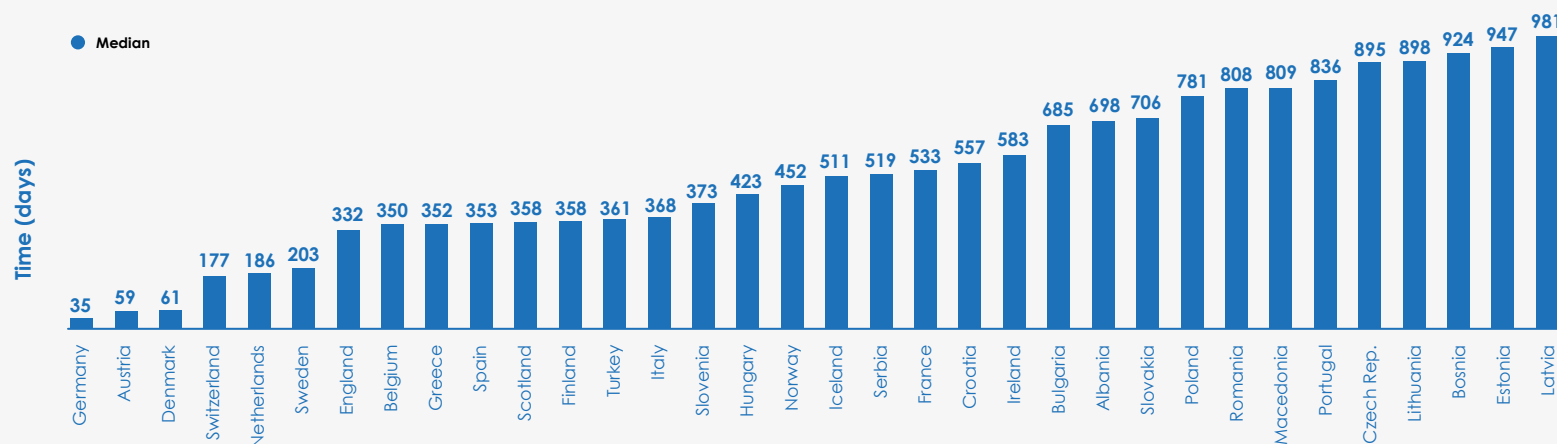
Hyperthermic Intraperitoneal Chemotherapy (HIPEC) is a process in which heated chemotherapy is pumped directly into the abdomen after surgery. Used with surgery, this treatment targets abdominal cancers that have spread into the lining of the abdominal cavity (peritoneum and/or peritoneal cavity). These advanced cancers are notoriously difficult to treat. Surgery alone is rarely successful, and traditional chemotherapy yields limited results.

Best practice

The process from discovery to approval is a long one, and may take over ten years, but the process between actual approval by the European Medicines Agency and the approval for pricing and reimbursement at national level may take many years too. Despite the facts that many of these drugs are life-saving for patients, the average time to market after approval is more than one year.

The best practice is to be found in Germany, where drugs become immediately available with price and reimbursement discussions taking place after market entry. The average delay between market authorisation and patient access for oncology products is between 2 months to over 2.5 years⁵⁶. The countries with the highest presence of newly approved oncology drugs are Germany, Austria, Denmark and the Netherlands (more than 80% of drugs approved in the previous three years).

Figure 9: Oncology median time to availability (2015 – 2018)



56 IQVIA - EFPIA Patient W.A.I.T. Indicator 2019 survey, 2020

A second aspect is to be able to identify which drug should be used for which treatment. If the genetic cause is identified, it may be better to have a targeted treatment that works on the cause, either before or after surgery, sometimes in combination with chemotherapy. These genetic tests allow the correct identification of the cause of the disease, and its subsequent treatment.

One other new technique that is currently being launched in Europe is the creation of micro-tumours with cells of the patient's tumour so that in the lab the best pharmaceutical treatment can be identified based on the effect observed on the micro-tumour. The technology can also be used for pharmaceuticals not indicated for colorectal cancer (off-label). This can be done within a week's time. The technology measures treatment effectiveness and resistance for the individual cancer patient. The right individual cancer treatment saves the patient from unnecessary side effects and provides cost efficiency in drug-spending.

Recommendations

Once a drug has been approved by the European Medicines Agency and the European Commission, it is unacceptable that patients should have to wait years for new treatments to become available, including biosimilars. Industry and public health authorities should work on more patient-centric approaches to make innovation rapidly accessible to patients who need them.

Molecular and genetic testing should be done once the diagnosis has been made in order to identify the best possible treatment for the patient.

Expected outcomes

Even if the standard of care in chemotherapy is no longer under patent, and generics and biosimilars are already available for the treatment of colorectal cancer, the newest treatments are primarily indicated for limited segments of the patient population.

When biosimilars are available, they should also be used. Here, we refer to our Position Paper on the Use of Biosimilars⁵⁷.

The voice of patients

- 22% of patients said they were tested for RAS mutation⁵⁸
- 74% of patients were given clear information about the treatment side-effects

The role of patient organisations

Patient organisations can assist patients with their treatment options. The consequences of chemotherapy can be harsh, resulting in physical discomfort and long absence from work, or social isolation. Patient organisations can assist with the non-medical aspects, including guidance on nutrition, physical exercise, psycho-oncology, work-related topics and paperwork.

Patient organisations can also assist with the identification of new treatments that are available abroad and that might be of help in a cross-border setting or more experimental treatments that are at the moment under clinical investigation.



⁵⁷ Digestive Cancers Europe - Position Paper on the Use of Biosimilars, 2019

⁵⁸ Understanding the Experience and Needs of Patients with Metastatic Colorectal Cancer – Results of a European Patient Survey, Digestive Cancers Europe, 2020 - <https://www.digesticancers.eu/wp-content/uploads/2020/09/mCRCsurvey-FINAL.pdf>

Nutrition & Physical activity

during treatment

Nutrition

While bad lifestyle habits can be a risk factor for cancer, nutrition is a critical aspect of the treatment too.

During treatment, and especially because of chemotherapy, patients will lose appetite, suffer from nausea and vomiting, and may suffer from changed taste perceptions.

For example, during chemotherapy, weight loss occurs in 40%–92% of patients 65 years and older, depending on the tumor site⁵⁹.

Many studies have demonstrated that maintaining a good nutritional status through nutrition intervention can help individuals with cancer improve outcomes including⁶⁰:

- Increased energy and protein intake
- Maintain and gain body weight
- Improve quality of life
- Improve strength and energy levels
- Manage treatment-related side effects
- Avoid dose reduction and treatment delays
- Reduce unplanned hospital admissions

Malnutrition is prevalent with cancer, and both percent weight loss and BMI predict survival independently of conventional prognostic factors⁶¹. In cancer patients, malnutrition is associated with treatment toxicity, complications, reduced physical functioning, and decreased survival⁶². Accordingly, newly published expert guidelines advise nutrition screening and assessment for all cancer patients⁶³.

The European Society for Clinical Nutrition and Metabolism (ESPEN) has published Guidelines on Nutrition in Cancer Patients with the added expert group Recommendations for Action against Cancer-related Malnutrition.

In patients with colorectal cancer, followed up after radiotherapy for a median 6.5 years, those who received individualised nutritional counseling to maintain protein and energy intake experienced less treatment toxicity, better quality of life, and lower mortality compared to patients randomised to either oral supplements and usual diet, or only their usual diet⁶⁴.

Cachexia is a condition of malnutrition defined by more than 10% of weight loss and a Body Mass Index (BMI) below 20. An unexpectedly high proportion of patients meet the criteria for cachexia.

59 Sánchez-Lara K, Ugalde-Morales E, Motola-Kuba D, Green D. Gastrointestinal symptoms and weight loss in cancer patients receiving chemotherapy. Br J Nutr 2013;109:894-7.

60 Malnutrition in Patients With Cancer: An Often Overlooked and Undertreated Problem, in Supportive Care, October 30, 2013

61 Martin L, Senesse P, Gioulbasanis I, Antoun S, Bozzetti F, Deans C, Strasser F, Thoresen L, Jagoe RT, Chasen M, Lundholm K, Bosaeus I, Fearon KH, Baracos VE. Diagnostic criteria for the classification of cancer-associated weight loss. J Clin Oncol. 2015; 33:90-99.

62 Maurizio Muscaritoli et al. Prevalence of malnutrition in patients at first medical oncology visit: the PreMiO study, Oncotarget, 2017

63 Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, Fearon K, Hutterer E, Isenring E, Kaasa S, Krznaric Z, Laird B, Larsson M, et al. ESPEN guidelines on nutrition in cancer patients. Clin Nutr. 2017; 36:11-48

64 Macmillan Cancer Support. Macmillan Learnzone. Weight Loss and Eating. Available from: <http://www.learnzone.org.uk/courses/course.php?id=40>.

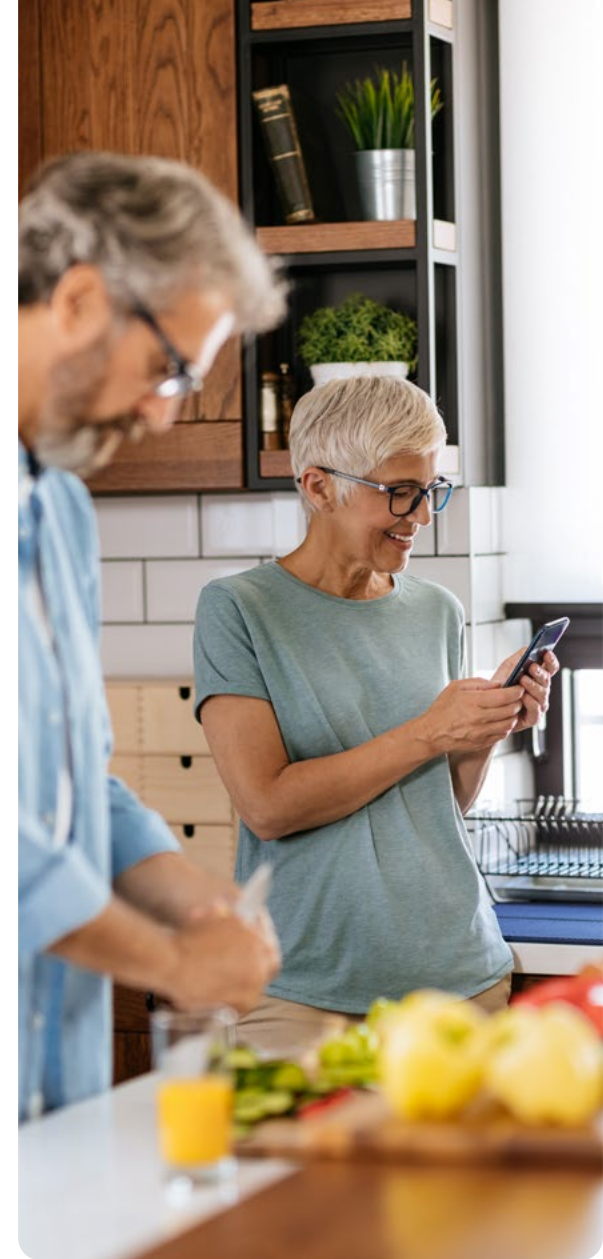
A recent study in Italy demonstrated that more than 60% of colorectal cancer patients could be classified as cachectic, based on BMI and weight loss⁶⁵. The study also comes to the following observations:

- Even for cancer patients who are not malnourished before surgery, 14-day pre-surgical nutrition therapy significantly improved nutritional status and reduced post-operative surgical complications
- Nutritional status affects acceptability and tolerability of anticancer therapies, in turn altering therapeutic choices. An accurate evaluation of nutritional status is of paramount importance in treating cancer patients, especially in early stages. The efficacy of chemotherapy, for example, could be impaired by a reduction in the patient's therapy tolerance, which is influenced by a poor nutritional status
- The relationship between disease curability/severity and subjective symptoms, such as appetite loss or degree of malnutrition, underlines the need for an integrated support team including a psycho-oncologist, who can address and treat psychological aspects (depression, loss of hope, and anxiety) while other team members deal with medical issues

A survey conducted by the European Cancer Patient Coalition demonstrates that the majority of physicians (53,9%; n=467) did not check the nutritional status of their patients, including their body weight, or did not refer patients with feeding problems to a nutrition specialist (76,7%; n=462)⁶⁶. Hospital studies in Europe showed that only one in three cancer patients at risk of malnutrition in fact received nutritional support^{67,68}.

In the early nineties, even up to 20% of patients died of malnutrition and not of their cancer⁶⁹. This issue has improved, but it still occurs especially among elderly patients⁷⁰.

The issue is even more severe for colorectal cancer patients who are usually in the older age groups, who have a higher prevalence of high cholesterol and type 2 diabetes. These patients are more likely to be on a low-fat and low-sugar diet even before treatment. If they continue with their diet during chemotherapy, the consequences are even more severe. Patients could be advised to switch back to a high calorie, high fat and high sugar diet. Again, it is critical that the treating medical team is fully informed of the patient's full condition in order to give complete advice.



65 Muscaritoli M, Lucia S, Farcomeni A, et al. Prevalence of malnutrition in patients at first medical oncology visit: the PreMiO study. *Oncotarget*. 2017;8(45):79884-79896. Published 2017 Aug 10. doi:10.18632/oncotarget.20168

66 European Cancer Patient Coalition: Living Well During Treatment, 2019

67 Prevalence of malnutrition and current use of nutrition support in patients with cancer. Hébuterne X, Lemarié E, Michallet M, de Montreuil CB, Schneider SM, Goldwasser F. *JPN J Parenter Enteral Nutr*. 2014 Feb; 38(2):196-204

68 Prevalence of hospital malnutrition in cancer patients: a sub-analysis of the PREDyCES® study. Planas M, Álvarez-Hernández J, León-Sanz M, Celaya-Pérez S, Araujo K, García de Lorenzo A, PREDyCES® researchers. *Support Care Cancer*. 2016 Jan; 24(1):429-435.

69 Ottery FD. Cancer cachexia: prevention, early diagnosis, and management. *Cancer Pract*. 1994;2:123-131.

70 Zhang et al. Malnutrition and overall survival in older patients with cancer, in *Clinical Nutrition*, July 1, 2020

Physical activity

Physical activity is as important as good nutrition, and both go hand-in-hand. Physical activity facilitates recovery, improves nutritional intake and has positive effects on mental states.

Physical activity starts with normal activities in the home, moving then to daily walks, to specific fitness training, until the former physical shape is regained. This physical strengthening can be a rewarding project under the patient's control.

Regular exercise during cancer treatment has the following positive effects:

- Keeps or improves your physical abilities (how well you can use your body to do things)
- Improves balance, lower risk of falls and broken bones
- Keeps muscles from wasting due to inactivity
- Lowers the risk of heart disease
- Lessens the risk of osteoporosis (weak bones that are more likely to break)
- Improves blood flow to your legs and lowers the risk of blood clots



- Makes you less dependent on others for help with normal activities of daily living
- Improves your self-esteem
- Lowers the risk of being anxious and depressed
- Lessens nausea
- Improves your ability to keep social contacts
- Lessens symptoms of tiredness (fatigue)
- Helps you control your weight
- Improves your quality of life

At least 20 studies of people with breast, colorectal, prostate, and ovarian cancer have suggested that physically active cancer survivors have a lower risk of cancer recurrence and improved survival compared with those who are inactive⁷¹.

Despite its relative importance, only 53% of physicians gave their cancer patients advice on physical activity⁷².

The health economic aspect of nutrition and physical activity

Nutrition and physical activity are among the most cost-effective means of impacting patient well-being and even in some cases to increase outcomes. It is disturbing to see how their importance is undervalued in medical practice.

The role of patient organisations

Patient organisations play a very important role in making the patient alert to all the aspects of the disease and to help identify possible issues and to answer questions. Some patient organisations offer nutritional counsel, and most will be able to refer their members to specialised cancer dietitians.



⁷¹ American Cancer Society, website, consulted 2020

⁷² European Cancer Patient Coalition: Living Well During Treatment, 2019

Quality of Life and Survivorship

Cancer survivors live between celebration and concern⁷³. The diagnosis to be free of cancer is a relief, but they live with the fear of recurrence. For five years after treatment, the patient will have to be followed up with frequent tests, quarterly, every six months or annually: colonoscopy, CT and MR scans. This implies that the emotional stress within the family about the future prospects of the patient remains.

The patient will want to re-integrate into normal life, even if the shadow of cancer will remain a presence in every decision they make about work, holidays, travel, or other family decisions.

Clinical consequences

Research has shown that physical and mental quality of life for colorectal cancer survivors was inferior when compared with age-matched individuals without cancer. Although issues and symptoms were most prominent during the first three

years, long-term effects of treatment can persist and include fatigue, sleep difficulty, fear of recurrence, anxiety, depression, negative body image, sensory neuropathy, gastrointestinal problems, urinary incontinence, and sexual dysfunction. The unique challenges and issues of colorectal cancer survivors can and should be addressed by health care providers and the research community to ensure effective interventions and models of care to manage these problems⁷⁴.

At the psychological level, fear, anxiety, sleep difficulties, negative body image, change of perspective on life, and fatigue may play a significant role. This again stresses the importance of timely psychosocial care to reduce symptoms and increase Quality of Life.

Social consequences

In the work environment, the situation will also be changed, even if the patient returns to his or her previous job. Will he or she still be able to function as before? What about the physical aspect of the work? Sometimes stigma plays a role and the

anticipation among employers that the disease might return, limiting prospects for specific jobs requiring physical effort, a promotion or undertaking international functions. Chemotherapy may also have long-lasting effects on the individual's energy levels. Discussing all these aspects is a must, including the preparation of teamwork and possible changes in task division and temporary assignments.

Many patients lose their jobs or change jobs because of the disease. The disease itself will result in unexpected financial demands, and even if in most European countries, healthcare costs are reimbursed, the other costs related to the disease are not (absence from work of carers, transport to the hospital, medication that is not reimbursed, psychological support, etc.).

Once you have been diagnosed with cancer, it is difficult to get new financial services at a reasonable cost, including loans, mortgages and insurances, including travel insurance.

⁷³ For more see the section on Survivorship and rehabilitation. In European Guide for Quality National Cancer Control Programmes. Tit Albreht, Jose M. Martin-Moreno, Marjetka Jelenc, Lydia Gorgojo, Meggan Harris (Eds). National Institute of Public Health, Ljubljana, Slovenia, 2015.

⁷⁴ Crystal Denlinger, The Challenges of Colorectal Cancer Survivorship, J Natl Compr Canc Netw. 2009

The voice of the patient

The highest needs as identified by patients are⁷⁵:

- 26% professional psychological support
- 25% talking to other patients
- 23% patient support programs

Around one quarter of patients say that their disease negatively impacted their income.



Recommendation

All patients should be offered the possibility to have their survivorship needs assessed and a survivorship care plan established to address them as stated by the National Comprehensive Cancer Network (NCCN) Survivorship Guidelines⁷⁶

⁷⁵ Understanding the Experience and Needs of Patients with Metastatic Colorectal Cancer – Results of a European Patient Survey, Digestive Cancers Europe, 2020 - <https://www.digestivecancers.eu/wp-content/uploads/2020/09/mCRCsurvey-FINAL.pdf>

⁷⁶ NCCN Survivorship Guidelines : https://www.nccn.org/professionals/physician_gls/pdf/survivorship.pdf



Back-to-work strategies

The current situation

Most patients want to be able to pick up their lives as soon as possible, and that includes going back to work. Unfortunately, because of their disease, patients can lose their job, and find it hard to get back to work. Healthcare expenditure is often looked at in isolation by politicians who decide about budgets, but the economic cost of skilled people not being employed is high. Governments should invest, together with employers, unions and insurers, to have more proactive initiatives to help patients get back to work.

For patients whose absence is temporary and who have the certainty to keep their role, it is critical to be able to remain in contact with supervisors and colleagues. It is also of high importance to agree on how the patient returns to work, in which work regimen, and with a good task division within the team. Surgery and chemotherapy have a significant impact on a patient's level of energy, and it is advisable to return to work with a clear appreciation of the change the disease may have had on the patient, even after being declared free of cancer.

Best practice

The best practice is again to be found in the Netherlands, where employers have the obligation to continue to pay the employee for two years, with an additional obligation for both parties to keep working on a back-to-work strategy. In this way, the employee never formally leaves the company during the two-year period.

In many countries, organisations exist to help coach patients back to work, whether specifically for cancer patients or for all patients.

We also advocate for the 'right to be forgotten'. Patients who survive their disease are no longer patients and should not be considered as such. Their employers should give them the same chances and opportunities like any other member of the staff. This 'right to be forgotten' is equally important towards financial institutions in order to get loans, insurance or mortgages. France, Belgium and the Netherlands have already implemented laws to that effect.



Health economic aspects

In the European Union, the current estimate of absence from work in the active population because of colorectal cancer is estimated to be around 1.7 billion euro⁷⁷. The potential value for patients and society to facilitate reintegration in a work environment is important and should be taken into consideration when making health economic investment decisions.

Recommendations

Many models are possible within the context of the social legislation in each country. The critical thing is to get patients back to work when they are ready for it, and preferably in a way that is both acceptable to the employee and the employer. Over and above the legislative context, employers, insurers, unions and patients can devise approaches and best practices that can be expanded to other organisations.

In 2017, the European Cancer And Work Network (CANWON), which was funded by a European research grant stopped existing. Its recommendations and guidelines remained unused. Despite the clear value for patients and society, this project has been discontinued.

The 'Right-to-be-Forgotten' should be applied in the legislation of every country.

The role of patient organisations

Patient organisations can assist patients with the paperwork that is needed for their employer and (public) health insurance. Patient organisations can share experiences of other patients, or recommend the patient to specialised organisations to get a job after a disease.



⁷⁷ Hofmarcher, T., Lindgren, P. (2020) The Cost of Cancers of the Digestive System in Europe. IHE Report 2020:XX. IHE: Lund, Sweden

End of life

The current situation

Like with every step of the patient journey, the individual choice of the patient is critical, and even if he or she is not a clinical expert, patients should receive complete and correct information, so that they can make a choice about the next steps. The same holds true for end-of-life choices. Patients diagnosed in stage IV, have limited prospects for recovery.

Clinical staff should have honest and open discussions with the patient and their family about the prospects. Therapeutic obstinacy should be avoided, but at the same time if patients are willing to continue their treatment, they should also have that option. The risk perception among physicians and carers is often of a different nature and scale than what the patients themselves perceive.

The context of the patient is important, such as general health and co-morbidities, age or social situation.

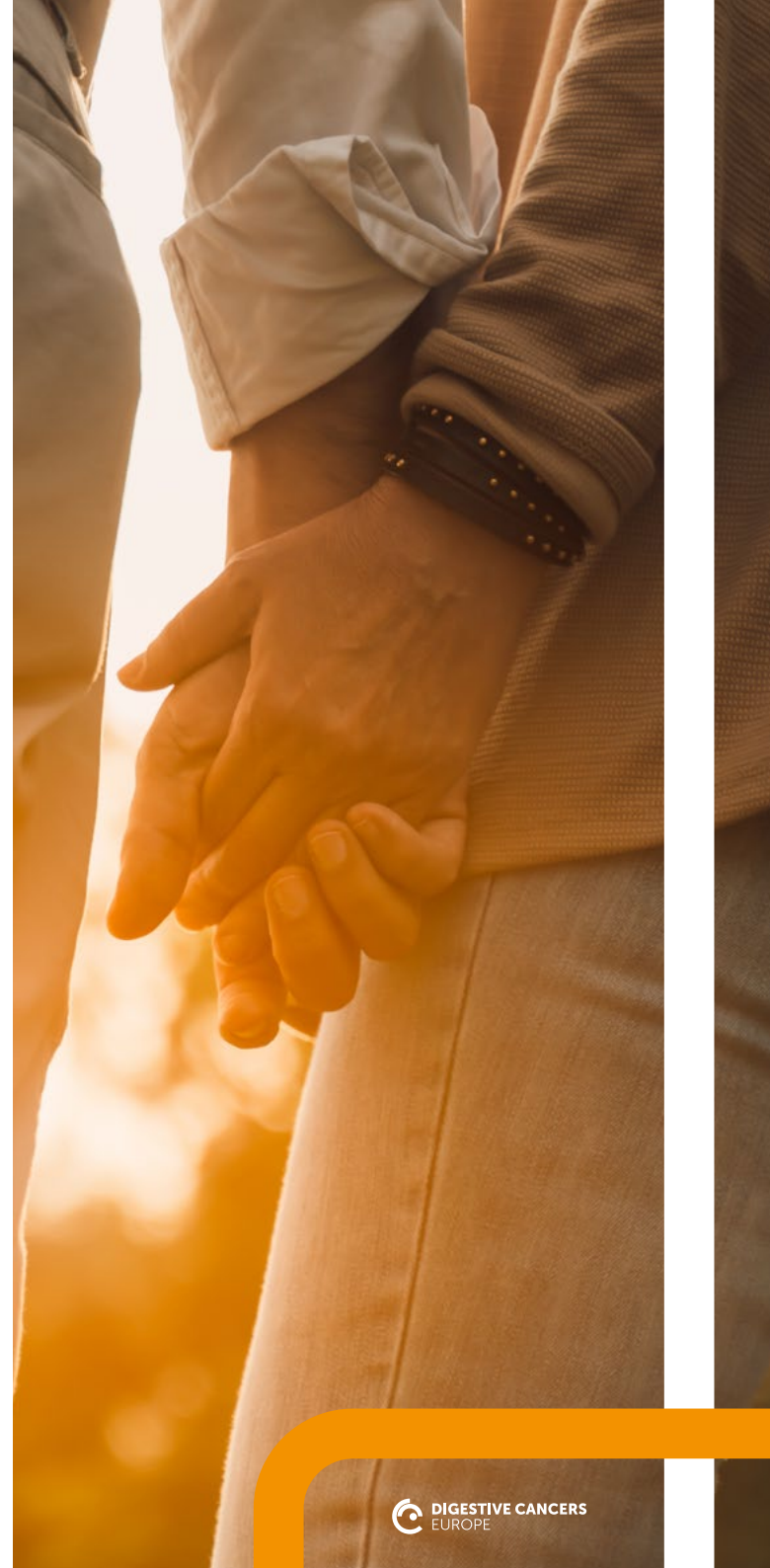
Best practice

The more options patients have, the more choice they will have. But the option not to be treated should also be presented to the patient. Palliative care should be organised often much earlier than is currently the case, and patients should have the chance to live the last months of their life with good pain management, with dignity and quality care.

Studies have demonstrated the importance for patients with untreatable disease to speak to lay non-medical staff about their life and their care, resulting in more patient satisfaction and less aggressive treatments⁷⁸.

In some countries, such as Belgium and Switzerland, patients can ask for active euthanasia.

⁷⁸ Patel MI, Sundaram V, Desai M, et al. Effect of a Lay Health Worker Intervention on Goals-of-Care Documentation and on Health Care Use, Costs, and Satisfaction Among Patients With Cancer: A Randomized Clinical Trial. *JAMA Oncol.* 2018;4(10):1359–1366. doi:10.1001/jamaoncol.2018.2446



Palliative Care

Palliative care is the right to receive timely pain control and symptom relief. It is often narrowly interpreted as the end of all treatment and managing pain before the end of life, but it can also refer to pain management while waiting for treatment. We can refer to the European Guide for Quality National Cancer Control Programmes for more details on how to organise this⁷⁹.

Recommendations

The choice to no longer be treated is a very personal one, but the more options a patient has, the more the individual's personal choice can be respected.

Expected outcomes

The expected outcome should be a marked improvement of the 'quality of death', with lots of needless suffering avoided.

The role of patient organisations

Patient organisations are usually well informed about the legal, ethical issues of end-of-life choices. They can help patients to understand all the options and consequences. They can refer the patient to more specialised organisations for further assistance.



79 Tit Albrecht, Jose M. Martin-Moreno, Marjetka Jelenc, Lydia Gorgojo, Meggan Harris (Eds): European Guide for Quality National Cancer Control Programmes National Institute of Public Health, Ljubljana, Slovenia, 2015.

The role of patient organisations

The current situation

Patient organisations create value. They create value for individual patients, to help them navigate the healthcare system, to assist with the non-medical aspects of their illness. Patient organisations offer value to healthcare systems by providing insights based on the collective intelligence and experience of all their members, and they offer value to hospitals, by acting as an extension of the hospital team for all non-medical aspects of treatment.

In most European countries, patient organisations exist that are dedicated to patients with colon and rectal cancer. It is important for patients to speak with and listen to patients who have gone through the same process as they have. They can share insights, practical tips and coping strategies. If anything, patients who are a part of a patient organisation are less isolated.

Once a patient has been diagnosed, he or she should be referred to a disease-specific patient organisation. This should become standard medical practice. Hospitals and patient organisations

can set up a basic mode of working, organise patient information sessions, peer-to-peer conversations, educational material and other help desk facilities.

Despite the obvious value of patient organisations, they are not publicly funded in most European countries and they have to rely on donations by individuals, foundations and companies, making their revenue unpredictable and unstable, with limited possibility for long-term planning. In times of a pandemic or economic recession, the impact of revenue loss to patient organisations is devastating.

We advocate for a more formal role of patient organisations by disease area, including funding and decision-making.

Best practices

The following services are offered by member organisations of Digestive Cancers Europe, with the aspiration to offer this across Europe.

- **Health literacy and education** - information on prevention, screening, risk profiles, awareness
- **Patient navigation** - how to navigate the healthcare system, where to go for specific medical and non-medical needs
- **Living with the disease** - how to live with the disease
- **Non-medical counselling**
 - Nutrition
 - Social and insurance
 - Psycho-oncology
 - Work-related counselling
 - Paperwork and bureaucracy
 - Social network
- **Advocating and helping to organise prevention and screening**

Patients who are looked after have better health outcomes: faster recovery, better recovery, better mental health, faster return-to-work situations.



Recommendation

At European and national level, disease-specific patient organisations should get publicly funded with the clear mandate to improve the current situation and to engage with all the different stakeholders to refine the current roadmap in action steps.

They will work with the ministry of health to determine priorities, to ensure policy coherence between the regional, national and European level.

They will counsel individual patients to improve their situation.

Patient organisations should also be part of all colorectal cancer research projects, first to help prioritise the importance and relevance of new research for patients, and second to include the patient perspective in all research projects. Despite the obvious value of integrating the patient perspective in research, this is still more exceptional than the rule.



Research

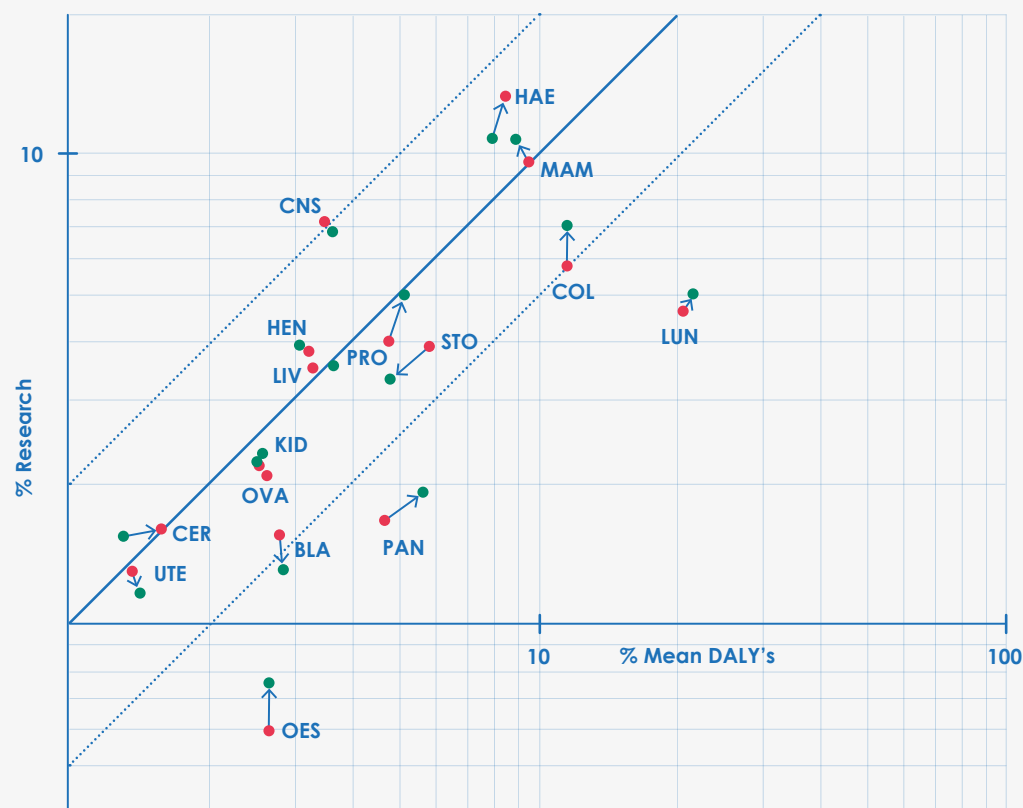
The current situation

All digestive cancers are under-researched compared to their burden of disease. A recent study makes this link and demonstrates this fact⁸⁰. The number of publications (as an indicator of research investments) is correlated with the burden of disease (Disability Adjusted Life Years: DALYs). Compared to lung cancer, oesophageal and pancreatic cancer, research on colorectal cancer performs better, but below average. A similar picture is seen in the United States.

Much more cancer research is needed, including in colorectal cancer. Next to medical and pharmaceutical research, health economic research seems also to be under-represented. Despite the huge burden of disease for patients and society, there are barely any data about the cost of treatment, the social and economic cost for patients and society. There is no research about the effectiveness of health systems, about treatment results, about best practices, or about back-to-work strategies.

⁸⁰ Mursheda Begum, Grant Lewison, Mark Lawler, Richard Sullivan : Mapping the European cancer research landscape: An evidence base for national and Pan-European research and funding, in: European Journal of Cancer, 2018

Figure 10: Cancer Research in Europe in Relation to the Burden of Disease



As we have seen from all the previous chapters, other elements that play a critical role in colorectal cancer treatment remain without any research at all:

- What is the health economic cost of colorectal cancer?
- How many patients go back to work after treatment?
- How can we evaluate colorectal cancer prevention measures in light of the expected outcomes?
- How can citizens be motivated to adapt their lifestyle choices in a sustainable manner?
- What are high performing countries in colorectal cancer screening doing to reach such citizen participation?
- What are the colorectal cancer mortality and survival rates by hospital?
- Why are there such big survival differences between hospitals in the same country?
- How can we organise colorectal cancer care in the best performing centers?
- Which measures need to be in place to avoid malnutrition?
- Which physical activity strategies will lead to highest patient participation and best outcomes?

- What is the value of being a member of a Patient Organisation in terms of outcomes and Quality of Life?
- What is the impact of Shared Decision-Making Models on patient outcomes?
- How can all outcomes data be centralised, and become accessible and transparent for all stakeholders?
- ...

Today, research is not prioritised. Research calls are organised in such a way that investigators can participate based on their insights and ideas, but without any direct relevance to prioritisation as patients would see them. If research is taken seriously – in terms of offering societal value – then patients should be part of all decision-making processes.

Pharmaceutical research in digestive cancers is primarily organised by pharmaceutical companies and predominantly by companies headquartered in the United States. Of the 27 drugs against colorectal cancer in development (Phase II & III), 10 are being developed by European companies, according to our own calculations.

Please refer to our 'Research Mission' for digestive cancers on this topic.

Recommendation

For current research, it is critical to involve patient organisations and patients.

As the custodians of the patient journey, patient organisations can identify the priority areas for research. This is critical because a lot of money is being spent on research that does not necessarily focus on meaningful patient outcomes.

Once research topics have been determined, it is also of the highest importance for the research to involve patients. It has been demonstrated that the real-life application and the actual value of new treatments are much higher depending on the active involvement of patient organisations in the design of the study, the recruitment and the process management⁸¹.

⁸¹ Jan Geissler, Dipl.-Kfm., Bettina Ryll, PhD, MD, Susanna Leto di Priolo, PharmD, and Mary Uhlenhopp, RN, MS, MPH : Improving Patient Involvement in Medicines Research and Development: A Practical Roadmap, in: Therapeutic Innovation & Regulatory Science, 2017,

In conclusion

In conclusion, there are a lot of best practices in Europe. Our continent may have the highest incidence of colorectal cancer, but the best-performing countries in terms of prevention and treatment are also found in Europe. Even without innovation, without new research and new technologies, the potential upside of applying best practices in Europe is huge.

The patient journey below demonstrates this. Although not everything is immediately applicable or applicable without effort or investment, it shows the way forward and where the big gains are to be achieved if we want to reduce the huge burden of colorectal cancer in Europe.

Better prevention can potentially lead to 55% of colorectal cancers being avoided, resulting in hundreds of thousands citizens never getting the diagnosis and not dying from the disease.

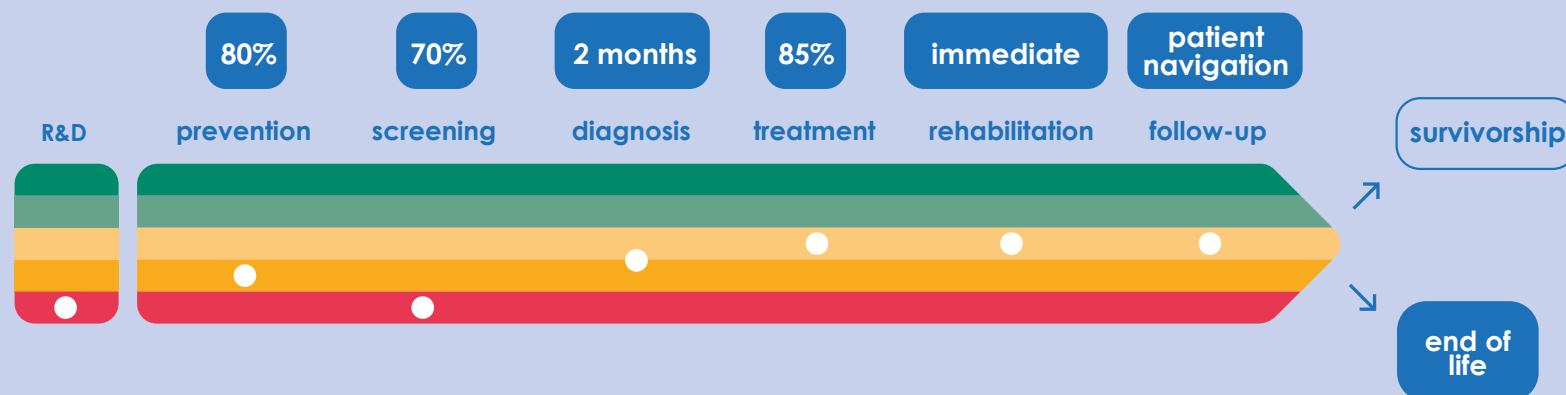
If the whole of Europe applied the best practices in screening, with 70% of the population between 50 and 74 years old participating, with 48% of patients diagnosed in Stage I as compared to 13% on average in the EU, tens of thousands of citizens would continue living full active lives.

We recommend to aspire to a much better and faster diagnosis of 2 months on average. The quantitative outcome is hard to evaluate, but it will mean a lot in reduced anxiety and loss of time.

Today, colorectal cancer patients treated in the best performing hospitals achieve a 5-year survival of 85%. This shows that every hospital should be able to attain the same level or at least patients should be led to the hospitals that reach that outcome.

In regards to the introduction of pharmaceutical innovation, it is critical that patients get immediate access to the best possible treatment, and that they don't have to wait years. Because the newest pharmaceuticals are very effective on small patient populations the total effect is hard to estimate, but substantial for the individual patients.

The total value of patient organisations in assisting patients throughout the patient journey with both medical and non-medical advice will lead to a more effective and efficient process, and we estimate the potential value of patient organisations can offer a 30% increase in both effectiveness and efficiency.



The table below gives an indication of what can be achieved by reaching the champion status everywhere in Europe. This is an ideal of course, and impossible to reach, but at least it helps to give a sense of direction and it indicates the magnitude of what can be achieved. This is where research money should be invested: to monitor where substantial benefits can be attained for the patients and for the whole of society.

Patient organisations will become the custodians of the patient journey, advocating for the best and most efficient way to treat the highest number of patients. They will advocate for policy changes, the application of best practices, and the seamless integration of all non-medical aspects related to the disease.

Today, politicians feel responsible for the healthcare budget, healthcare professionals feel responsible for their individual patients. We believe that with a more concerted and visionary approach significant improvements can be made that currently remain under the radar.

We have 500,000 additional colorectal cancer patients every year. It is unacceptable that they are diagnosed too late and not treated properly, and as a result 250,000 of them die. We are convinced that we can save half of these, or 125,000 lives - additionally every year by 2028 if all best practices are applied.

	Base of calculation number of annual new cases	Average of survival (current situation)	Champions of survival (potential upside)	Difference	Population-based upside if best practices are used	Health economic value if best practices are used
Prevention	487,714	NA	55%	55%		
Screening: stage I diagnosis		13%	48%	35%	To be calculated	To be calculated
Hospital care	487,714	60%	85%	25%	To be calculated	To be calculated



Statistical Sources

- The European Cancer Information System: <https://ecis.jrc.ec.europa.eu>
- The Global Cancer Observatory: <https://gco.iarc.fr>
- International Association of Cancer Registries: <http://www.iacr.com.fr>
- Institute of Health Metrics & Evaluation: <http://www.healthdata.org>
- World Health Organisation Global Mortality Database: <https://www.who.int/data/data-collection-tools/who-mortality-database>

CONCORD programme: Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Nikšić M, Bonaventure A, Valkov MY, Johnson CJ, Estève J, Ogunbiyi OJ, Azevedo e Silva G, Chen W-Q, Eser S, Engholm G, Stiller CA, Monnereau A, Woods RR, Visser O, Lim GH, Aitken J, Weir HK, Coleman MP, CONCORD Working Group. 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: 1-53.

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DIGESTIVE CANCERS
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The European Colorectal Cancer Road Map



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