

The impact of the COVID-19 pandemic on colorectal cancer care in the Netherlands: a population-based study

Master Thesis



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Abstract

Background. The COVID-19 pandemic disrupted health care services worldwide. In the Netherlands, the first confirmed COVID-19 infection was on February 27, 2020. We aimed to investigate the impact of the COVID-19 pandemic on (time to) care for colorectal cancer patients in the Netherlands.

Methods. Colorectal cancer patients were selected from the Netherlands Cancer Registry (NCR) and patients diagnosed during three periods in weeks 9-26 of 2020 were compared with patients diagnosed in weeks 2-8 of 2020. For all analyses, colon cancer patients were stratified based on the pathological stage and clinical stage in cases where pathological stage was unknown, and rectal cancer patients were stratified based on the clinical stage. The weekly average number of patients treated per type of first treatment was analyzed using the Mantel-Haenszel test adjusted for age. Median time between diagnosis and treatment and median time between (neo)adjuvant therapy and surgery were analyzed using the Mann Whitney test. Percentages of (acute) resection, stoma and (neo)adjuvant therapy were analyzed using the Chi-squared test.

Results. A resection was more often performed as first treatment in colon cancer patients in case of: age >75 years and stage I, age <55 or >75 years and stage III, and all ages and stage IV. Patients with stage III colon cancer aged 55-75 years less often had a resection as their first treatment and patients with clinical stage I rectal cancer aged >75 years more often had local surgery as their first treatment. Median time between diagnosis and first treatment decreased on average by 4.5 days for almost all periods, except for rectal cancer patients treated in the North/East of the Netherlands during weeks 18-26 of 2020. For colon cancer patients, significant more patients received a stoma during the pandemic ($p < 0.01$), except for weeks 18-26 of 2020 compared to weeks 2-8 of 2020. No differences were found between the period before and during the pandemic in percentages resection and (neo)adjuvant therapy.

Conclusion. Despite the disruptive impact of the COVID-19 pandemic on global health care, the impact on colorectal cancer care in the Netherlands was found to be limited. Only slight changes in colorectal cancer care during the COVID-19 pandemic were shown, which partly was due to a higher proportion of symptomatic patients during the pandemic.

Introduction

The coronavirus disease 2019 (COVID-19) started in Wuhan, China, and is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). In the Netherlands, the first confirmed COVID-19 infection was on February 27, 2020 (2). After this, the coronavirus spread fast through the whole country. To prevent COVID-19 from spreading any further, the Dutch government has taken various societal measures such as social distancing, closing stores and schools, and urging people to only leave their houses if necessary (3).

The COVID-19 pandemic also had a major impact on the health care services worldwide (4-7). Because of the outbreak of COVID-19, patients who were infected with the coronavirus got priority within the health care services. Therefore, non-COVID-19 patients became less prioritized. This led to a situation in which patients were less likely to go to the general practitioner (GP) with complaints, which led to a lower number of patients being diagnosed with cancer during the COVID-19 pandemic (5, 6, 8, 9). Moreover, national screening programs were halted due to the COVID-19 pandemic, including that for colorectal cancer between half March 2020 and half May 2020 (4, 8). Evidence is found that the amount of diagnosis in colorectal cancer in the Netherlands has dropped mainly in the age group eligible for screening, 55-75 years, from early May 2020 until late June 2020 (4, 8).

In the beginning of March 2020, the first recommended measures were published on how to deal with the COVID-19 pandemic within health care services in the Netherlands. Those recommended measures have been published by associations such as the Foundation of Oncological Cooperation (SONCOS) and the Dutch Association for Medical Oncology (NVMO). Examples of the recommended measures for colorectal cancer care are: 1) replace chemoradiation with a pre-operative short schedule of radiotherapy and a long waiting time before surgery; 2) omit pre-operative radiotherapy if short-term resection is possible; 3) consider postponing surgery for rectal cancer up to 12 weeks if patients have been treated with neoadjuvant therapy; and 4) consider postponing adjuvant therapy up to 12 weeks postoperative.

The aim of this study is to research the impact of the COVID-19 pandemic on (time to) colorectal cancer care in the Netherlands in 2020 and whether patients received treatment according to the recommended measures published for colorectal cancer care during the COVID-19 pandemic.

Methods

Patients

Patients older than 17 years diagnosed with colorectal cancer during weeks 2-26 of 2020 were included in this study. Data were selected from the Netherlands Cancer Registry (NCR). The NCR registers all newly diagnosed malignancies based on notification by the National Pathology Archive (PALGA) since 1989 and is hosted by the Netherlands Comprehensive Cancer Organisation (IKNL). Data were derived from 25 of the 70 hospitals in the Netherlands. This were 10 general hospitals, 11 top clinical hospitals and 4 academic hospitals spread through the whole country. For patients included during this study, the following data were gathered: patient characteristics (e.g., age at diagnosis, gender, performance status, and comorbidity), tumor characteristics (e.g., clinical stage, pathological stage, and ileus), type of treatments (e.g., systemic therapy, radiotherapy, and resection), interval between different events (e.g., number of days between diagnosis and first treatment), and the hospital where the patients received their treatment.

Definitions

For all patients, age at diagnosis was grouped into ages <55, 55-75 and >75 years.

The selected period was divided in four periods based on national data from PALGA to see which week numbers included less or more than 75% fewer screening colonoscopies during the period the screening program for colorectal cancer was halted: period A, weeks 2-8 (i.e., period before the COVID-19 pandemic); period B, weeks 9-11 (i.e., period during the COVID-19 pandemic but before screening program was halted); period C, weeks 12-17 (i.e., period during the COVID-19 pandemic and not more than 75% fewer screening colonoscopies); and period D, weeks 18-26 (i.e., period during the COVID-19 pandemic and more than 75% fewer screening colonoscopies). Periods B, C and D separately as well as combined were compared to period A since this was seen as the period before the COVID-19 pandemic.

Analyzing neoadjuvant therapy, type of first treatment and lead times, patients were divided in these four periods based on the incidence date. Analyzing adjuvant therapy, patients were divided in these four periods based on the surgery date.

TNM classification was used for staging the tumors (10). Stage of tumors (stage I, II, III or IV) were grouped different for the two types of colorectal cancer: colon cancer tumors were grouped based on the pathological stage and clinical in cases where pathological stage was unknown and rectal cancer tumors were grouped based on the clinical stage.

Hospitals where patients received their treatment for colorectal cancer were categorized into different regions (provinces) in the Netherlands: the North/East (Friesland, Groningen, Overijssel, Gelderland), the South (Noord-Brabant, Limburg) and the West (Zeeland, Zuid-Holland, Noord-Holland, Utrecht).

Statistical analysis

The baseline characteristics of colorectal cancer patients diagnosed in weeks 2-26 of 2020 were tested by chi-squared tests to determine if there were any significant differences between the patients diagnosed in period B, C and D of 2020 separately compared to period A of 2020.

To analyze type of first treatment, the average weekly incidence of patients per type of first treatment was calculated by type of cancer, tumor stage and period. The average weekly incidences in period B, C and D were separately compared with the average weekly incidence in period A using the Mantel-Haenszel test adjusted for age.

The median time between diagnosis and first treatment was calculated by type of cancer, region, and period. The median time between neoadjuvant therapy and surgery was calculated for patients diagnosed with rectal cancer stage II or III by type of neoadjuvant therapy and period. The median time between surgery and adjuvant therapy was calculated for patients diagnosed with colon cancer stage III by period. All median times of period B, C and D were separately compared with period A using the Mann Whitney test.

The proportion of patients that received a resection or a stoma was calculated by type of cancer, tumor stage and period. Also, the percentage of neoadjuvant therapy was calculated for patients diagnosed with rectal cancer stage II or III by type of neoadjuvant therapy and period. For patients diagnosed with colon cancer stage III, the percentage of adjuvant therapy was calculated by period. Here, all percentages of period B, C and D separately as well as combined were compared with period A using the Chi-squared test.

Stata version 16.1 software was used to analyze all data and for all tests performed, a two-sided p-value of <0.05 was considered statistically significant.

Results

Research population

The baseline characteristics of patients diagnosed with colon cancer in weeks 2-26 of 2020 are presented in Table 1a. Compared to period A, the proportion of patients aged 55-75 years was lower and the proportion of patients aged <55 and >75 was higher in period D ($p<0.01$). The proportion of patients diagnosed with colon cancer stage I or II was lower in period C ($p=0.04$) and D ($p<0.01$). Furthermore, the proportion of colon cancer patients with ileus was higher during period C ($p=0.03$) and D ($p<0.01$).

The baseline characteristics of rectal cancer patients in weeks 2-26 of 2020 are presented in Table 1b. Compared to period A, the proportion of patients aged <55 years was lower and the proportion of patients aged 55-75 and >75 years was higher in period D ($p<0.01$). Finally, the proportion of patients diagnosed with rectal cancer with a good performance status was lower in period D ($p=0.03$) compared to period A, respectively 37% versus 51%.

Type of first treatment

Differences between type of first treatment over the different periods for colon cancer patients are summarized in Figure 1a and for rectal cancer patients in Figure 1b.

Compared to period A, the proportion of patients diagnosed with colon cancer stage II during period B that received a combination of stoma and resection on the same day increased with 11.7%. The proportion of patients diagnosed with colon cancer stage IV in period C that received a resection increased with 18.8%. Those significant increases were seen for all age groups. Furthermore, the proportion of patients diagnosed with colon cancer stage I older than 75 years that received a resection was higher in period C ($p<0.01$) compared to period A, respectively 91.7% versus 48.4%. Fewer patients received local surgery and no treatment during this period. The proportion of patients diagnosed with colon cancer stage III older than 75 years in period B that received a resection increased significantly with 20.5%. All patients received a resection during period B, no other type of first treatment was given. In addition, for patients with colon cancer stage III younger than 55 years, the proportion of patients that received a resection was higher in period D ($p<0.01$) compared to period A, respectively 91.7% versus 25.0%. Here, all patients received a resection, except for one patient who received a combination of stoma and resection on the same day. By contrast, the proportion of patients with colon cancer stage III

aged 55-75 years that received a resection in period D decreased significantly with 34.9%. Here, more patients received a stoma or a combination of stoma and resection on the same day.

Finally, compared to period A, the proportion of rectal cancer patients diagnosed with stage I older than 75 years that received local surgery in period B increased significantly with 58.3%. For rectal cancer patients diagnosed with stage II, III or IV, no significant differences were found between the different periods of 2020.

Time between diagnosis and first treatment

For colon cancer patients, the median time between diagnosis and first treatment in period A was 23 days, compared with 22 days in period B, 14 days in period C ($p<0.01$), and 20 days in period D ($p=0.01$) (Supplementary Figure 1). For colon cancer patients in the region North/East, the median time between diagnosis and first treatment was significantly shorter in all the periods of 2020 ($p<0.01$) compared separately to period A of 2020 (Supplementary Figure 2). Moreover, for colon patients in the regions South and West, the median times between diagnosis and first treatment were significantly shorter in period C ($p=0.01$ and $p<0.01$) compared to period A (Supplementary Figure 3 and 4).

Furthermore, shorter intervals were seen for rectal cancer patients. The median time between diagnosis and first treatment in period A was 30 days, compared with 26 days in period B, 23 days in period C ($p<0.01$), and 28 days in period D (Supplementary Figure 5). For rectal cancer patients in the region North/East, no significant differences were found (Supplementary Figure 6). However, for rectal cancer patients in the region South, the median time between diagnosis and first treatment was significantly shorter in period B ($p=0.03$) compared to period A (Supplementary Figure 7). Finally, for rectal cancer patients in the region West, the median time between diagnosis and first treatment only was significantly shorter in period C ($p=0.03$) compared to period A (Supplementary Figure 8).

Time between (neo)adjuvant therapy and surgery

For patients with rectal cancer stage II or III who received neoadjuvant chemoradiation, the median time between neoadjuvant therapy and surgery in period A was 90 days, compared with 85 days in period B, 85.5 days in period C and 94 days in period D (Supplementary Figure 9). Moreover, for patients with rectal cancer stage II or III who received neoadjuvant radiotherapy, the median time between neoadjuvant therapy and surgery in period A was 6.5 days, compared with 87 days in period B, 62 days in period C and 8.5 days in period D (Supplementary Figure 10). Finally, for patients with colon cancer

stage III, the median time between surgery and adjuvant therapy in period A was 40 days, compared with 52 days in period B, 45.5 days in period C and 36 days in period D (Supplementary Figure 11). For all median times mentioned above, no significant differences were found.

Treatment

The percentages of (acute) resection, stoma and adjuvant therapy for colon cancer patients are shown in Table 2a. The percentages of (acute) resection, stoma and neoadjuvant therapy for rectal cancer patients are shown in Table 2b.

For the percentages of resection for colon and rectal cancer patients, no significant differences were found between the periods B-D compared separately as well as compared combined to period A. Using subanalyses per stage, for patients diagnosed with rectal cancer stage II, a significant lower resection percentage was found in period B ($p=0.01$) compared to period A, namely 44.4% versus 83.8%.

Compared to period A, the proportion of colon cancer patients that received an acute resection increased during period C ($p<0.01$) and D ($p=0.02$) separately, as well as during period B-D ($p=0.02$) combined. Analyzing the proportion of rectal cancer patients that received an acute resection, no significant differences were found while period B-D was compared separately as well as compared combined to period A.

For colon cancer patients, a higher stoma percentage in period B-D combined ($p<0.01$) was found compared to period A. Furthermore, period C ($p=0.01$) and D ($p=0.01$) separately compared to period A showed a higher stoma percentage. Subanalyses per stage showed for colon cancer patients diagnosed with stage III a higher stoma percentage in period D ($p<0.01$) compared to period A, namely 27.2% versus 12.1%. For this stage, also a higher stoma percentage was found while period B-D combined ($p=0.02$) was compared to period A, namely 23.9% versus 12.1%. However, no significant differences were found for rectal cancer patients.

Analyzing the percentages of adjuvant therapy, no significant differences were found for periods B-D compared separately as well as compared combined to period A. Furthermore, analyzing the percentages of neoadjuvant therapy, no significant differences were found while periods B-D was compared separately as well as compared combined to period A. Finally, the percentages of neoadjuvant radiotherapy and neoadjuvant chemoradiation also were calculated separately but showed no significant differences.

Discussion

This population-based study showed the impact of the COVID-19 pandemic on colorectal cancer care in the Netherlands. Despite the disruptive impact of the COVID-19 pandemic on global health care, the impact on colorectal cancer care in the Netherlands was found to be limited.

Results found in this study showed that during period C and D, colon cancer patients more often had ileus or received an acute resection. Possible explanations could be the Dutch official authorities suggesting to only visit the GP with serious complaints and the temporary halt of the colorectal cancer screening program. This led to a situation where patients were reluctant to seek care in an earlier stage and therefore more patients with serious complaints visited the hospital during the COVID-19 pandemic (4, 8). Our results also showed that colon cancer patients diagnosed with stage I, III or IV more often received a resection as their first treatment during the COVID-19 pandemic instead of systemic therapy, local surgery or no treatment. This can be related to the finding that more patients with serious complaints visited the hospital during the COVID-19 pandemic.

Besides the fact that the number of colorectal cancer diagnoses decreased during the COVID-19 pandemic, the number of diagnoses of other cancer types also decreased, and many (high risk) surgeries were postponed (9). Therefore, more capacity was available within the hospitals, which could result in less lead time. This could be a possible explanation for the reduction in median time between diagnosis and first treatment found in our results.

Analyzing median time between diagnosis and first treatment for the different regions in the Netherlands, the North/East of the Netherlands showed a significant decrease for colon patients during the whole COVID-19 pandemic. Since the North/East of the Netherlands was least affected by COVID-19, those hospitals might had more time to treat their patients since there were less COVID-19 patients compared with hospitals in the other regions (11). By contrast, this was not applied to rectal cancer patients diagnosed in period D. Here, the median time between diagnosis and first treatment became longer compared to period A. Analyzing this specific patient group, a lower performance status was shown. Therefore, to avoid risk of getting infected with the coronavirus, those patients may have received their first treatment later than usual. To be sure the decreases in median time between diagnosis and first treatment during the COVID-19 pandemic were related to the COVID-19 pandemic and had nothing to do with for example holidays, the median time between diagnosis and first treatment for weeks 2-26 of

2019 were calculated (data not shown). However, the median times of 2019 did not possess similarities to the median times of 2020, and therefore the decreases in median time between diagnosis and first treatment during the COVID-19 pandemic are likely COVID-19 related.

Analyzing the median time between (neo)adjuvant therapy and surgery, our results showed that the median time changed a little during the COVID-19 pandemic. This little change could be partly related to the recommended measures to postpone surgery after neoadjuvant therapy and adjuvant therapy after surgery. Yet, this could also partly be related to the normal clinical practice in which a longer waiting time between neoadjuvant therapy and surgery is applied more often (12). However, the number of patients that received (neo)adjuvant therapy seems to be declined during the COVID-19 pandemic: from 45 to 27 patients that received neoadjuvant therapy and from 53 to 42 patients that received adjuvant therapy. Due to the low number of patients, these results were not significant.

Results of our study showed that the percentage of patients that received a stoma increased significantly during the COVID-19 period. A possible explanation could be the changed patient group, since there were more patients with serious complaints visiting the hospital during the COVID-19 pandemic. Another explanation for this finding could be that undergoing a resection can involve risks, for example wound infection or anastomotic leakage, and therefore patients might need to be taken to the Intensive Care Unit (ICU). To reduce the risk of such complications, a colostomy may have been performed preventively (13, 14). During the COVID-19 pandemic, many COVID-19 patients were admitted to the ICU, which led to a situation where almost all the ICU beds were occupied (15). Possibly, to reduce the risk of complications and even higher pressure on the IC, more stoma's have been placed during the COVID-19 pandemic.

A recommended measure published during the COVID-19 pandemic was to replace neoadjuvant chemoradiation with neoadjuvant radiotherapy and a long waiting time before a resection. However, results of our study showed no significant differences in percentage neoadjuvant chemoradiation and neoadjuvant radiotherapy. Another recommended measure published during the COVID-19 pandemic was to omit a pre-operative schedule of radiotherapy if short-term resection was possible. Similarly, no significant differences in percentage neoadjuvant radiotherapy were found in our results. Therefore, our study did not show results that reflect an implementation of these recommended measures during the COVID-19 pandemic.

The COVID-19 pandemic period was not compared to the exact same period of previous year(s), but to the weeks 2-8 of 2020. During the past years, the number of colorectal cancer diagnoses decreased (16). Therefore, comparing the number of diagnoses during the COVID-19 pandemic with the exact same periods of previous years would have given a distorted interpretation of our results. In order to make a proper comparison between the different periods of 2020 the weekly average was used, since the number of weeks differed per period.

To our knowledge, this was the first study to report on the impact of the COVID-19 pandemic on colorectal cancer care in the Netherlands. However, there was one limitation, namely the number of colorectal cancer patients included during this study was small because we used data from 25 hospitals instead of all the 70 hospitals in the Netherlands. Therefore, the impact of data fluctuations unrelated to the COVID-19 pandemic cannot be excluded and interpretations of these results had to be made with caution.

Conclusion

Despite the disruptive impact of the COVID-19 pandemic on global health care, the impact on colorectal cancer care in the Netherlands was found to be limited. Only slight changes in colorectal cancer care during the COVID-19 pandemic were shown, which partly was due to a higher proportion of symptomatic patients during the pandemic. First, several changes in receiving a certain type of first treatment can be due to a changed patient group during the COVID-19 pandemic because the colorectal cancer screening program was temporarily halted and the Dutch authorities recommended to only visit the GP with serious complaints. Second, colorectal cancer patients experienced no delay in receiving first treatment after diagnosis, this time became even shorter since there was more capacity available within the hospitals because there were less cancer diagnosis and less (high risk) surgeries during the COVID-19 pandemic. Last, the percentage of patients receiving a stoma during the COVID-19 pandemic was higher. On the one hand, because of the changed patient group and, on the other hand, possibly to avoid risks on complications and therefore a higher pressure on the ICU, since the ICU was almost fully occupied with patients infected with the coronavirus.

Figures

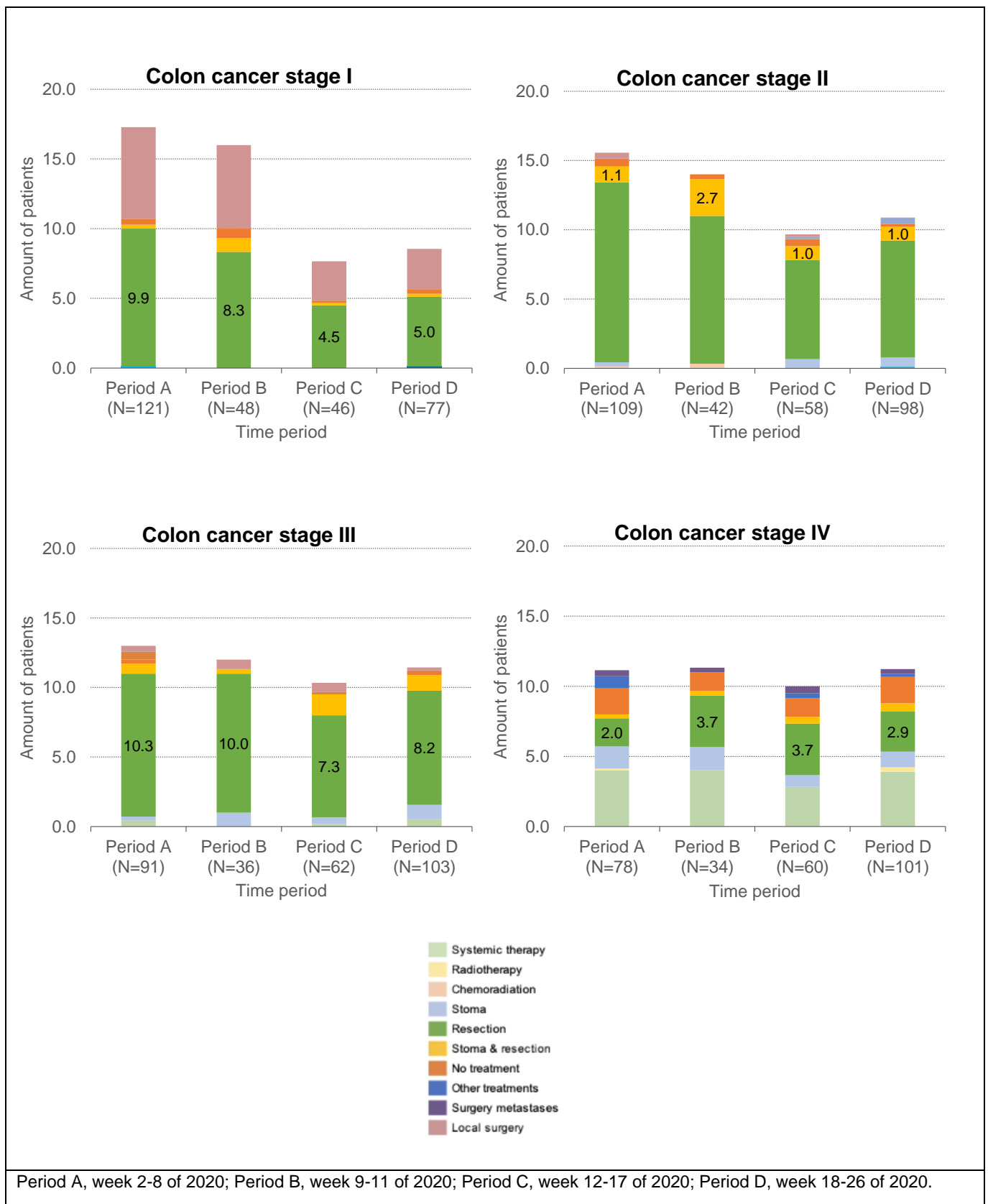


Figure 1a Average number of colon cancer patients treated per week, per tumor stage and per type of first treatment

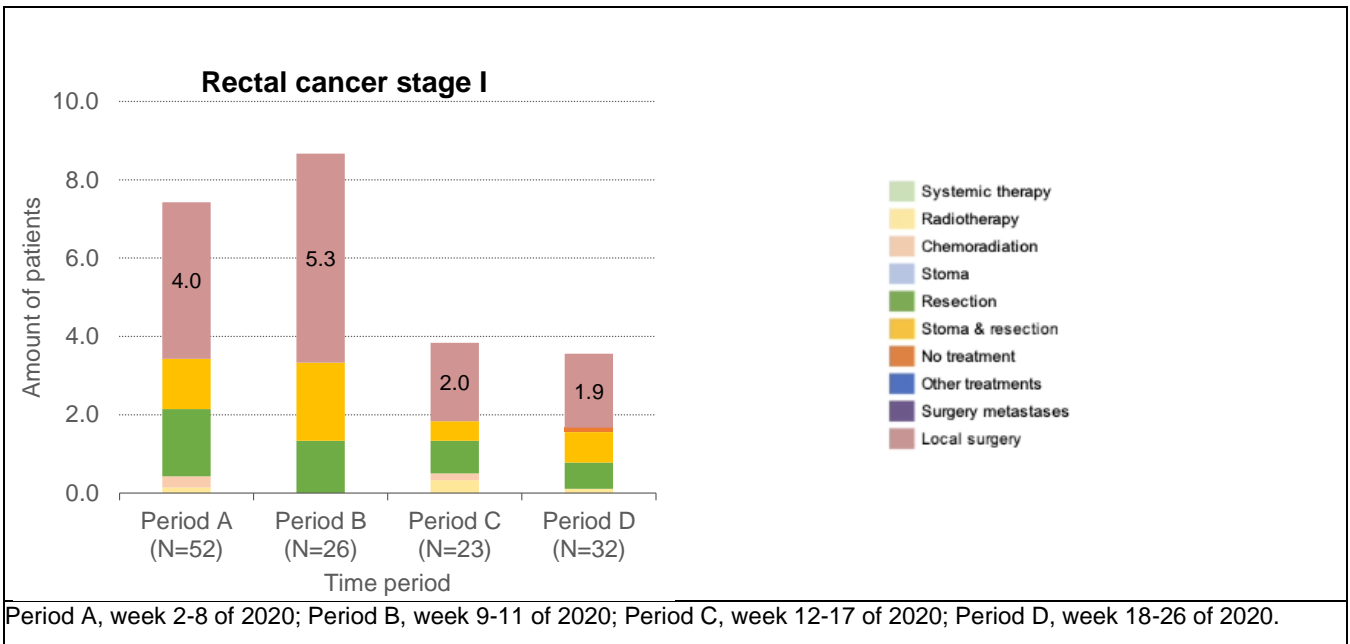


Figure 1b Average number of rectal cancer patients treated per week, per tumor stage and per type of first treatment

Tables

Table 1a Characteristics of patients diagnosed with colon cancer in periods A, B, C and D of 2020

		Period A	Period B		Period C		Period D	
		N (%)	N (%)	P-value	N (%)	P-value	N (%)	P-value
Patients	N	410	161		231		385	
Age (years)	<55	28 (6.9)	15 (9.3)	0.41	26 (11.3)	0.15	49 (12.7)	<0.01
	55-75	225 (54.9)	92 (57.1)		123 (53.2)		169 (43.9)	
	>75	157 (38.3)	54 (33.5)		82 (35.5)		167 (43.4)	
Gender	Men	209 (51.0)	81 (50.3)	0.89	116 (50.2)	0.85	197 (51.2)	0.96
	Woman	201 (49.0)	80 (49.7)		115 (50.0)		188 (48.8)	
Performance status	Good performance	148 (36.1)	66 (41.0)	0.25	86 (37.2)	0.33	116 (30.1)	0.11
	Restricted performance	77 (18.8)	30 (18.6)		33 (14.3)		78 (20.3)	
	Disability	29 (7.1)	6 (3.7)		20 (8.7)		39 (10.1)	
	Unknown	156 (38.0)	59 (36.6)		92 (39.8)		152 (39.5)	
Comorbidity	No comorbidity	160 (39.0)	61 (37.9)	0.89	114 (49.4)	0.04	140 (36.4)	0.43
	One comorbidity	120 (29.3)	49 (30.4)		54 (23.4)		110 (28.6)	
	Two comorbidities	65 (15.9)	28 (17.4)		30 (13.0)		74 (19.2)	
	Unknown	65 (15.9)	23 (14.3)		33 (14.3)		61 (15.8)	
Pathological stage	Stage I	121 (29.5)	48 (29.8)	0.63	46 (19.9)	0.04	77 (20.0)	<0.01
	Stage II	109 (26.6)	42 (26.1)		58 (25.1)		98 (25.5)	
	Stage III	91 (22.2)	36 (22.4)		62 (26.8)		103 (26.8)	
	Stage IV	78 (19.0)	34 (21.1)		60 (26.0)		101 (26.2)	
	Stage X	11 (2.7)	1 (0.01)		5 (2.2)		6 (1.6)	
Ileus	No	311 (75.9)	124 (77.0)	0.42	164 (71.0)	0.03	249 (64.7)	<0.01
	Yes	33 (8.0)	17 (10.6)		32 (13.9)		55 (14.3)	
	Unknown	66 (16.1)	20 (12.4)		35 (15.1)		81 (21.0)	
Region	North/East	97 (23.7)	36 (22.4)	0.56	59 (25.5)	0.14	97 (25.2)	0.82
	South	204 (49.8)	75 (46.6)		97 (42.0)		192 (49.9)	
	West	109 (26.6)	50 (31.1)		75 (32.5)		96 (24.9)	

Period A, week 2-8; Period B, week 9-11; Period C, week 12-17; Period D, week 18-26.

The p-value was calculated excluding missing values, using the chi-squared test to compare patients diagnosed in period B, C or D of 2020 with patients diagnosed in period A of 2020.

Table 1b Characteristics of patients diagnosed with rectal cancer in periods A, B, C and D of 2020

		Period A	Period B		Period C		Period D	
		N (%)	N (%)	P-value	N (%)	P-value	N (%)	P-value
Patients	N	174	68		84		140	
Age (years)	<55	29 (16.7)	11 (16.2)	0.46	8 (9.5)	0.27	23 (16.4)	<0.01
	55-75	102 (58.6)	45 (66.2)		51 (60.7)		60 (42.9)	
	>75	43 (24.7)	12 (17.6)		25 (29.8)		57 (40.7)	
Gender	Men	121 (69.5)	44 (64.7)	0.47	52 (61.9)	0.22	72 (51.4)	<0.01
	Woman	53 (30.5)	24 (35.3)		32 (38.1)		68 (48.6)	
Performance status	Good performance	89 (51.1)	35 (51.5)	0.66	38 (45.2)	0.49	52 (37.1)	0.03
	Restricted performance	28 (16.1)	12 (17.6)		15 (17.9)		37 (26.4)	
	Disability	13 (7.5)	7 (10.3)		3 (3.6)		11 (7.9)	
	Unknown	44 (25.3)	13 (19.1)		28 (33.3)		40 (28.6)	
Comorbidity	No comorbidity	74 (42.5)	29 (42.6)	0.92	39 (46.4)	0.88	54 (38.6)	0.60
	One comorbidity	51 (29.3)	19 (27.9)		23 (27.4)		39 (27.9)	
	Two comorbidities	19 (10.9)	6 (8.8)		9 (10.7)		20 (14.3)	
	Unknown	30 (17.2)	14 (20.6)		13 (15.5)		27 (19.3)	
Clinical stage	Stage I	52 (29.9)	26 (38.2)	0.53	23 (27.4)	0.35	32 (22.9)	0.54
	Stage II	37 (21.3)	9 (13.2)		10 (11.9)		26 (18.6)	
	Stage III	52 (29.9)	18 (26.5)		31 (36.9)		50 (35.7)	
	Stage IV	27 (15.5)	12 (17.6)		17 (20.2)		26 (18.6)	
	Stage X	6 (3.4)	3 (4.4)		3 (3.6)		6 (4.3)	
Ileus	No	137 (78.7)	51 (75.0)	0.74	64 (76.2)	0.94	93 (66.4)	0.90
	Yes	4 (2.3)	2 (2.9)		2 (2.4)		3 (2.1)	
	Unknown	33 (19.0)	15 (22.1)		18 (21.4)		44 (31.5)	
Region	North/East	41 (23.6)	19 (27.9)	0.77	11 (13.1)	0.14	29 (20.7)	0.72
	South	80 (46.0)	29 (42.6)		42 (50.0)		63 (45.0)	
	West	53 (30.5)	20 (29.4)		31 (36.9)		48 (34.3)	

Period A, week 2-8; Period B, week 9-11; Period C, week 12-17; Period D, week 18-26.

The p-value was calculated excluding missing values, using the chi-squared test to compare patients diagnosed in period B, C or D of 2020 with patients diagnosed in period A of 2020.

Table 2a Number of colon cancer patients that received (acute) resection, adjuvant therapy, or stoma per period

		Period A	Period B		Period C		Period D		Period B-D	
		N (%)	N (%)	P-value	N (%)	P-value	N (%)	P-value	N (%)	P-value
Patients	N	410	161		231		385		777	
Resection	All	305 (74.4)	126 (78.3)	0.33	179 (77.5)	0.38	293 (76.1)	0.58	598 (77.0)	0.32
	Acute <12 hours	16 (5.3)	3 (2.4)	0.23	15 (8.4)	<0.01	28 (9.6)	0.02	46 (7.7)	0.02
	Acute >12 hours	8 (2.6)	6 (4.8)		15 (8.4)		16 (5.5)		37 (6.2)	
	Adjuvant therapy*	53 (55.8)	19 (57.6)	0.86	62 (62.6)	0.33	46 (53.5)	0.76	127 (58.3)	0.96
Stoma		50 (12.2)	28 (17.4)	0.10	45 (19.5)	0.01	72 (18.7)	0.01	145 (18.7)	<0.01

Period A, weeks 2-8 of 2020; Period B, weeks 9-11 of 2020; Period C, weeks 12-17 of 2020; Period D, weeks 18-26 of 2020; Period B-D, weeks 9-26 of 2020.

The p-value was calculated excluding missing values, using the chi-squared test to compare patients diagnosed in period B, C or D of 2020 with patients diagnosed in period A of 2020.

* Patients that received adjuvant therapy are divided in four periods based on surgery date, while the patients that received a resection are divided in four periods based on incidence date. Therefore, the percentages shown for adjuvant therapy are not calculated as a proportion of the total number of patients that received a resection shown in this table.

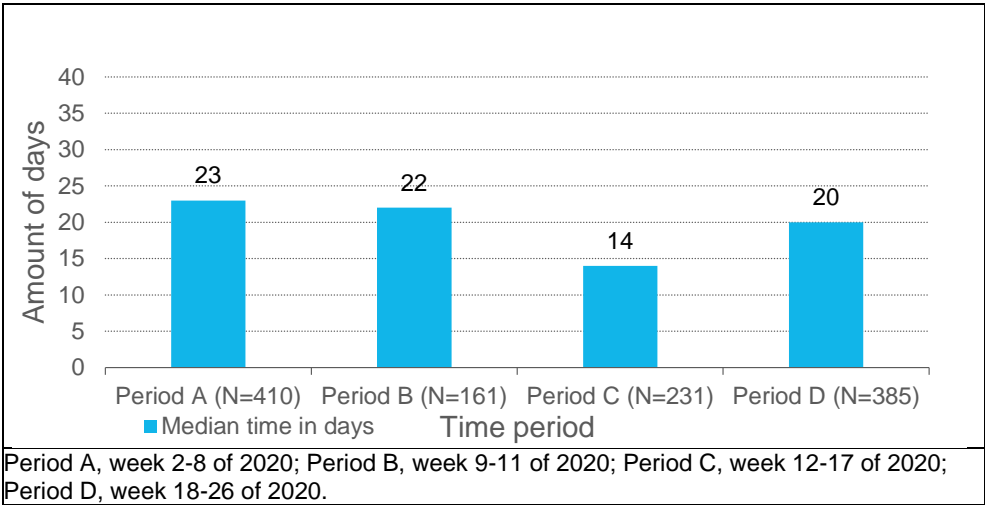
Table 2b Number of rectal cancer patients that received (acute) resection, neoadjuvant therapy, or stoma per period

		Period A	Period B		Period C		Period D		Period B-D	
		N (%)	N (%)	P-value	N (%)	P-value	N (%)	P-value	N (%)	P-value
Patients	N	174	68		84		140		292	
Resection	All	105 (60.3)	33 (48.5)	0.10	47 (56.0)	0.50	77 (55.0)	0.34	157 (53.8)	0.17
	Acute <12 hours	1 (1.0)	0 (0.0)	0.57	0 (0.0)	0.50	1 (1.3)	0.83	1 (0.6)	0.77
	Acute >12 hours	0 (0.0)	0 (0.0)		0 (0.0)		0 (0.0)			
	Neoadjuvant therapy	45 (35.7)	13 (10.3)	0.73	25 (19.8)	0.24	43 (34.1)	0.08	81 (64.3)	0.17
Stoma		77 (44.3)	27 (39.7)	0.52	38 (45.2)	0.88	66 (47.1)	0.61	131 (44.9)	0.90

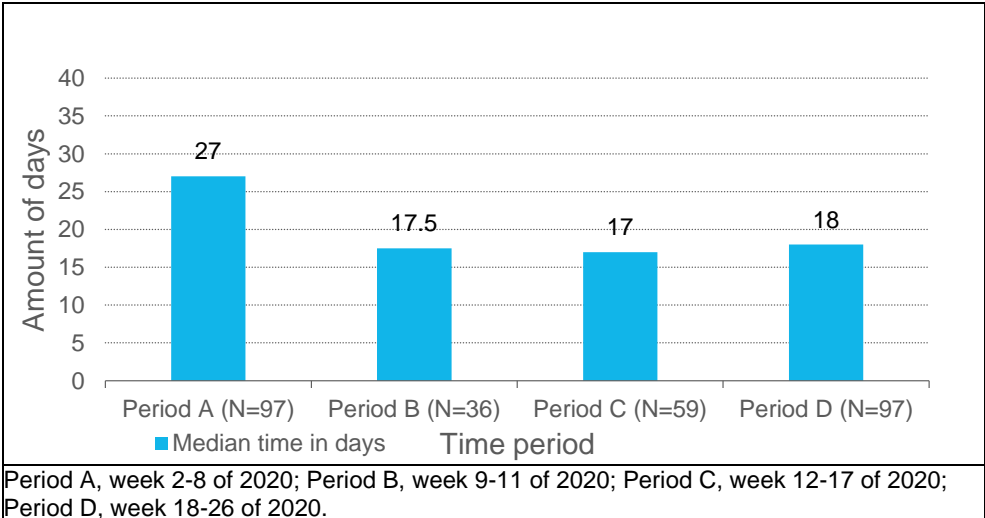
Period A, weeks 2-8 of 2020; Period B, weeks 9-11 of 2020; Period C, weeks 12-17 of 2020; Period D, weeks 18-26 of 2020; Period B-D, weeks 9-26 of 2020.

The p-value was calculated excluding missing values, using the chi-squared test to compare patients diagnosed in period B, C or D of 2020 with patients diagnosed in period A of 2020.

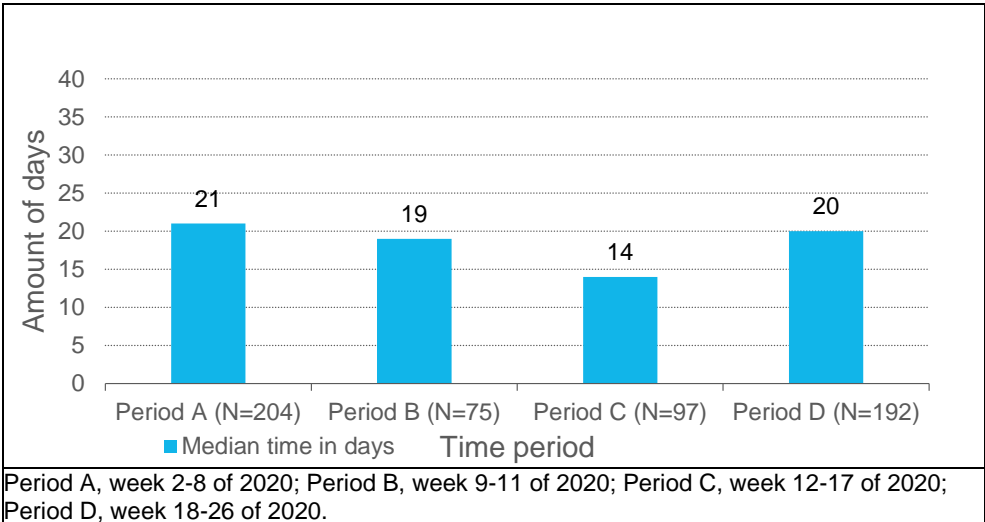
Supplementary Materials



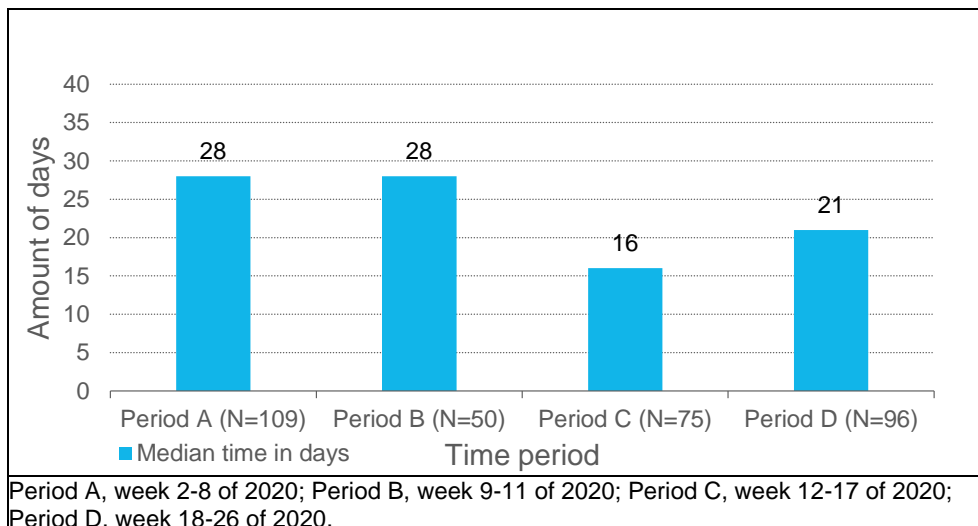
Supplementary Figure 1 Median time between diagnosis and first treatment for colon cancer patients



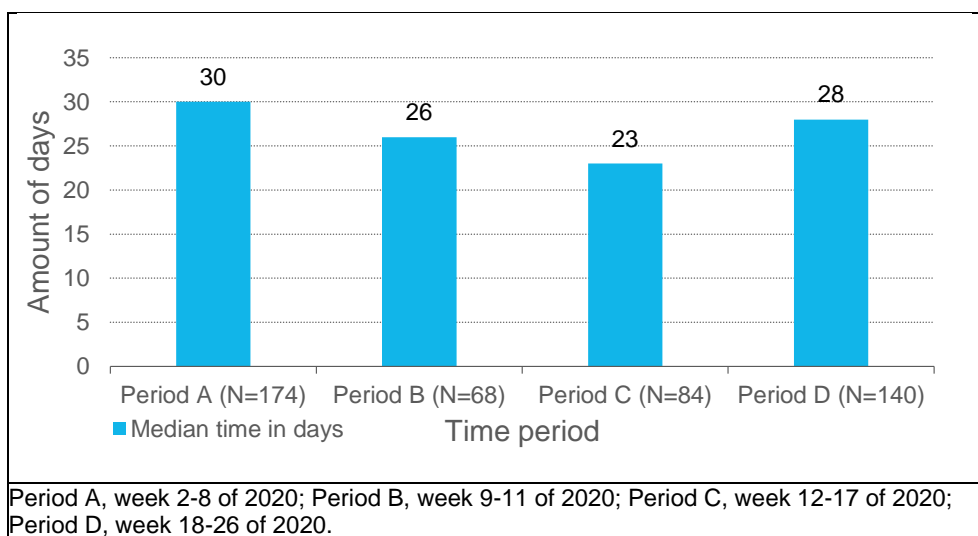
Supplementary Figure 2 Median time between diagnosis and first treatment for colon cancer patients treated in hospitals in the region North/East



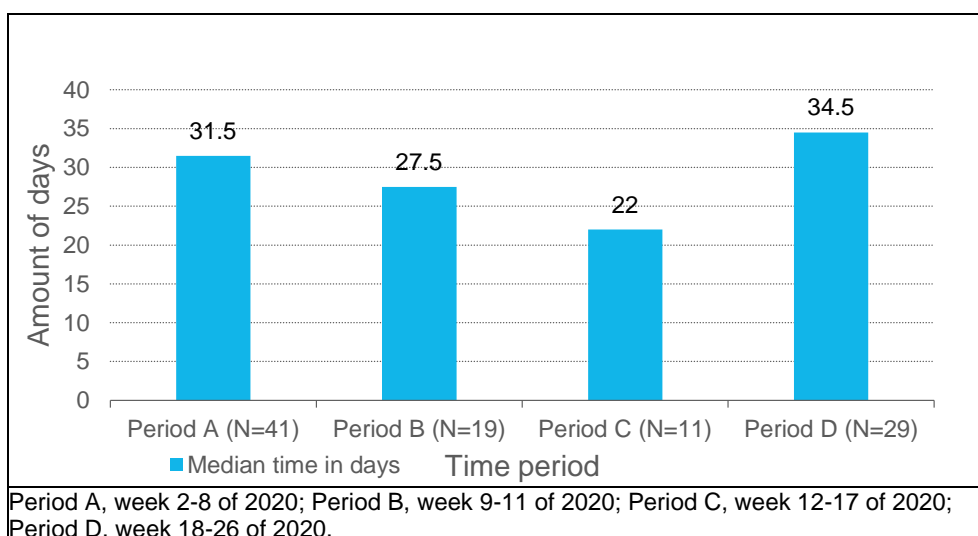
Supplementary Figure 3 Median time between diagnosis and first treatment for colon cancer patients treated in hospitals in the region South



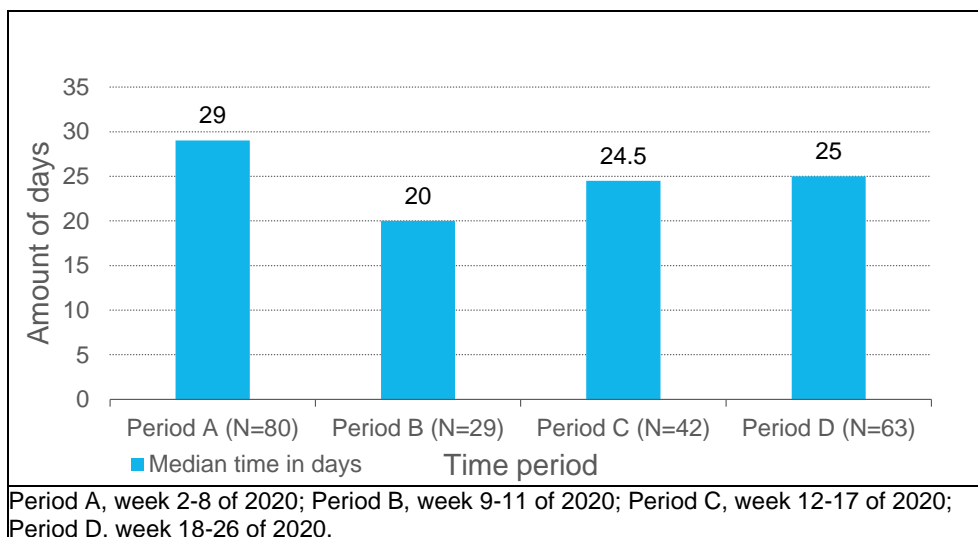
Supplementary Figure 4 Median time between diagnosis and first treatment for colon cancer patients treated in hospitals in the region West



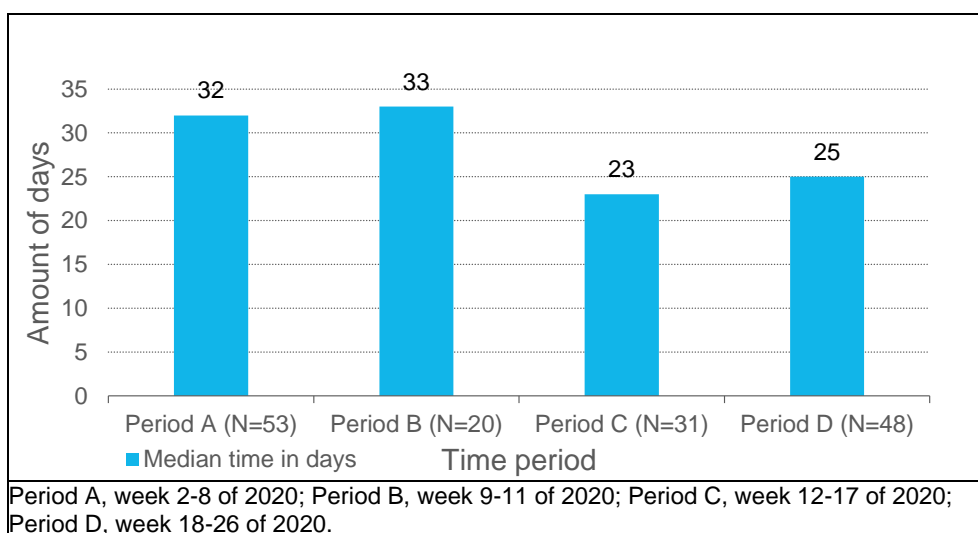
Supplementary Figure 5 Median time between diagnosis and first treatment for rectal cancer patients treated in hospitals in the region West



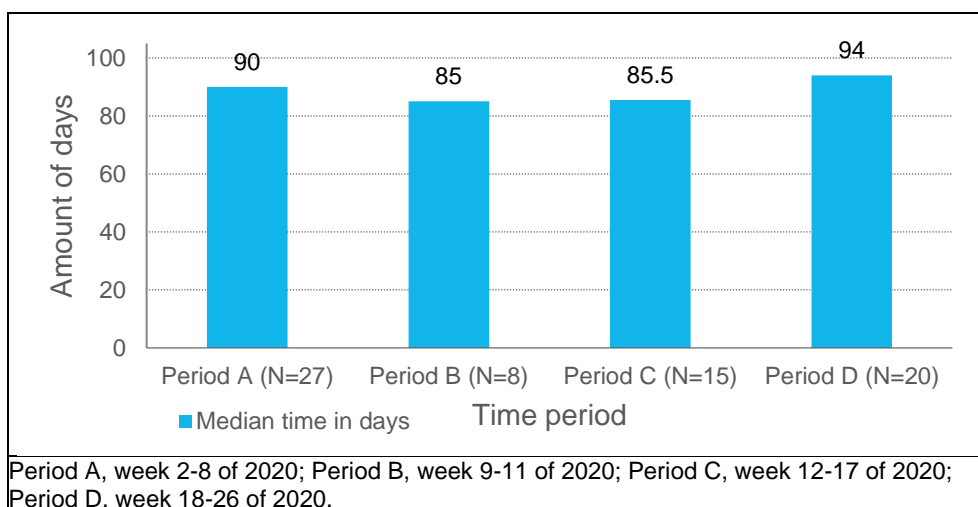
Supplementary Figure 6 Median time between diagnosis and first treatment for rectal cancer patients treated in hospitals in the region North/East



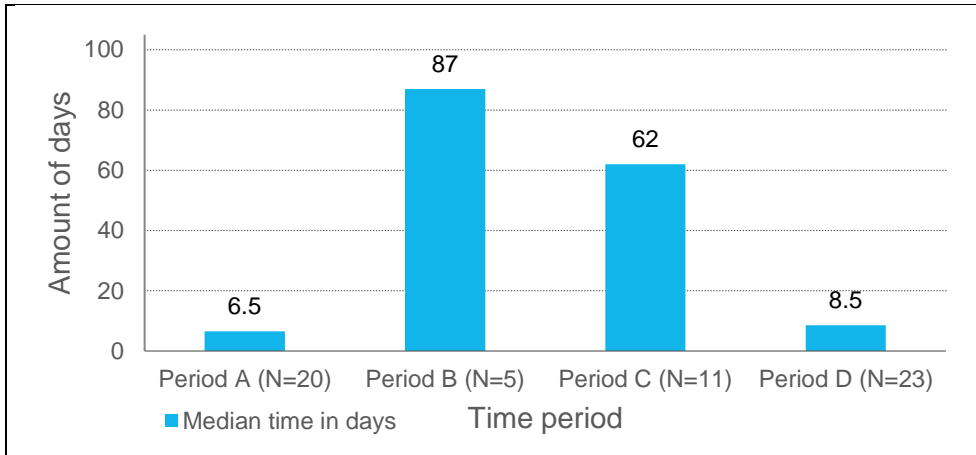
Supplementary Figure 7 Median time between diagnosis and first treatment for rectal cancer patients treated in hospitals in the region South



Supplementary Figure 8 Median time between diagnosis and first treatment for rectal cancer patients treated in hospitals in the region West

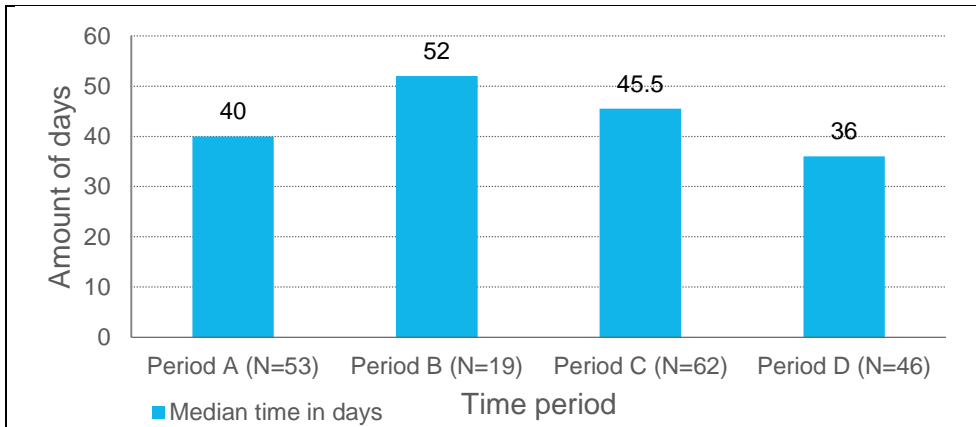


Supplementary Figure 9 Median time between chemoradiation and operation for patients with rectal cancer clinical stage 2 and 3



Period A, week 2-8 of 2020; Period B, week 9-11 of 2020; Period C, week 12-17 of 2020; Period D, week 18-26 of 2020.

Supplementary Figure 10 Median time between radiotherapy and operation for patients with rectal cancer clinical stage 2 and 3



Period A, week 2-8 of 2020; Period B, week 9-11 of 2020; Period C, week 12-17 of 2020; Period D, week 18-26 of 2020.

Supplementary Figure 11 Median time between operation and adjuvant therapy for patients with colon cancer stage 3

Supplementary Table 1a Weekly average number of patients diagnosed with colon cancer per type of first treatment, per period based on incidence date, and per pathological tumor stage

	Total	ST	RT	CR	Stoma	Resection	S&R	NT	OT	SM	LS
Stage I											
Period A	17.3	0.0 (0.0)	0.1 (0.8)	0.0 (0.0)	0.0 (0.0)	9.9 (57.0)	0.3 (1.7)	0.4 (2.5)	0.0 (0.0)	0.0 (0.0)	6.6 (38.0)
Period B	16.0	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	8.3 (52.1)	1.0 (6.3)	0.7 (4.2)	0.0 (0.0)	0.0 (0.0)	6.0 (37.5)
Period C	7.7	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	4.5 (58.7) ^a	0.2 (2.2)	0.2 (2.2)	0.0 (0.0)	0.0 (0.0)	2.8 (37.0)
Period D	8.6	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.1 (1.3)	5.0 (58.4)	0.2 (2.6)	0.3 (3.9)	0.0 (0.0)	0.0 (0.0)	2.9 (33.8)
Stage II											
Period A	15.6	0.0 (0.0)	0.0 (0.0)	0.1 (0.9)	0.3 (1.8)	13.0 (83.5)	1.1 (7.3)	0.6 (3.7)	0.0 (0.0)	0.0 (0.0)	0.4 (2.8)
Period B	14.0	0.0 (0.0)	0.0 (0.0)	0.3 (2.4)	0.0 (0.0)	10.7 (76.2)	2.7 (19.0) [↑]	0.3 (2.4)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Period C	9.7	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.7 (6.9)	7.2 (74.1)	1.0 (10.3)	0.5 (5.2)	0.2 (1.7)	0.0 (0.0)	0.2 (1.7)
Period D	10.9	0.1 (1.0)	0.0 (0.0)	0.0 (0.0)	0.7 (6.1)	8.4 (77.6)	1.0 (9.2)	0.2 (2.0)	0.4 (4.1)	0.0 (0.0)	0.0 (0.0)
Stage III											
Period A	13.0	0.4 (3.3)	0.0 (0.0)	0.0 (0.0)	0.3 (2.2)	10.3 (79.1)	0.7 (5.5)	0.3 (2.2)	0.6 (4.4)	0.0 (0.0)	0.4 (3.3)
Period B	12.0	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	1.0 (8.3)	10.0 (83.3) ^b	0.3 (2.8)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.7 (5.6)
Period C	10.3	0.2 (1.6)	0.0 (0.0)	0.0 (0.0)	0.5 (4.8)	7.3 (71.0)	1.5 (14.5)	0.0 (0.0)	0.2 (1.6)	0.0 (0.0)	0.7 (6.5)
Period D	11.4	0.6 (4.9)	0.0 (0.0)	0.0 (0.0)	1.0 (8.7)	8.2 (71.8) ^{c,d}	1.1 (9.7)	0.2 (1.9)	0.1 (1.0)	0.0 (0.0)	0.2 (1.9)
Stage IV											
Period A	11.1	4.0 (35.9)	0.1 (1.3)	0.0 (0.0)	1.6 (14.1)	2.0 (17.9)	0.3 (2.6)	1.9 (16.7)	0.9 (7.7)	0.4 (3.8)	0.0 (0.0)
Period B	11.3	4.0 (35.3)	0.0 (0.0)	0.0 (0.0)	1.7 (14.7)	3.7 (32.4)	0.3 (2.9)	1.3 (11.8)	0.0 (0.0)	0.3 (2.9)	0.0 (0.0)
Period C	10.0	2.8 (28.3)	0.0 (0.0)	0.0 (0.0)	0.8 (8.3)	3.7 (36.7) [↑]	0.5 (5.0)	1.3 (13.3)	0.3 (3.3)	0.5 (5.0)	0.0 (0.0)
Period D	11.2	3.9 (34.7)	0.3 (3.0)	0.0 (0.0)	1.1 (9.9)	2.9 (25.7)	0.6 (5.0)	1.9 (16.8)	0.2 (2.0)	0.3 (3.0)	0.0 (0.0)

ST, systemic therapy; RT, radiotherapy; CR, chemoradiation; S&R, stoma & resection; NT, no treatment; OT, other treatment; SM, surgery metastases; LS, local surgery; Period A, week 2-8 of 2020; Period B, week 9-11 of 2020; Period C, week 12-17 of 2020; Period D, week 18-26 of 2020.

Data are shown as average n (%). We compared data of period B-D (the COVID-19 period) with data of period A (the before COVID-19 period) using the Mantel-Haenszel test. This has been adjusted for different age groups (<55, 55-75, >75 years).

The arrows show statistically significant data corrected for age: ↑ = higher proportion of patients received this treatment; ↓ = lower proportion of patients received this treatment.

The analyses adjusted for the different age groups are performed and significant differences are explained:

a: higher proportion of patients aged >75 years diagnosed with colon cancer stage I received resection

b: higher proportion of patients aged >75 years diagnosed with colon cancer stage III received resection

c: higher proportion of patients aged <55 years diagnosed with colon cancer stage III received resection

d: lower proportion of patients aged 55-75 years diagnosed with colon cancer stage III received resection

Supplementary Table 1b Weekly average number of patients diagnosed with rectal cancer per type of first treatment, per period based on incidence date, and per clinical tumor stage

	Total	ST	RT	CR	Stoma	Resection	S&R	NT	OT	SM	LS
Stage I											
Period A	7.4	0.0 (0.0)	0.1 (1.9)	0.3 (3.8)	0.0 (0.0)	1.7 (23.1)	1.3 (17.3)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	4.0 (53.8)
Period B	8.7	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	1.3 (15.4)	2.0 (23.1)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	5.3 (61.5) ^a
Period C	3.8	0.0 (0.0)	0.3 (8.7)	0.2 (4.3)	0.0 (0.0)	0.8 (21.7)	0.5 (13.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	2.0 (52.2)
Period D	3.6	0.0 (0.0)	0.1 (3.1)	0.0 (0.0)	0.0 (0.0)	0.7 (18.8)	0.8 (21.9)	0.1 (3.1)	0.0 (0.0)	0.0 (0.0)	1.9 (53.1)
Stage II											
Period A	5.3	0.0 (0.0)	0.7 (13.5)	0.9 (16.2)	0.6 (10.8)	1.4 (27.0)	1.1 (21.6)	0.4 (8.1)	0.0 (0.0)	0.0 (0.0)	0.1 (2.7)
Period B	3.0	0.0 (0.0)	0.7 (22.2)	0.7 (22.2)	0.3 (11.1)	0.3 (11.1)	0.7 (22.2)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.3 (11.1)
Period C	1.7	0.0 (0.0)	0.5 (30.0)	0.7 (40.0)	0.0 (0.0)	0.5 (30.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Period D	2.9	0.0 (0.0)	0.7 (23.1)	0.1 (3.8)	0.6 (19.2)	0.6 (19.2)	0.9 (30.8)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.1 (3.8)
Stage III											
Period A	7.4	0.1 (1.9)	2.0 (26.9)	4.0 (53.8)	1.0 (13.5)	0.1 (1.9)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.1 (1.9)
Period B	6.0	0.0 (0.0)	1.7 (27.8)	2.7 (44.4)	1.3 (22.2)	0.3 (5.6)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Period C	5.2	0.0 (0.0)	2.0 (38.7)	2.2 (41.9)	0.5 (9.7)	0.3 (6.5)	0.2 (3.2)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Period D	5.6	0.0 (0.0)	1.9 (34.0)	2.3 (42.0)	0.7 (12.0)	0.4 (8.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.2 (4.0)
Stage IV											
Period A	3.7	0.6 (15.4)	1.0 (26.9)	0.1 (3.8)	1.3 (34.6)	0.0 (0.0)	0.0 (0.0)	0.6 (15.4)	0.0 (0.0)	0.0 (0.0)	0.1 (3.8)
Period B	4.0	0.7 (16.7)	1.3 (33.3)	0.3 (8.3)	0.7 (16.7)	0.0 (0.0)	0.3 (8.3)	0.7 (16.7)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Period C	2.8	0.5 (17.6)	0.3 (11.8)	0.5 (17.6)	0.7 (23.5)	0.3 (11.8)	0.2 (5.9)	0.0 (0.0)	0.2 (5.9)	0.2 (5.9)	0.0 (0.0)
Period D	3.0	0.9 (29.6)	0.8 (25.9)	0.2 (7.4)	0.6 (18.5)	0.0 (0.0)	0.0 (0.0)	0.1 (3.7)	0.3 (11.1)	0.1 (3.7)	0.0 (0.0)

ST, systemic therapy; RT, radiotherapy; CR, chemoradiation; S&R, stoma & resection; NT, no treatment; OT, other treatment; SM, surgery metastases; LS, local surgery; Period A, week 2-8 of 2020; Period B, week 9-11 of 2020; Period C, week 12-17 of 2020; Period D, week 18-26 of 2020.

Data are shown as average n (%). We compared data of period B-D (the COVID-19 period) with data of period A (the before COVID-19 period) using the Mantel-Haenszel test. This has been adjusted for the different age groups (<55, 55-75, >75 years).

The analyses adjusted for the different age groups are performed and significant differences are explained:
a: higher proportion of patients aged >75 years diagnosed with rectal cancer stage I received local surgery

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