

Impact of the COVID-19 pandemic on the in hospital diagnostic pathway of breast and colorectal cancer in the Netherlands: a population-based study

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Abstract

Objective

The COVID-19 pandemic has had an impact on health care. In the Netherlands, hospital capacity for non-covid care was limited and population screening for cancer was temporarily halted. The aim of this study was to investigate the impact of the pandemic on the in hospital diagnostic pathway of patients with breast or colorectal cancer.

Methods

In this study, 48,425 patients with breast cancer and 27,810 patients with colorectal cancer with a primary tumor were selected from the Netherlands Cancer Registry and the Dutch Hospital Data. Patients diagnosed between January 2020 and July 2021 were divided into six periods, based on the number of hospitalizations due to COVID-19, and compared to the same periods in 2017-2019. A t-test was performed to compare the number of diagnosed patients per period. Patient characteristics were compared using chi-squared tests. The impact on the diagnostic procedures performed was analysed using logistic regression. The median time between pathologically confirmed diagnosis and therapy and the median time between first diagnostic procedure and therapy were analysed using Cox Proportional Hazards Regression. Analyses were stratified for cancer type and corrected for age, gender (only for colorectal cancer), stage and region.

Results

During the first peak of the pandemic in 2020, significantly fewer patients were diagnosed with breast and colorectal cancer, respectively -48% and -35%. This decrease was mainly seen in lower stage tumors. Mammography and echography were performed significantly less for patients with breast cancer during the first recovery period in 2020 (OR=0.83 and 0.85 respectively) compared to 2017-2019. PET-CT was performed significantly more often during the first recovery period (OR=1.39). For patients with colorectal cancer, echography, endoscopy and radiologic imaging were performed significantly less during the first peak in 2020 (OR=0.75, 0.82 and 0.71 respectively). CT and MRI were performed significantly more during the first COVID-19 peak in 2020 (OR=1.55 and 1.39 respectively). The median time between pathologically confirmed breast cancer diagnosis and start of therapy and the median time between first diagnostic procedure and start of therapy significantly decreased during all covid periods in 2020. The

largest decrease for patients with breast cancer was observed during the first peak in 2020 with 3 and 4 days (HR=1.26 and HR=1.25) respectively. For colorectal cancer, the largest decrease was observed in the same period by 8 and 7 days (HR=1.42 and HR=1.34) respectively.

Conclusion

Significant differences were found in the procedures performed, but these differences do not seem to have had a major impact on the in hospital diagnostic pathway. The decreased number of diagnoses was related to the temporary halt of the national screening programs. Breast cancer procedure PET-CT was performed more often during the COVID-19 period, possibly reflecting the increased proportion of patients diagnosed at a higher stage. The number of breast and colorectal cancer diagnoses for early stage tumors was limited. A reduced time of the diagnostic pathway may be the result of fewer referred patients with cancer and the large effort on keeping the oncology care in place. In conclusion, throughout the Netherlands good cancer care was performed during COVID-19.

Keywords

COVID-19, breast cancer, colorectal cancer, diagnostic pathway, diagnosis, lead time, diagnostic procedures, population based

Introduction

Late 2019, a new infection known as COVID-19 disease, was identified in Wuhan, China [1]. The coronavirus spread quickly, became a worldwide problem and impacted cancer care. Delays in screening, diagnosis and treatment were observed which may result in an increase in cancer deaths in the future [2,3,4]. March 2020, the first measures against the coronavirus were taken in the Netherlands [5]. The Dutch government announced general measures to combat the coronavirus such as keeping a minimum distance of 1.5 meter of each other, washing hands, sneezing in the elbow and no more shaking hands [6]. In March 2020, an 'intelligent lockdown' was implemented to reduce the number of infected people [5]. The intelligent lockdown was a partial lockdown; hotels, restaurants, schools, and childcare facilities were closed [6]. People were advised to visit the general practitioner (GP) only in case of severe complaints and referrals to the hospital were postponed [5]. In addition, surgeries were postponed [7], population screening for breast and colorectal cancer was temporarily halted [8] and fewer diagnoses and treatments were performed [9,10]. The number of infections were not equally spread over the Netherlands, most infections were in the south of the Netherlands. Patients were transferred to other hospitals when there were no hospital beds left [6]. After temporarily halting population screening from mid-March 2020 to mid-May 2020, screening was restarted gradually. Mid 2021, breast cancer screening capacity was 85% and colorectal cancer screening had the same capacity in October 2021 as in the years before the pandemic [11]. By the end of 2020, measures were less stringent but there were still fewer patients with cancer referred to the hospital by their GP [12]. Fewer and delayed referrals possibly influenced the diagnostic pathway in the hospital [13].

In this study, the impact of COVID-19 on the diagnostic pathway of cancer in hospitals throughout the Netherlands was investigated. The period until mid-2021 was selected to investigate the impact during the first wave and the short-term impact after the first wave. Two types of cancer with population screening, breast and colorectal cancer [14,15], were investigated. Up to now, studies focused on the first months of the pandemic or focused on treatment, follow-up and the predicted long-term impact. Few studies focused on the impact of the COVID-19 pandemic on cancer diagnosis. Some studies revealed an enormous impact on cancer care [4] or colorectal cancer specifically [16]. Another study revealed

postponed cancer care and patients with poorer patient and tumor characteristics during the pandemic [17].

No studies were found focussing on the total diagnostic pathway, therefore the objective of this study was to investigate the impact of the COVID-19 pandemic on the in hospital diagnostic pathway until start of therapy by analysing the diagnostic procedures performed per patient and the diagnostic time to start of therapy.

Method

Data collection

This study is a retrospective cohort study, based on data from the Netherlands Cancer Registry (NCR) and Dutch Hospital Data (DHD). Data was retrieved from 69 Dutch hospitals. The data set consists of data on patient and tumor characteristics (e.g., age, gender, type of cancer, stage of disease, region in the Netherlands) and the diagnostic pathway (e.g., diagnostic procedure performed, date of diagnosis, date of first diagnostic procedure, date of start therapy). Only primary cancer diagnoses were included in this study.

Patients

Patients aged 18 years or older diagnosed with primary breast or colorectal cancer during the period from January 2017 to July 2021 were included in this study. Data from DHD and the NCR were probabilistic merged on patient level using patient number, date of birth, gender and postal code. The maximum time allowed between first cancer related appointment in a hospital and start of therapy is six weeks according to the SONCOS-norm [18]. Therefore, diagnostic procedures more than six months prior to diagnosis date were removed to avoid including non-cancer related diagnostic procedures in the analysis. Patients without known hospital diagnostic procedures, an unknown start date of therapy or a start date of therapy before diagnosis date were excluded from the dataset.

Definitions

Periods

The study period between January 2017 to July 2021 was divided in six periods based on hospitalizations due to COVID-19 in the Netherlands. Period A covers weeks 1-11 of 2020 (i.e., pre-COVID); period B weeks 12-20 of 2020 (i.e., first peak); period C weeks 21-41 of 2020 (i.e., first recovery); period D weeks 42-53 of 2020 (i.e., second peak); period E weeks 1-20 of 2021 (i.e., third peak) and period F weeks 21-30 of 2021 (i.e., second recovery).

Age categories

Patients with breast and colorectal cancer were categorized in age categories, based on the age categories for population screening for breast and colorectal cancer: 50 to 75 [14] and 55 to 75 [15],

respectively. Therefore, patients with breast cancer were grouped into ages <50, 50-75 and >75 years and patients with colorectal cancer were grouped into ages <55, 55-75 and >75 years.

Gender

For breast cancer, only females were included. For colorectal cancer, males and females were included.

Stage of disease

Stage of disease was divided into stage 1 to 4 for both breast cancer and colorectal cancer, based on the TNM classification (18th edition) [19]. Pathological stage was used if available. When pathological stage was unknown, clinical stage was used. Any remaining unknown stage was classified as stage "X".

Region

Patients were categorized into a region, based on the hospital where a patient was diagnosed. In total, the Netherlands was divided into five regions [20], these are the north (Friesland, Groningen, Drenthe), the middle east (Overijssel, Flevoland), the middle (Utrecht, Gelderland), the west (Noord-Holland, Zuid-Holland, Zeeland) and the south (Noord-Brabant, Limburg).

Lead times

The lead time of the diagnostic pathway per patient was calculated for the time between pathologically confirmed diagnosis and start of therapy and the time between first diagnostic procedure and start of therapy. The date of diagnosis is registered by data managers of the NCR with different registration rules and the date of first procedure was not registered consequently, therefore both were included to investigate if there were differences in outcome.

Diagnostic procedures

Per type of cancer, different diagnostic procedures were analyzed based on common diagnostic procedures per type of cancer [21]. Diagnostic procedures were divided into mammography, echography, PET-CT and CT for breast cancer and echography, endoscopy, CT, MRI, PET-CT and radiology imaging for colorectal cancer.

Statistical analysis

The data was analysed to determine the impact of the COVID-19 pandemic on the diagnostic pathway of cancer in the Netherlands. The years 2017 to 2019 were the period before the COVID-19 pandemic and was used as control group. Periods during COVID-19 were compared to the same period in 2017 to 2019

to determine differences between periods during the pandemic. The diagnostic procedures performed and the lead times of the diagnostic pathway were investigated. Breast and colorectal cancer were analysed separately. Patient and tumor characteristics (i.e., type of cancer, age, gender, stage of disease, region, period) were described at the time of diagnosis. Patient characteristics of the study population were investigated using Chi-squared test. An unpaired t-test was performed to analyze the number of diagnosed patients per period. Possible confounders were based on available data and literature and included in the regression analysis. For breast cancer, confounding variables in the regression models were age, stage of disease and region. For colorectal cancer, confounding variables were age, gender, stage of disease and region. In addition, confounders during the first wave were investigated. During this period, population screening was temporarily halted and the number of infections were not equally spread over the Netherlands. Therefore, confounders were investigated to determine the impact of confounders separately.

The diagnostic procedures performed per patient during the COVID-19 periods were compared to the same period before the pandemic (2017 to 2019). The diagnostic procedures performed per patient were analyzed as 1 (performed) or 0 (not performed) using logistic regression. The median time to therapy during the COVID-19 periods was compared to the same period before the pandemic (2017 to 2019) and analyzed using Cox Proportional Hazards Regression.

Data were analyzed using Stata version 17.0. A two-sided p-value of <0.05 was considered statistically significant.

Results

Research population

In total, 48,425 patients with breast cancer and 27,810 patients with colorectal cancer were included. During the pandemic, proportionally fewer patients in the screening age were diagnosed and patients were diagnosed at a higher stage. The baseline characteristics of patients with breast and colorectal cancer were shown in table 1a and 1b respectively. The number of diagnosed patients with breast cancer significantly decreased during the first peak, first recovery, third peak and second recovery. Colorectal cancer diagnoses significantly decreased during all periods excluding the second peak. The number of diagnosed patients had the largest decrease during the first peak in 2020, -48% and -35% for breast cancer (figure 1a) and colorectal cancer (figure 1b) respectively.

Diagnostic procedures

Breast cancer

Breast cancer diagnostic procedures performed per patient were shown in table 2a. Adjusted for age, stage and region, the percentage of patients who received mammography was significantly decreased during the first recovery (from 86% to 84%, OR=0.83). The percentage of patients who received echography was significantly decreased during the first recovery (from 93% to 92%, OR=0.85). The percentage of patients who received PET-CT was significantly increased during the first peak (from 2% to 5%, OR=1.94) and first recovery (from 2% to 3%, OR=1.39) and the percentage of patients who received CT was significantly decreased in the pre-COVID period (from 4% to 3%, OR=0.69), third peak (from 4.5% to 3.6%, OR=0.83) and second recovery (from 4% to 3%, OR=0.68).

Colorectal cancer

Colorectal cancer diagnostic procedures performed per patient were shown in table 2b. After adjusting for age, gender, stage and region, the percentage of patients who received echography was significantly decreased during the first peak (from 16% to 13%, OR=0.75) and second recovery (from 15% to 12%, OR=0.59). The percentage of patients who received endoscopy was significantly decreased during the first peak, first recovery, second peak and third peak. The percentage of patients who received CT was significantly increased during the first peak (from 39% to 52%, OR=1.55), first recovery (from 41% to 47%, OR=1.25) and third peak (from 38% to 43%, OR=1.25). The percentage of patients who received

MRI was significantly increased during the first peak (from 7% to 10%, OR=1.39), first recovery (from 7% to 9%, OR=0.67) and third peak (from 7% to 9%, OR=1.33) and the percentage of patients who received radiology imaging was significantly decreased in all periods.

Lead times

Breast cancer

The median time of the diagnostic pathway of breast cancer was shown in figure 2a. The hazard ratios and p-values were shown in table 3. After adjustment for age, stage and region, the time between breast cancer diagnosis and start of therapy significantly increased during the pre-COVID period and the second recovery with 2 days (HR =0.82 and HR=0.88 respectively) and during the third peak with 1 day (HR=0.90). This median lead time significantly decreased during the first peak with 3 days (HR=1.26) and first recovery and second peak with 1 day (HR=1.04 and HR=1.16 respectively). The time between first diagnostic procedure and start of therapy significantly increased during the pre-COVID period with 4 days (HR=0.79) and third peak and second recovery with 2 days (HR=0.89 and HR=0.85 respectively.) This median lead time significantly decreased during the first peak with 4 days (HR=1.25), first recovery with 1 day (HR=1.04) and second peak with 2 days (HR=1.13).

Colorectal cancer

The median time of the diagnostic pathway of colorectal cancer was shown in figure 2b. The hazard ratios and p-values were shown in table 3. After adjustment for age, gender, stage and region, the time between colorectal cancer diagnosis and start of therapy significantly increased during the second peak with 2 days (HR=0.90). This lead time significantly decreased during the first peak with 8 days (HR=1.42), first recovery with 3 days (HR=1.09) and second peak with 2 days (HR=1.07). The time between first diagnostic procedure and start of therapy significantly increased during the second recovery with 3 days (HR=0.82). This lead time significantly decreased during the first peak with 7 days (HR=1.34) and first recovery with 3.5 days (HR=1.08).

Confounders

During the first peak, the median time to therapy increased for patients in the age group >75 compared to the population in the screening age. There were no notable differences for gender, stage, and region in terms of the lead time of the diagnostic pathway for both breast (figure 4a) and colorectal cancer (figure 4b).

Discussion

In this study, the impact of the COVID-19 pandemic on the in hospital diagnostic pathway of cancer in the Netherlands was investigated. Related to the measures taken, i.e., the temporary halt of the national screening program, the number of breast and colorectal cancer diagnoses decreased, as shown in previous studies [22,23]. Compared to the years 2017 to 2019, the frequency of hospital diagnostic procedures decreased for both tumor types. In addition, the diagnostic procedures were performed within a shorter time interval.

The revealed lower number of breast and colorectal cancer diagnoses during the pandemic was to be expected and was mainly seen in lower stage tumors. Patients without cancer-related symptoms were not diagnosed during the temporary halt of screening. In addition, a decreasing trend in the number of colorectal cancer diagnoses has been present for the past years [24]. However, during the first peak of the pandemic, there was a lower number in diagnoses compared to the other periods.

There were significant differences found in the diagnostic procedures performed per patient. For breast cancer, the percentage of patients who received mammography, echography and a CT-scan significantly decreased during the COVID-19 period and the percentage of patients who received PET-CT significantly increased. The percentage of patients with colorectal cancer who received echography, endoscopy and radiology imaging significantly decreased during the pandemic and the percentage of patients who received CT and MRI significantly increased. This decrease in the percentage of patients who received PET-CT, CT and MRI during the pandemic may be due to the fact that patients were diagnosed at a higher stage, which is associated with more symptoms, therefore other diagnostic procedures were performed compared to people without symptoms.

Time between date of diagnoses to start of therapy and first diagnostic procedure and start of therapy were both included in the analysis, due to differences in date of first diagnostic procedure and date of diagnosis. However, the results of both are comparable. This study revealed that significant shorter lead times of the diagnostic pathway of breast and colorectal cancer existed during the pandemic, which was consistent with other studies [13,20,25]. This decrease may be due to the fact that fewer patients were referred to the hospital, which allowed diagnostics to be performed more quickly. Secondly, the decrease may be due to the actively postponement of surgeries [7] and hormonal treatment or radiotherapy was

given first or earlier, which led to an earlier start of therapy. Thirdly, the decrease may be due to the fact that patients were diagnosed at a higher stage, therefore diagnosis is easier and treatment can start earlier. Comparing the first peak in the pandemic with the years 2017 to 2019, the confounders of lead times showed minor differences in terms of stage of disease and region. Differences in age categories were found, the time to therapy for the elderly was longer in comparison with younger patients. This may be due to the fact elderly people had a fear of visiting the GP and the hospital, because of a higher risk of a large impact of a COVID-19 infection.

There were some limitations in this study. In total, data was available from 69 of the 76 hospitals in the Netherlands and not all patients had sufficient available data to be merged. The percentage of patients with breast and colorectal cancer who received biopsy and the percentage of patients with breast cancer who received MRI were not representative and therefore not included. In a follow-up study, the impact of COVID-19 on biopsy and MRI should be examined.

Conclusion

In conclusion, throughout the Netherlands good cancer care was performed during COVID-19. Significant differences were found in the diagnostic pathway of cancer, but these differences do not seem to have had a major impact. The impact of the pandemic was mainly seen in 2020, particularly during the first peak. Diagnostics of breast and colorectal cancer in 2021 were comparable with the pre-covid period (period A). The impact of the pandemic on breast and colorectal cancer was comparable. There was a drop in number of diagnoses related to the temporary halt of population screening, the percentage of patients who received diagnostic procedures for early stage tumors decreased (i.e., less mammography for breast cancer, less endoscopy for colorectal cancer), and a shortened time to therapy was seen, probably as a result of less hospitalized patients with cancer and the effort on keeping the oncology care in place. A follow-up study is needed to examine the impact on biopsy, MRI and the long-term influence of the differences aforementioned and found in this study.

1 Appendix

2 Table 1a: Patient characteristics of the included patients with breast cancer

		period A 2017- 2019	period A pre covid		period B 2017- 2019	period B peak 1		period C 2017- 2019	period C recovery 1		period D 2017- 2019	period D peak 2		period E 2017- 2019	period E peak 3		period F 2017- 2019	period F recovery 2	
		N (%)	N (%)	P- value	N (%)	N (%)	P- value	N (%)	N (%)	P- value	N (%)	N (%)	P- value	N (%)	N (%)	P- value	N (%)	N (%)	P- value
Patients	N	6765	2354		5826	1005		13272	3558		7093	2342		13167	4236		6380	1974	
Age (years)	<55	1345 (20)	435 (18)	0.118	1060 (18)	278 (28)	<0.01	2405 (18)	783 (22)	<0.01	1154 (16)	404 (17)	0.534	2532 (19)	771 (18)	0.179	1190 (19)	297 (15)	<0.01
	55-75	4392 (65)	1526 (65)		3846 (66)	545 (54)		8606 (65)	2020 (57)		4838 (68)	1582 (68)		8581 (65)	2766 (65)		4090 (64)	1338 (68)	
	>75	1028 (15)	393 (17)		920 (16)	182 (18)		2261 (17)	755 (21)		1101 (16)	356 (15)		2054 (16)	699 (17)		1100 (17)	339 (17)	
Stage of disease	Stage I	3612 (53)	1217 (52)	0.645	3068 (53)	411 (41)	<0.01	6928 (52)	1525 (43)	<0.01	3893 (55)	1191 (51)	<0.01	6963 (53)	2201 (52)	<0.01	3316 (52)	963 (49)	<0.01
	Stage II	2196 (32)	782 (33)		1929 (33)	398 (40)		4543 (34)	1414 (40)		2293 (32)	819 (35)		4342 (33)	1436 (34)		2189 (34)	716 (36)	
	Stage III	632 (9)	230 (10)		554 (10)	124 (12)		1205 (9)	394 (11)		575 (8)	206 (9)		1236 (9)	378 (9)		588 (9)	171 (9)	
	Stage IV	312 (5)	120 (5)		265 (5)	67 (7)		566 (4)	219 (6)		319 (4)	116 (5)		602 (5)	192 (5)		274 (4)	87 (4)	
	Stage X	13 (0)	5 (0)		10 (0)	5 (0)		30 (0)	6 (0)		13 (0)	10 (0)		24 (0)	29 (1)		13 (0)	37 (2)	
Region	Middle	1448 (21)	541 (23)	<0.01	1249 (21)	209 (21)	0.041	2791 (21)	684 (19)	<0.01	1628 (23)	457 (20)	<0.01	2812 (21)	823 (19)	<0.01	1303 (20)	409 (21)	<0.01
	Middle east	761 (11)	325 (14)		680 (12)	147 (15)		1504 (11)	516 (15)		816 (12)	355 (15)		1513 (11)	621 (15)		743 (12)	293 (15)	
	North	881 (13)	242 (10)		772 (13)	133 (13)		1845 (14)	422 (12)		911 (13)	283 (12)		1725 (13)	488 (12)		937 (15)	276 (14)	
	South	1147 (17)	446 (19)		1067 (18)	182 (18)		2400 (18)	632 (18)		1211 (17)	406 (17)		2314 (18)	818 (19)		1106 (17)	340 (17)	
	West	2522 (37)	796 (34)		2056 (35)	332 (33)		4720 (36)	1303 (37)		2520 (36)	835 (36)		4794 (36)	1466 (35)		2284 (36)	631 (32)	
	Unknown	6 (0)	4 (0)		2 (0)	2 (0)		12 (0)	1 (0)		7 (0)	6 (0)		9 (0)	20 (0)		7 (0)	25 (1)	

Period A (pre covid), week 1-11 (2020); Period B (peak 1), week 12-20 (2020); Period C (recovery 1), week 21-41 (2020); Period D (peak 2), week 42-53 (2020); Period E (peak 3), week 1-20 (2021); Period F (recovery 2), week 21-30 (2021); Pathological stage X, unknown.

The p-value was calculated excluding missing values, using the chi-squared test to compare patients diagnosed in period A, B, C, D, E or F with patients diagnosed in the same period during 2017-2019.

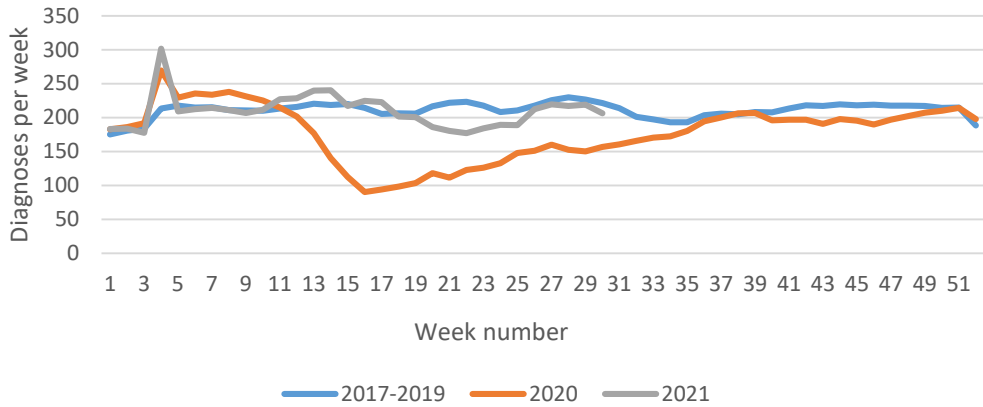
3 Table 1b: Patient characteristics of the included patients with colorectal cancer

		period A 2017- 2019	period A pre covid		period B 2017- 2019	period B peak 1		period C 2017- 2019	period C recovery 1		period D 2017- 2019	period D peak 2		period E 2017- 2019	period E peak 3		period F 2017- 2019	period F recovery 2	
		N (%)	N (%)	P- value	N (%)	N (%)	P- value	N (%)	N (%)	P- value	N (%)	N (%)	P- value	N (%)	N (%)	P- value	N (%)	N (%)	P- value
Patients	N	4239	1176		3421	740		7842	2244		4034	1214		7964	2074		3767	826	
Age (years)	<55	445 (10)	148 (13)	<0.01	399 (12)	106 (14)	0.013	844 (11)	316 (14)	<0.01	460 (11)	143 (12)	0.863	886 (11)	246 (12)	0.139	421 (11)	91 (11)	0.408
	55-75	2306 (54)	577 (49)		1787 (52)	345 (47)		4069 (52)	1010 (45)		2064 (51)	626 (52)		4255 (53)	1140 (55)		1938 (51)	406 (49)	
	>75	1488 (35)	451 (38)		1235 (36)	289 (39)		2929 (37)	918 (41)		1510 (37)	445 (37)		2823 (35)	688 (33)		1408 (37)	329 (40)	
Gender	Men	2331 (55)	659 (56)	0.523	1887 (55)	389 (53)	0.199	4220 (54)	1181 (53)	0.322	2162 (54)	598 (49)	<0.01	4381 (55)	1106 (53)	0.170	2010 (53)	431 (52)	0.539
	Woman	1908 (45)	517 (44)		1534 (45)	351 (47)		3622 (46)	1063 (47)		1872 (46)	616 (51)		3583 (45)	968 (47)		1757 (47)	395 (48)	
Stage of disease	Stage I	911 (21)	261 (22)	0.780	669 (20)	126 (17)	<0.01	1637 (21)	374 (17)	<0.01	836 (21)	231 (19)	0.197	1649 (21)	408 (20)	<0.01	805 (21)	116 (14)	<0.01
	Stage II	1060 (25)	300 (26)		914 (27)	170 (23)		1987 (25)	579 (26)		1042 (26)	338 (28)		2042 (26)	536 (26)		951 (25)	160 (19)	
	Stage III	1322 (31)	346 (29)		1046 (31)	219 (30)		2408 (31)	702 (31)		1246 (31)	362 (30)		2462 (31)	637 (31)		1148 (30)	176 (21)	
	Stage IV	876 (21)	246 (21)		739 (22)	217 (29)		1690 (22)	559 (25)		843 (21)	270 (22)		1682 (21)	480 (23)		810 (22)	370 (45)	
	Stage X	70 (2)	23 (2)		53 (2)	8 (1)		120 (2)	30 (1)		67 (2)	13 (1)		129 (2)	13 (1)		53 (1)	4 (0)	
Region	Middle	843 (20)	232 (20)	0.175	660 (19)	159 (21)	0.112	1556 (20)	447 (20)	0.699	769 (19)	253 (21)	0.247	1568 (20)	395 (19)	<0.01	715 (19)	124 (15)	<0.01
	Middle east	552 (13)	134 (11)		432 (13)	73 (10)		866 (11)	259 (12)		451 (11)	120 (10)		1021 (13)	218 (11)		411 (11)	100 (12)	
	North	448 (11)	110 (9)		372 (11)	65 (9)		830 (11)	211 (9)		432 (11)	130 (11)		845 (11)	219 (11)		416 (11)	75 (9)	
	South	945 (22)	282 (24)		771 (23)	172 (23)		1866 (24)	547 (24)		986 (24)	275 (23)		1794 (23)	442 (21)		895 (24)	206 (25)	
	West	1417 (33)	402 (34)		1158 (34)	266 (36)		2656 (34)	761 (34)		1357 (34)	418 (34)		2671 (34)	784 (38)		1298 (34)	296 (36)	
	Unknown	34 (1)	16 (1)		28 (1)	5 (1)		68 (1)	19 (1)		39 (1)	18 (1)		65 (1)	16 (1)		32 (1)	25 (3)	

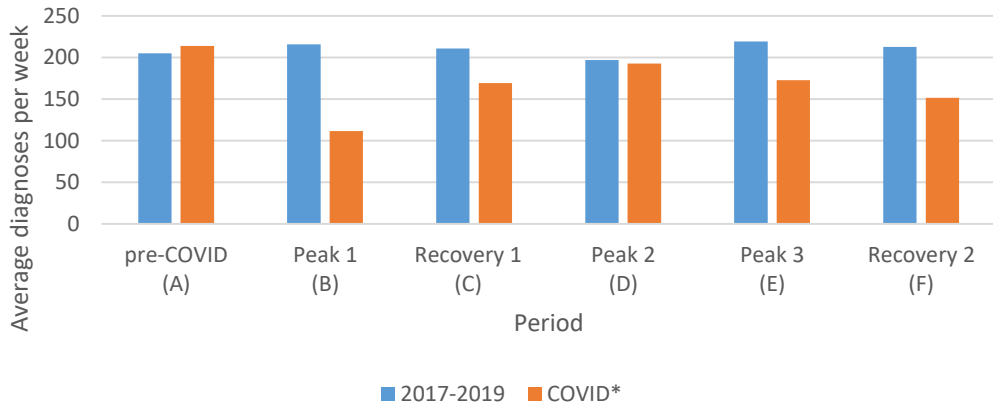
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The p-value was calculated excluding missing values, using the chi-squared test to compare patients diagnosed in period A, B, C, D, E or F with patients diagnosed in the same period during 2017-2019.

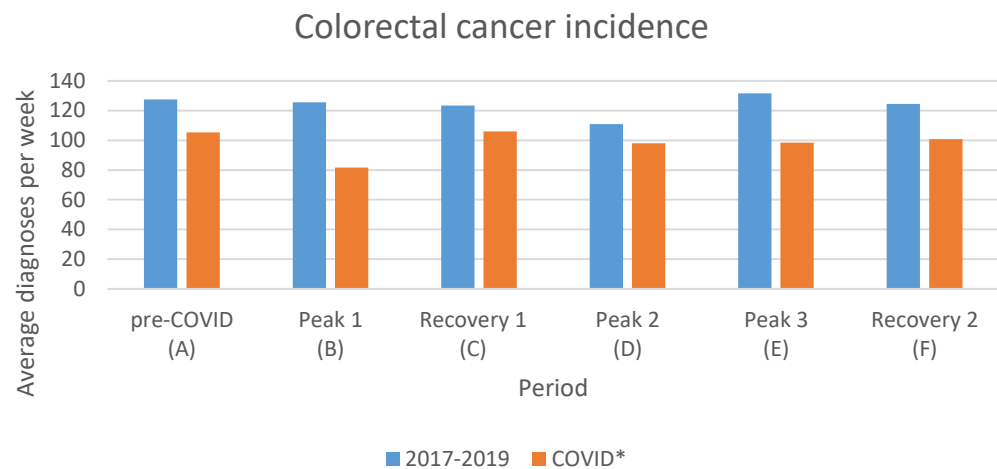
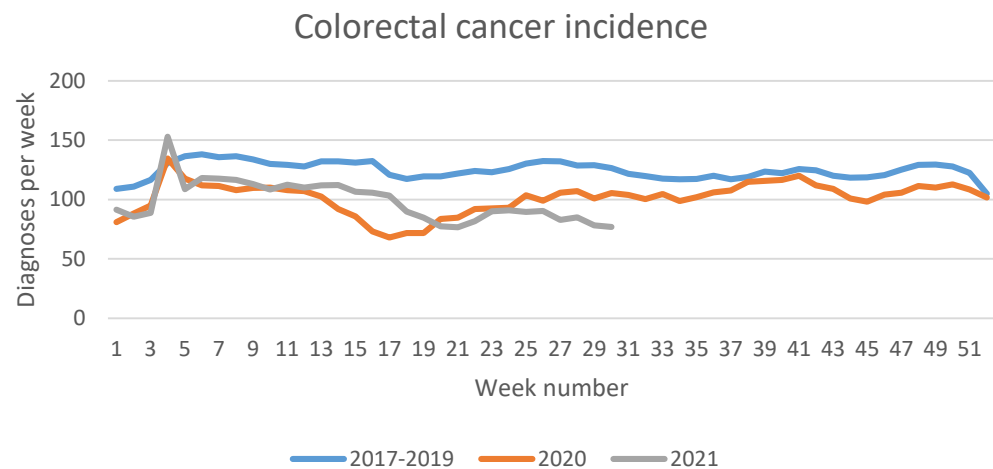
Breast cancer incidence



Breast cancer incidence



4 Figure 1a: Breast cancer diagnoses (average diagnoses per year in period 2017-2019)
 5 *Period A (pre covid), week 1-11 (2020); Period B (peak 1), week 12-20 (2020); Period C (recovery 1), week 21-41 (2020); Period D (peak 2), week 42-53 (2020);
 6 Period E (peak 3), week 1-20 (2021); Period F (recovery 2), week 21-30 (2021); All periods were significantly different.
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8 Figure 1b: Colorectal cancer diagnoses (average of diagnoses per year in period 2017-2019)

9 *Period A (pre covid), week 1-11 (2020); Period B (peak 1), week 12-20 (2020); Period C (recovery 1), week 21-41 (2020); Period D (peak 2), week 42-53 (2020);

10 Period E (peak 3), week 1-20 (2021); Period F (recovery 2), week 21-30 (2021); All periods were significantly different.

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12 Table 2a: Breast cancer diagnostic procedures performed per patient

		period A 2017- 2019			period B 2017- 2019			period C 2017-2019			period D 2017- 2019			period E 2017-2019			period F 2017- 2019		
		period A pre covid			period B peak 1			period C recovery 1			period D peak 2			period E peak 3			period F recovery 2		
		N (%)	N (%)	OR	N (%)	N (%)	OR	N (%)	N (%)	OR	N (%)	N (%)	OR	N (%)	N (%)	OR	N (%)	N (%)	OR
Patients	N	6765	2354		5826	1005		13272	3558		7093	2342		13167	4236		6380	1974	
Mammo graphy	Yes	5816 (86)	2053 (87)	1,1	4993 (86)	866 (86)	1,1	11416 (86)	2974 (84)	0,83**	6006 (85)	2016 (86)	1,11	11299 (86)	3654 (86)	1,02	5494 (86)	1720 (87)	1,07
	No	949 (14)	301 (13)		833 (14)	139 (14)		1856 (14)	584 (16)		1087 (15)	326 (14)		1868 (14)	582 (14)		886 (14)	254 (13)	
Echogra phy	Yes	6239 (92)	2197 (93)	1,17	5394 (93)	929 (92)	0,89	12332 (93)	3283 (92)	0,85*	6555 (92)	2152 (92)	0,92	12170 (92)	3885 (92)	0,9	5911 (93)	1843 (93)	1,07
	No	526 (8)	157 (7)		432 (7)	76 (8)		940 (7)	275 (8)		538 (8)	190 (8)		997 (8)	351 (8)		469 (7)	131 (7)	
PET-CT	Yes	156 (2)	55 (2)	0,98	137 (2)	55 (5)	1,94**	281 (2)	118 (3)	1,39**	155 (2)	64 (3)	1,2	309 (2)	117 (3)	1,21	130 (2)	44 (2)	1,04
	No	6609 (98)	2299 (98)		5689 (98)	950 (95)		12991 (98)	3440 (97)		6938 (98)	2278 (97)		12858 (98)	4119 (97)		6250 (98)	1930 (98)	
CT	Yes	301 (4)	73 (3)	0,69**	237 (4)	58 (6)	1,35	516 (4)	162 (5)	1,12	247 (3)	102 (4)	1,25	562 (4)	149 (4)	0,83*	266 (4)	56 (3)	0,68*
	No	6464 (96)	2281 (97)		5589 (96)	947 (94)		12756 (96)	3396 (95)		6846 (97)	2240 (96)		12605 (96)	4087 (96)		6114 (96)	1918 (97)	

Period A (pre covid), week 1-11 (2020); Period B (peak 1), week 12-20 (2020); Period C (recovery 1), week 21-41 (2020); Period D (peak 2), week 42-53 (2020); Period E (peak 3), week 1-20 (2021); Period F (recovery 2), week 21-30 (2021).

OR: Odds ratio, was calculated using the logistic regression.

* significant difference between periods (P<0.05)

** significant difference between periods (P<0.01)

13 Table 2b: Colorectal cancer diagnostic procedures performed per patient

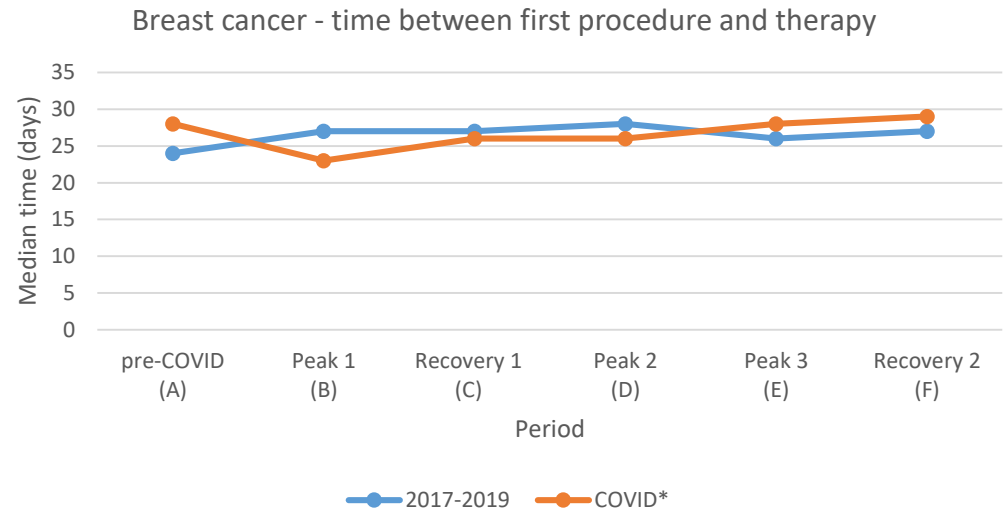
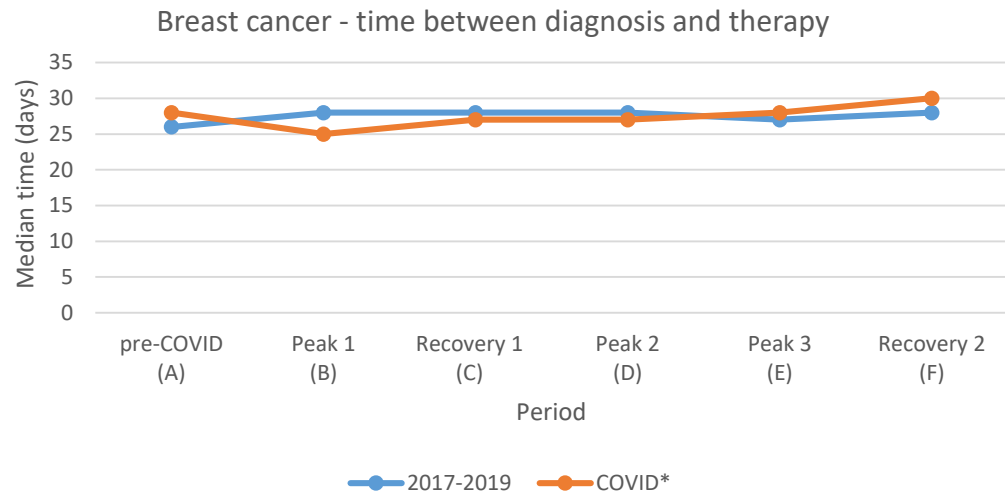
		period A 2017- 2019	period A pre covid		period B 2017- 2019	period B peak 1		period C 2017- 2019	period C recovery 1		period D 2017- 2019	period D peak 2		period E 2017- 2019	period E peak 3		period F 2017- 2019	period F recovery 2	
		N (%)	N (%)	OR	N (%)	N (%)	OR	N (%)	N (%)	OR	N (%)	N (%)	OR	N (%)	N (%)	OR	N (%)	N (%)	OR
Patients	N	4239	1176		3421	740		7842	2244		4034	1214		7964	2074		3767	826	
Echogr aphy	Yes	611 (14)	161 (14)	0,93	533 (16)	99 (13)	0,75*	1113 (14)	319 (14)	0,94	555 (14)	167 (14)	0,96	1179 (15)	282 (14)	0,87	556 (15)	102 (12)	0,59**
	No	3628 (86)	1015 (86)		2888 (84)	641 (87)		6729 (86)	1925 (86)		3479 (86)	1047 (86)		6785 (85)	1792 (86)		3211 (85)	724 (88)	
Endosc opy	Yes	3255 (77)	873 (74)	0,88	2606 (76)	525 (71)	0,82*	5911 (75)	1624 (72)	0,89*	3010 (75)	860 (71)	0,85*	6091 (76)	1498 (72)	0,82**	2837 (75)	600 (73)	1,01
	No	984 (23)	303 (26)		815 (24)	215 (29)		1931 (25)	620 (28)		1024 (25)	354 (29)		1873 (24)	576 (28)		930 (25)	226 (27)	
CT	Yes	1541 (36)	462 (39)	1,12	1343 (39)	382 (52)	1,55**	3178 (41)	1059 (47)	1,25**	1628 (40)	529 (44)	1,11	3009 (38)	896 (43)	1,25**	1520 (40)	332 (40)	0,83*
	No	2698 (64)	714 (61)		2078 (61)	358 (48)		4664 (59)	1185 (53)		2406 (60)	685 (56)		4955 (62)	1178 (57)		2247 (60)	494 (60)	
MRI	Yes	295 (7)	96 (8)	1,2	251 (7)	77 (10)	1,39*	577 (7)	199 (9)	1,21*	299 (7)	107 (9)	1,21	567 (7)	193 (9)	1,33**	3498 (93)	66 (8)	1,13
	No	3944 (93)	1080 (92)		3170 (93)	663 (90)		7265 (93)	2045 (91)		3735 (93)	1107 (91)		7397 (93)	1881 (91)		269 (7)	760 (92)	
PET-CT	Yes	42 (1)	18 (2)	1,53	51 (1)	13 (2)	1,11	106 (1)	37 (2)	1,21	43 (1)	20 (2)	1,49	97 (1)	23 (1)	0,94	45 (1)	7 (1)	0,6
	No	4197 (99)	1158 (98)		3370 (99)	727 (98)		7736 (99)	2207 (98)		3991 (99)	1194 (98)		7867 (99)	2051 (99)		3722 (99)	819 (99)	
Radiol. Imaging	Yes	325 (8)	68 (6)	0,72*	261 (8)	42 (6)	0,71*	566 (7)	142 (6)	0,82*	284 (7)	60 (5)	0,67**	606 (8)	92 (4)	0,55**	299 (8)	52 (6)	0,7*
	No	3914 (92)	1108 (94)		3160 (92)	698 (94)		7276 (93)	2102 (94)		3747 (93)	1154 (95)		7358 (92)	1982 (96)		3468 (92)	774 (94)	

Period A (pre covid), week 1-11 (2020); Period B (peak 1), week 12-20 (2020); Period C (recovery 1), week 21-41 (2020); Period D (peak 2), week 42-53 (2020); Period E (peak 3), week 1-20 (2021); Period F (recovery 2), week 21-30 (2021).

OR: Odds ratio, was calculated using the logistic regression.

* significant difference between periods (P<0.05)

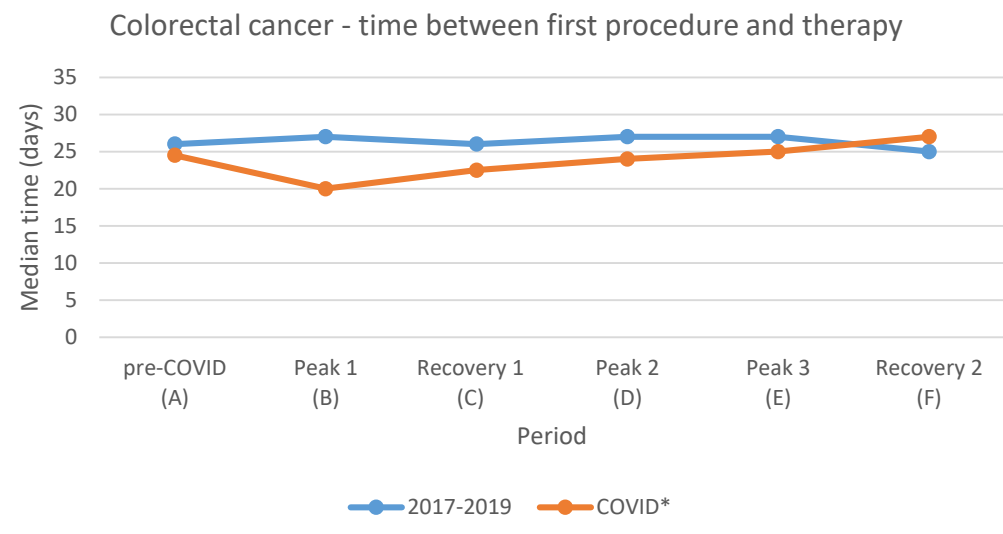
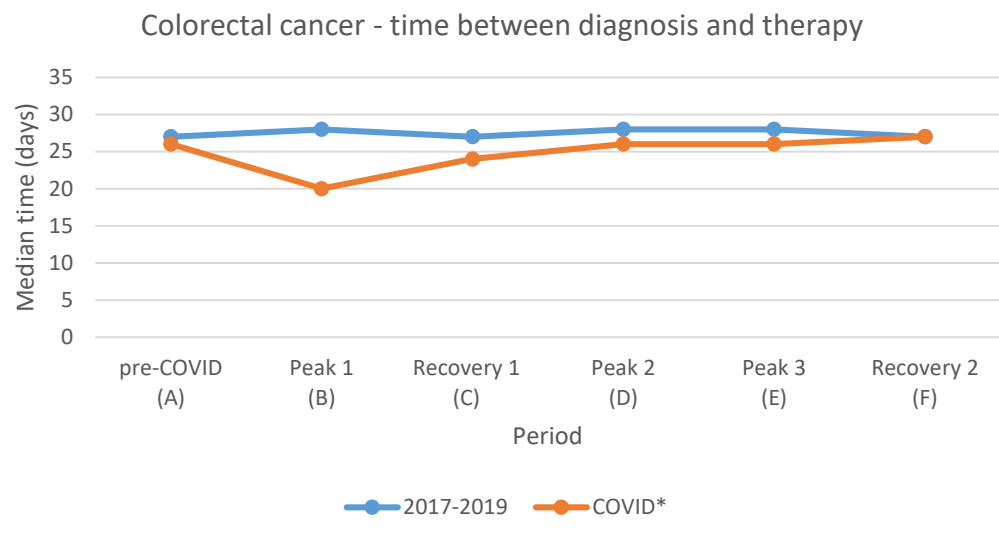
** significant difference between periods (P<0.01)



14 Figure 2a: Lead times of the diagnostic pathway of breast cancer

15 *Period A (pre covid), week 1-11 (2020); Period B (peak 1), week 12-20 (2020); Period C (recovery 1), week 21-41 (2020); Period D (peak 2), week 42-53 (2020);

16 Period E (peak 3), week 1-20 (2021); Period F (recovery 2), week 21-30 (2021).



17 Figure 2b: Lead times of the diagnostic pathway of colorectal cancer

18 *Period A (pre covid), week 1-11 (2020); Period B (peak 1), week 12-20 (2020); Period C (recovery 1), week 21-41 (2020); Period D (peak 2), week 42-53 (2020);

19 Period E (peak 3), week 1-20 (2021); Period F (recovery 2), week 21-30 (2021).

20 Table 3: Time to therapy of diagnostic pathway

Period		Hazards ratio (interval)					
		A (pre-covid)	B (peak 1)	C (recovery 1)	D (peak 2)	E (peak 3)	F (recovery 2)
Breast cancer	Diagnosis - therapy	0,82 (0,78-0,86)**	1,26 (1,18-1,35)**	1,04 (1,01-1,08)*	1,16 (1,11-1,22)**	0,9 (0,87-0,93)**	0,88 (0,84-0,93)**
	First procedure - therapy	0,79 (0,76-0,83)**	1,25 (1,17-1,34)**	1,04 (1-1,08)*	1,13 (1,08-1,19)**	0,89 (0,86-0,92)**	0,85 (0,81-0,9)**
Colorectal cancer	Diagnosis - therapy	0,97 (0,91-1,03)	1,42 (1,31-1,54)**	1,09 (1,04-1,14)**	1,07 (1,01-1,15)*	1,02 (0,97-1,07)	0,9 (0,83-0,97)**
	First procedure - therapy	0,94 (0,88-1,01)	1,34 (1,24-1,46)**	1,08 (1,03-1,13)**	1,04 (0,98-1,11)	1,01 (0,96-1,06)	0,82 (0,76-0,89)**

Period A (pre covid), week 1-11 (2020); Period B (peak 1), week 12-20 (2020); Period C (recovery 1), week 21-41 (2020); Period D (peak 2), week 42-53 (2020); Period E (peak 3), week 1-20 (2021); Period F (recovery 2), week 21-30 (2021); Corrected for age, gender (only colorectal cancer), stage and region.

* significant difference between periods $p < 0.05$

** significant difference between periods $p < 0.01$

21 Table 4a: Breast cancer lead times of diagnostic pathway confounders during the first peak

Breast cancer - diagnosis to therapy					Breast cancer - first procedure to therapy				
period B (peak 1)	2017-2019		2020		period B (peak 1)	2017-2019		2020	
	Hazard ratio (interval)	Median time (days)	Hazard ratio (interval)	Median time (days)		Hazard ratio (interval)	Median time (days)	Hazard ratio (interval)	Median time (days)
agecat					agecat				
50-75	1	28	1	26	50-75	1	28	1	24
<50	0,85 (0,8-0,91)**	30	0,96 (0,83-1,11)	26	<50	0,92 (0,85-0,98)*	28	1,06 (0,91-1,22)	23
>75	1,29 (1,2-1,39)**	23	1,42 (1,2-1,69)**	21	>75	1,25 (1,16-1,35)**	23	1,28 (1,07-1,52)**	21
stage					stage				
X	0,79 (0,39-1,59)	27	0,44 (0,14-1,39)	34	X	0,37 (0,18-0,74)**	34	0,4 (0,13-1,26)	42
1	1	28	1	25	1	1	28	1	23
2	1,03 (0,98-1,1)	28	0,96 (0,84-1,11)	26	2	1,06 (1-1,13)*	27	1,01 (0,88-1,17)	23.5
3	1,1 (1,01-1,21)*	28	0,99 (0,81-1,22)	25	3	1,16 (1,06-1,27)**	27	1,01 (0,82-1,24)	23
4	1,16 (1,03-1,32)*	22	1,53 (1,18-1,99)**	17	4	1,2 (1,06-1,36)**	22	1,31 (1,01-1,7)*	17
region					region				
middle	1,06 (0,98-1,15)	27	1,08 (0,88-1,31)	21	middle	1,08 (1-1,18)	27	0,97 (0,79-1,18)	21
middle east	1,06 (0,97-1,17)	28	0,86 (0,69-1,07)	27	middle east	1 (0,91-1,1)	29	0,69 (0,56-0,86)**	27
north	1,06 (0,96-1,16)	28	0,81 (0,65-1,02)	26	north	1,04 (0,95-1,15)	28	0,76 (0,61-0,95)*	25
south	1	27	1	23	south	1	27	1	21
unknown	11,03 (2,34-52,09)**	11.5	26,26 (4,31-160,18)**	7.5	unknown	17,1 (3,62-80,84)**	11.5	7,26 (1,2-43,99)*	11.5
west	0,93 (0,87-1,01)	29	0,77 (0,64-0,93)**	27	west	1,04 (0,97-1,12)	27	0,77 (0,64-0,93)**	24

Period B (peak 1), week 12-20 (2020)

*significant difference between periods $p < 0.05$

**significant difference between periods $p < 0.01$

22 Table 4b: Colorectal cancer lead times of diagnostic pathway confounders during the first peak

Colorectal cancer - diagnosis to therapy					Colorectal cancer - first procedure to therapy				
period B (peak 1)	2017-2019		2020		period B (peak 1)	2017-2019		2020	
	Hazard ratio (interval)	Median time (days)	Hazard ratio (interval)	Median time (days)		Hazard ratio (interval)	Median time (days)	Hazard ratio (interval)	Median time (days)
agecat					agecat				
55-75	1	29	1	20	55-75	1	27	1	19
<55	1,26 (1,13-1,41)**	25	1,31 (1,05-1,63)*	14,5	<55	1,21 (1,08-1,35)**	24	1,35 (1,08-1,68)**	15
>75	1,06 (0,99-1,15)	28	0,94 (0,8-1,1)	22	>75	0,97 (0,9-1,04)	28	0,85 (0,73-1)	22
gender					gender				
Female	1	27	1	16	Female	1	27	1	18
Male	0,92 (0,86-0,98)*	28	0,89 (0,77-1,03)	21	Male	0,96 (0,89-1,02)	28	0,97 (0,84-1,12)	21
stage					stage				
X	1,33 (0,99-1,78)	13	3,85 (1,27-11,66)*	5	X	1,35 (1,01-1,81)*	11	0,8 (0,29-2,23)	9
1	1	30	1	22,5	1	1	28	1	22
2	1,09 (0,99-1,21)	29	1,23 (0,98-1,56)	20	2	1,05 (0,95-1,17)	28	1,1 (0,87-1,39)	20
3	1,13 (1,02-1,24)*	28	1,23 (0,98-1,53)	20	3	1,1 (1-1,22)*	28	1,29 (1,03-1,61)*	19
4	1,17 (1,05-1,3)**	23	1,19 (0,95-1,48)	16	4	1,19 (1,07-1,32)**	23	1,15 (0,92-1,44)	18
region					region				
middle	0,97 (0,88-1,08)	26	1 (0,8-1,25)	19	middle	0,94 (0,85-1,04)	25	0,86 (0,69-1,07)	19
middle east	0,89 (0,79-1)*	30	0,89 (0,67-1,18)	22	middle east	0,84 (0,75-0,95)**	29	0,78 (0,59-1,03)	22
north	0,85 (0,75-0,96)*	30	0,86 (0,65-1,15)	20	north	0,83 (0,74-0,94)**	29	0,73 (0,55-0,97)*	20
south	1	28	1	17	south	1	26	1	16,5
unknown	1,07 (0,73-1,58)	3	0,56 (0,14-2,22)	6	unknown	0,8 (0,55-1,18)	23	2,08 (0,58-7,41)	6
west	0,91 (0,83-1)	28	0,86 (0,71-1,04)	21	west	0,87 (0,79-0,95)**	28	0,74 (0,61-0,9)**	21

Period B (peak 1), week 12-20 (2020)

*significant difference between periods $p < 0.05$

**significant difference between periods $p < 0.01$

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