Journal of Oncology Research and Therapy
Schulze S, et al. Oncol Res Ther 10: 10259.
www.doi.org/10.29011/2574-710X.10259
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Research Article

The Impact of the Covid-19 Pandemic Year 2020 on Cancer Care and the Two Years Outcome compared to 2018 and 2019: A Multicenter Observational Trial of the East German Study Group (OSHO)

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Citation: Schulze S, Sorge PF, Eiltzer L, Seseke F, Opitz B, et al. (2025) The Impact of the Covid-19 Pandemic Year 2020 on Cancer Care and the Two Years Outcome compared to 2018 and 2019: A Multicenter Observational Trial of the East German Study Group (OSHO). J Oncol Res Ther 10: 10259. DOI: 10.29011/2574-710X.10259.

Received Date: 23 December, 2024; **Accepted:** 02 January, 2025; **Published Date:** 04 January, 2025

Abstract

Background: To meet the burden of the COVID-19 pandemic on healthcare resources, oncology services had to be adapted. While a decline in newly-diagnosed cancers and therapies in 2020 was published, a coherent picture to long-term consequences of a temporary decrease in diagnostic scrutiny on outcome of cancer is missing. We report the cross-sectional and longitudinal results of COMA-19, a study designed to assess the impact of the pandemic on oncology care. **Methods:** Adult Patients with newly-diagnosed cancer in 2020, 2019 and 2018 from five certified cancer centers in Saxony-Anhalt, Germany were included. ADT (Arbeitsgemeinschaft-Deutscher-Tumorzentren)-based data were collected. The primary endpoint was the number of newly-diagnosed cancers in 2020 compared to previous years. Outcome after two years (survival, event-free survival, and time-to-progression) were key secondary endpoints. **Results:** 11855 patients were recruited (2020, n=3952; 2019, n=4176; 2018, n=3727). In 2020, the number of diagnoses was comparable to previous years (p=0·4). Alterations in patients and tumor characteristics, or delays in therapy were not seen. Systemic therapies (p=0·01) and surgeries (p=0·049) dropped by 4% each. Event-free-survival and time-to-progression were inferior in patients diagnosed in 2020 (p<0·001). Survival tended to be less favorable too (p=0.08). Negative outcomes were observed in ten entities including the four most common cancers (breast, lung, prostate, and colorectal). Minor treatment alterations in 2020 were key predictors for the negative outcome. **Conclusion:** Safeguarding access to oncological care under a pandemic is feasible. Yet, minor modifications in evidence-based therapy, even in high-economic regions, could have devastating consequences on outcome.

Keywords: Cancer Management; COVID-19; Oncology; Outcome; Pandemic; SARS-CoV-2;

Introduction

On 11 March 2020, the WHO declared the outbreak of severe acute respiratory syndrome corona virus 2 as the COVID-19 pandemic [1]. Far-reaching measures were imposed worldwide including social distancing (lockdowns). This pandemic placed a significant burden on healthcare resources. The infrastructure of almost all health care services was redirected to provide a maximum of intensive care resources. In many countries, health authorities advised health facilities to defer care for non-acute or non-life-threatening conditions, prioritize hospital care, and to reallocate staff to support critical COVID-19 care. The oncology care system had to be adapted to meet this storm. Early reports proposed an intentional postponing of adjuvant chemotherapy or elective surgery for "stable" cancer [2]. Screening programs were temporarily halted, diagnostic tests delayed, scheduled operations and some types of cancer treatment postponed or adapted [3-8]. Cancer societies rapidly published recommendations modifying the patients' cancer management to maintain, in theory, high-end cancer care [4, 9, 10].

It is not surprising that with a derailed oncological care, a significant decrease in new cancer diagnoses was to be expected. According to the Surveillance, Epidemiology, and End Results (SEER) program, incidence rates for all cancers combined fell 10% in 2020 relative to 2019 [11]. Publications objectified less diagnoses in 2020 and showed that the disruption in care to vary according to pandemic stage where the pause in diagnoses was more pronounced during higher restriction periods [5-7, 12-16].

Indeed, the capacities of different oncological care domains were associated with the number of COVID-19 cases, hospitalization rate, and utilization of intensive care units [17].

Yet and more than three years later, a coherent picture of the extent of disruptions in oncological care is still missing, particularly for cancer management such as delay in therapy and treatment types, partly due to the heterogeneity in data sources, factors insufficiently controlled for in statistical analyzes, and/or moderate evidence quality [18].

Long-term consequences of cancer care disruptions and pandemic management by healthcare systems are possible only after sufficient time has passed and relevant for future pandemics. Real-world data to long-term outcome is still lacking, although early modelling studies estimated increases in avoidable cancer deaths due to the decreased diagnostic scrutiny during the pandemic [19-21].

In a multicentre study of the East German Study Group for Hematology and Oncology (OSHO), the short-term oncological care, outcome including survival, and the impact of patient-, cancer-, and treatment-related factors on outcome of patients diagnosed and treated in all certified cancer centers in the federal state of Saxony-Anhalt, Germany in the pandemic year 2020 were compared to the years 2018 and 2019.

Methods

Study Design and Participants

COMA-19 is a multicenter, observational study of the OSHO. It was designed in 2020. Inclusion criteria were age ≥ 18 years and consecutive new cancer diagnoses in 2018, 2019, and 2020. Participating institutions were the five certified cancer centers in the federal state of Saxony-Anhalt according to the National Certification Program of the German Cancer Society prior to 2018. Pseudonymized data for 2018, 2019, and 2020 were collected on site in accordance with the uniform oncological basic data set of the Association of German Tumor Centers and Society of Epidemiological Cancer Registries in Germany. Data collected was identical with those reported to the cancer registry of the federal state (LKR) in accordance with applicable regulations. Coding of cancer was according to the International Statistical Classification of Diseases and Related Health Problems code (ICD-10).

Variables included were year of birth, gender, residence postcode, tumor type and date, stage of disease, therapy, date and cause of death.

Both 2018 and 2019 were included as comparators to avoid the accommodation of one-year which can influence the value of the annual percent change and challenge the interpretation of the trend measure.

Data on race and ethnicity were not collected, because all patients diagnosed with cancer were included consecutively irrespective of race or ethnicity which are not included as variables in the uniform oncological basic data set.

The protocol was submitted to and approved by the ethics committees and registered in the German Registry for Clinical Trails (DRKS00027370).

To minimize bias, the protocol was designed with defined objectives and endpoints, lost patients were accounted for in the sample size calculation, a standardize data set and validated measures for outcome were used, blind data collection was performed, outcome at enrollment was unknown as collection followed the two-step principle explained under procedures, and an independent analysis by other researchers was done.

The academic Krukenberg Cancer Center Halle (KKH) was the coordinating institution.

The study was conducted in accordance with applicable laws and regulations and in compliance with the International Conference

on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use - Good Clinical Practice (ICH-GCP) principles. By signing the protocol, investigators confirmed compliance with legal requirements, including data protection laws.

This study followed the STROBE reporting guideline [22]. Figure-1 illustrates the COMA-19 protocol.

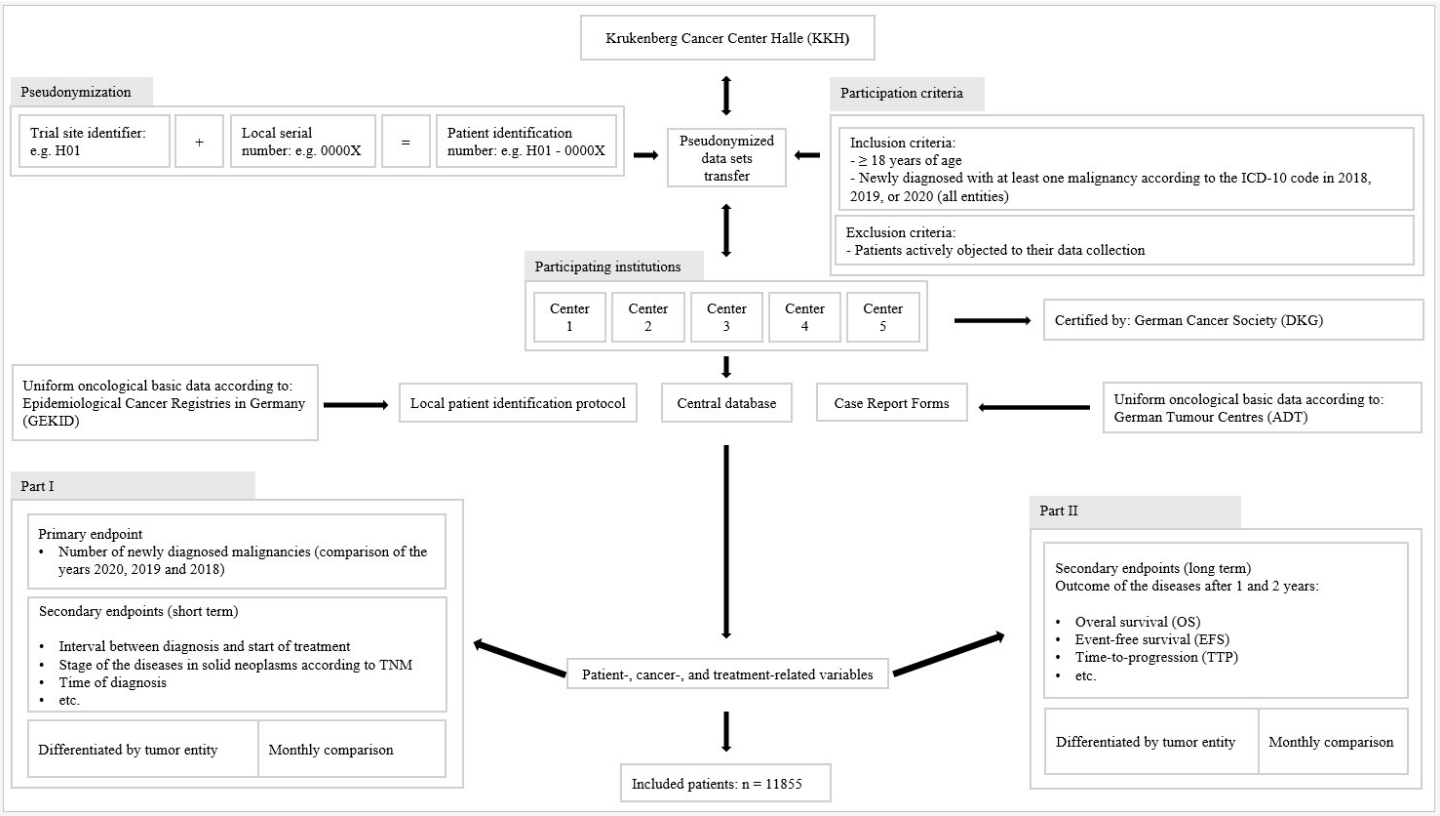

Figure-1: COMA-19 study protocol.

Procedures

The KKH collected the data centrally. Each center received a center identification number (ID). The patient ID and protocols were kept locally and filed in the study file of each center.

The protocol consisted of two parts with cross-sectional and longitudinal data. The cross-sectional data collection for the primary endpoint in 2021 (step one) was followed by the longitudinal data collection after one and two years in 2021 to 2023 (step two). Data were entered in a central database and analyzed at the KKH (Figure-1).

Outcomes

The primary endpoint of COMA-19 was the number of newly-diagnosed cancers in 2020 compared to 2018 and 2019. Outcome after one and two years including survival (OS), event-free survival (EFS), time-to-progression (TTP), and mortality incidence (MI) were key secondary endpoints. Other secondary endpoints were the number of newly-diagnosed cancer by site and time (2020 versus 2018 and 2019). Additionally, the official COVID-19 lock-downs of the Federal Republic of Germany were used to study the distribution of cases across 2020 compared to corresponding time points in 2018 and 2019. The first lock-down was from 16·03 to 04·05·2020 (lock-down-I) and the second lock-down was from 07·10 to 31·12·2020 (lock-down-II). The interval between diagnosis and therapy, stages of cancer, and the impact of patient-, disease-, and treatment-related variables on outcome for newly-diagnosed patients in 2020 compared to 2018 and 2019 were further secondary endpoints.

Statistical Analysis

We hypothesized that a monthly decline in the number of newly-diagnosed cancer of at least 10% per month is to be expected compared to 2018 and 2019. Based on known 2018 and 2019

numbers of the KKH, the number of new diagnoses was modelled using a Poisson univariate discrete probability distribution which can be used to model the number of events occurring at a constant mean rate independently of each other in a fixed time interval [23].

With alpha of 5% and a power of 80%, 1491 cases per year were required to represent a reduction of 10% (PASS software). To compensate for a failure rate (incomplete/incorrect data) of 15%, an additional 224 patients were required. Thus, a total of 1715 patients per year was calculated. Descriptive statistics were used. Continuous variables were presented as mean ± standard deviation (SD) if they are normally distributed. Otherwise as median with interquartile interval (IQR). Categorical factors are presented as absolute and relative frequencies. 95% confidence intervals were given to assess the estimated value of population parameters. Kaplan-Meier plots were used for OS, EFS, and TTP. Cox regression will estimate the influence of independent metric and categorical variables. Statistical tests were two-tailed and p values <0·05 were considered significant. Analyzes were performed using IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28·0. Armonk, NY, USA: IBM Corp.

Role of the funding source

The study funder, the OSHO, had oversight of study design and conduct and had no role in the data collection, data analysis, data interpretation, or writing of the publication. The funder is a non-profit registered association.

Results

A total of 11855 newly-diagnosed patients were included. Follow-up data were available for 7984 of these patients (67·3%). Follow-up rates for 2018, 2019, and 2020 were 73·1% (2723/3727), 69·2% (2890/4179), and 60·0% (2371/3952) respectively. The median follow-up for patients diagnosed in 2020 versus 2018 and 2019 were 10 (IQR 2–22) and 17 (IQR 3–36) months respectively. Figure-2 shows the CONSORT flowchart for the COMA-19 cohort.

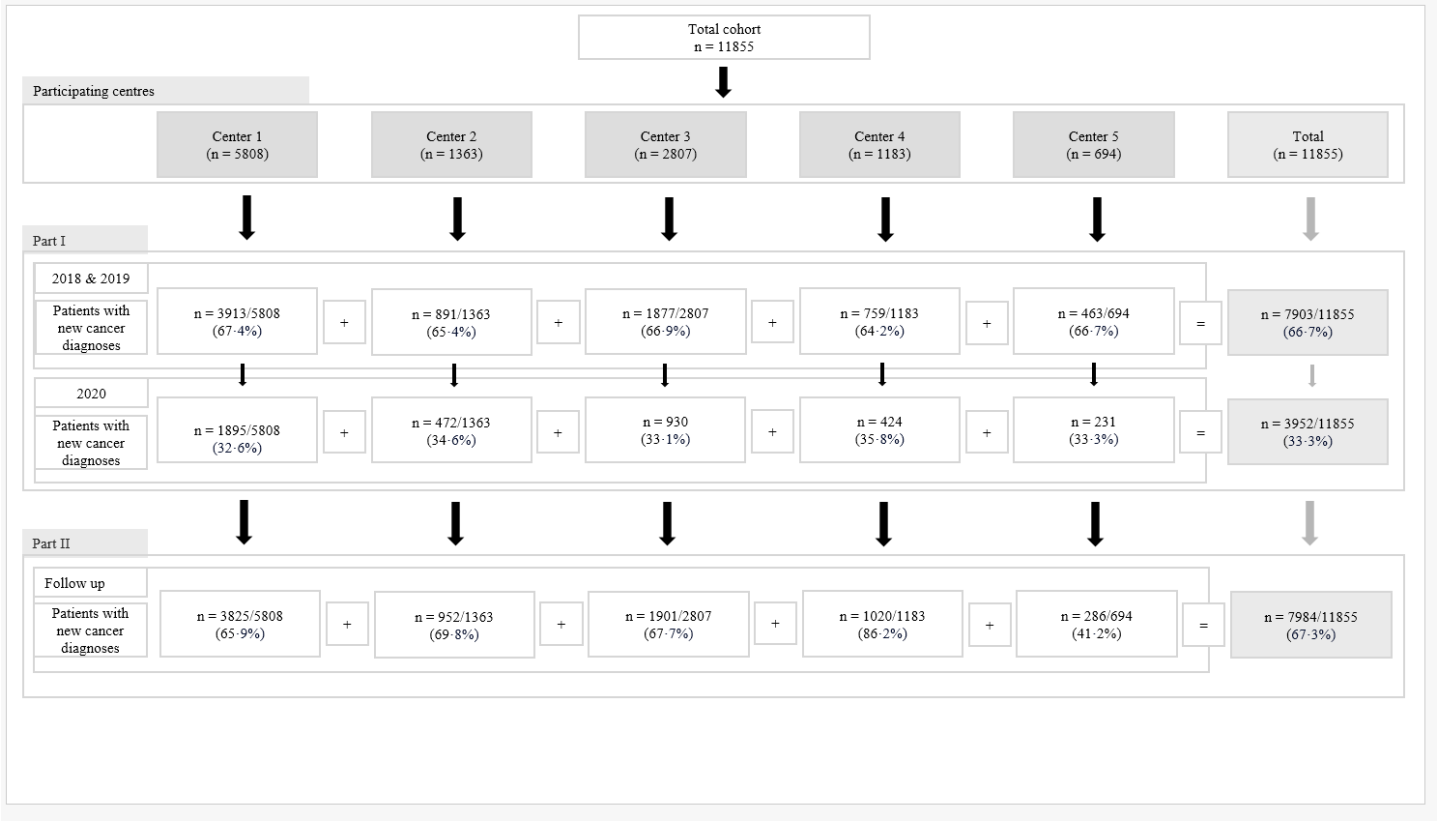

Figure-2: CONSORT flowchart of study population.

(I) Cancer Care

Newly-diagnosed patients 2020 compared to 2018 and 2019

The number of newly-diagnosed patients in 2020 (n=3952) was similar to that in 2019 (n=4176) and 2018 (n=3727) (p=0·4) (Figure-3).

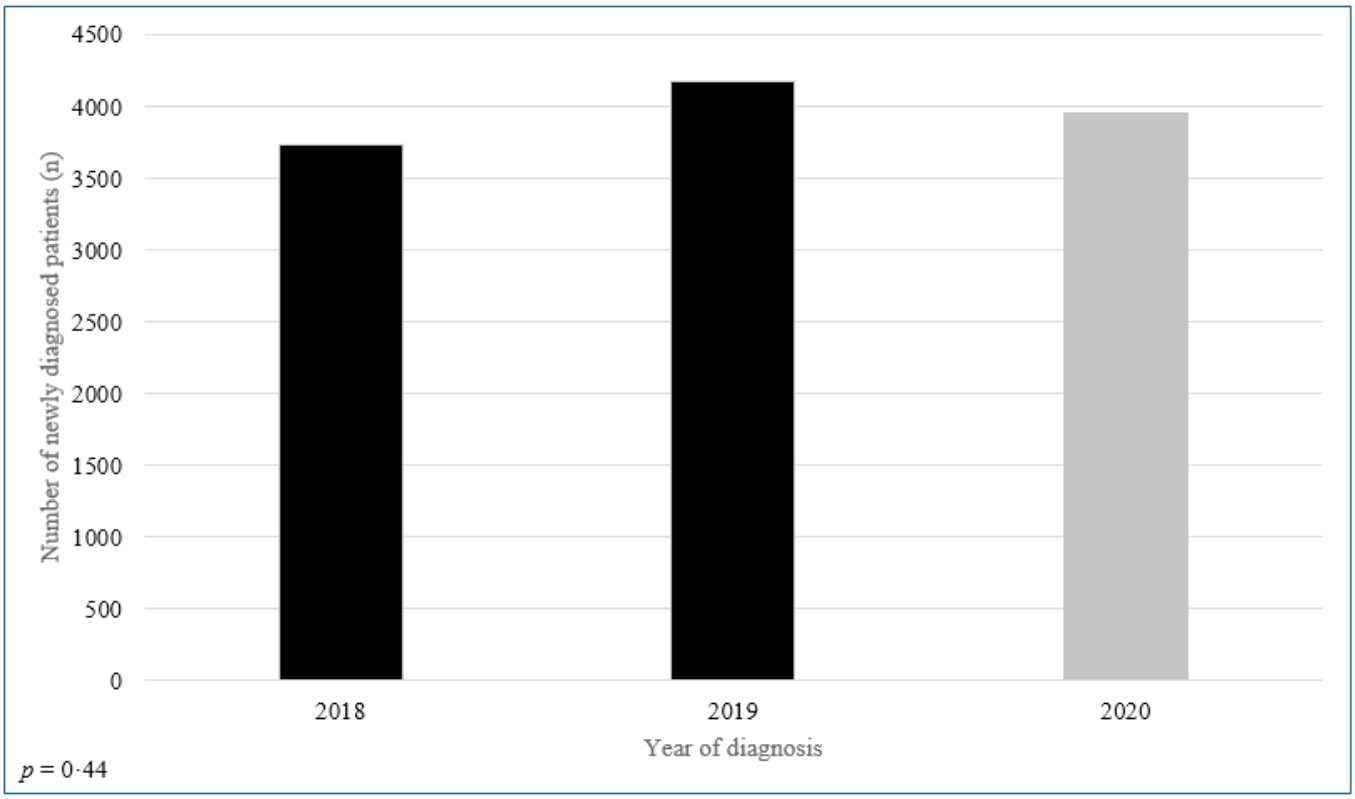

Figure-3: Newly diagnosed patients with cancer in 2020 compared to 2018 and 2019.

Patient, cancer, and treatment characteristics

The age distribution was similar in the three years with a median of 68 years (IQR 58·9–76·8). 43% of patients were ≥ 70 years old. Gender and place of residence (urban versus rural) were equally distributed in the three years (Table-1).

Variables	Total cohort	Cohort of 2018	Cohort of 2019	Cohort of 2020	*p* value*
	n = 11855	n = 3727	n = 4176	n = 3952	
Median age at time of diagnosis (IQR), (years)	67·8 (58·9–76·8)	67·5 (58·9–76·6)	67·8 (58·6–77·0)	68·0 (59·1–77·0)	0·37
Patients ≥ 70 years, n (%)	5094 (43·0)	1586 (42·6)	1792 (42·9)	1716 (43·4)	0·48
Gender, n (%)					
Male	6622 (55·9)	2051 (55·0)	2347 (56·2)	2224 (55·3)	0·52
Female	5233 (44·1)	1676 (45·0)	1829 (43·8)	1728 (43·7)	
Place of residence, n (%)					
Urban	4130 (34·8)	1342 (36·0)	1429 (34·2)	1359 (34·4)	0·42
Rural	7698 (64·9)	2373 (63·7)	2736 (65·5)	2589 (65·5)	
Missing	27 (0·2)	12 (0·3)	11 (0·3)	4 (0·1)	

Patients with former malignancies, n (%)					
Yes	832 (7·0)	222 (6·0)	311 (7·0)	299 (7·6)	
No	10965 (92·5)	3483 (93·5)	3844 (92·5)	3638 (92·1)	0·10
Missing	58 (0·5)	22 (0·6)	21 (0·5)	15 (0·4)	
Tumor staging (excluding hematologic malignancies), n (%) (neuro-oncologic tumors according to WHO, gynecologic tumors according to FIGO, all other solid tumors according to UICC)					0·94
Early tumor stages (0, I, and II)	5943 (50·1)	1797 (48·2)	2158 (51·7)	1988 (50·3)	
Advanced tumor stages (III and IV)	3734 (31·5)	1160 (31·1)	1322 (31·7)	1252 (31·7)	
Not applicable / missing	2178 (18·4)	770 (20·7)	696 (16·7)	712 (18·1)	
Treatment intention, n (%)					
Curative	8421 (71·0)	2855 (76·6)	2790 (66·8)	2776 (70·2)	
Palliative	1518 (12·8)	475 (12·7)	570 (13·6)	473 (12·0)	0·17
Missing	1916 (16·2)	397 (10·7)	816 (19·5)	703 (17·8)	
Therapy modalities, n (%)**					
Surgery	7860 (66·3)	2520 (66·3)	2832 (67·8)	2508 (63·5)	**0·049**
Radiotherapy	2792 (23·6)	967 (25·9)	937 (22·4)	888 (22·5)	0·39
Systemic medical therapy	4664 (39·3)	1559 (41·8)	1652 (39·6)	1453 (36·8)	**0·01**
Watch & Wait / Active surveillance	154 (1·3)	59 (1·6)	36 (0·9)	59 (1·5)	0·12
Best supportive care	2479 (20·9)	795 (21·3)	923 (22·1)	761 (19·6)	**0·03**
Missing	979 (8·3)	219 (5·9)	338 (8·1)	219 (5·9)	-
Abbreviation: Fédération Internationale de Gynécologie et d'Obstétrique (FIGO), Interquartile range (IQR), Union Internationale Contre le Cancer (UICC), World Health Organization (WHO)					
* *p* values for difference in mean between 2020 versus 2018 and 2019					
** more than one modality per patient possible					
Significant *p* values (<0·05) are highlighted (BOLD).					

Table 1: Patient, tumor, and treatment characteristics in 2020 compared to 2018 and 2019.

In Table-2 the cancer entities are illustrated. The most frequent cancers were breast followed by lung, prostate, and colorectal carcinomas. For most tumors, the number of new diagnoses in 2020 was comparable to that of 2018 and 2019. In 2020 more head and neck (p<0·001), hepatocellular (p=0·02), and renal (p=0·04) cancers were diagnosed. Only dermatologic tumors were less frequently diagnosed in 2020 (p=0·001). No differences in tumor stages were detected among the three years (p=0·94).

Treatment intension (curative versus palliative), radiotherapies, and active surveillance were similar in 2020 compared to 2018, and 2019. A 4% drop in systemic therapies (p=0·01) and surgery (p=0·049) in 2020 was noted (Table-1).

Tumor entity	Year of diagnosis (2018 and 2019 versus 2020)	Number (n)	*p* value
Breast cancer	2018 & 2019	1246	0·93
	2020	611	
	Total	1857	
Lung cancer	2018 & 2019	1033	0·78
	2020	501	
	Total	1534	
Prostate cancer	2018 & 2019	1017	0·94
	2020	499	
	Total	1516	
Colorectal cancer	2018 & 2019	797	0·14
	2020	357	
	Total	1154	
Melanoma and non-melanoma skin cancer	2018 & 2019	766	**0·001**
	2020	304	
	Total	1070	
Hematologic neoplasms	2018 & 2019	569	0·91
	2020	278	
	Total	847	
Renal cell carcinoma (incl. upper urinary tract)	2018 & 2019	417	**0·04**
	2020	242	
	Total	659	
Head and neck cancer	2018 & 2019	291	**< 0·001**
	2020	202	
	Total	493	
Urinary bladder (incl. lower urinary tract)	2018 & 2019	325	0·85
	2020	163	
	Total	488	
Gynecologic cancer	2018 & 2019	322	0·92
	2020	157	
	Total	479	

Pancreatic cancer	2018 & 2019	239	0·98
	2020	118	
	Total	357	
Endocrine malignancies	2018 & 2019	204	0·38
	2020	90	
	Total	294	
Hepatocellular and hepatobiliary cancer	2018 & 2019	144	**0·02**
	2020	96	
	Total	240	
Gastric cancer	2018 & 2019	139	0·66
	2020	73	
	Total	212	
Esophagus cancer	2018 & 2019	100	0·53
	2020	44	
	Total	144	
Central nervous system cancer	2018 & 2019	94	0·88
	2020	45	
	Total	139	
Sarcoma	2018 & 2019	50	0·31
	2020	31	
	Total	81	
Testicular cancer	2018 & 2019	40	0·27
	2020	26	
	Total	66	
Other*	2018 & 2019	110	-
	2020	115	
	Total	225	
Total cohort	2018 & 2019	7903	0·44
	2020	3952	
	Total	11855	
* Other include: cancer of unknown primary (n = 133), small bowl cancer (n = 45), penile cancer (n = 21), anal cancer (n = 17), cardiac, mediastinal, and pleural cancer (n = 6), cancer of another male genital tract (n = 3)			
Significant *p* values (<0·05) are highlighted (BOLD).			

Table 2: Tumor entities in 2020 compared to 2018 and 2019.

The interval between diagnosis and therapy was not impacted by the pandemic. The mean of 21 days (SD 34) in 2020 was six days less than that in 2018 and 2019 (mean 27 days, SD 65) and there was no therapy delay across all cancer entities (Figure-4).

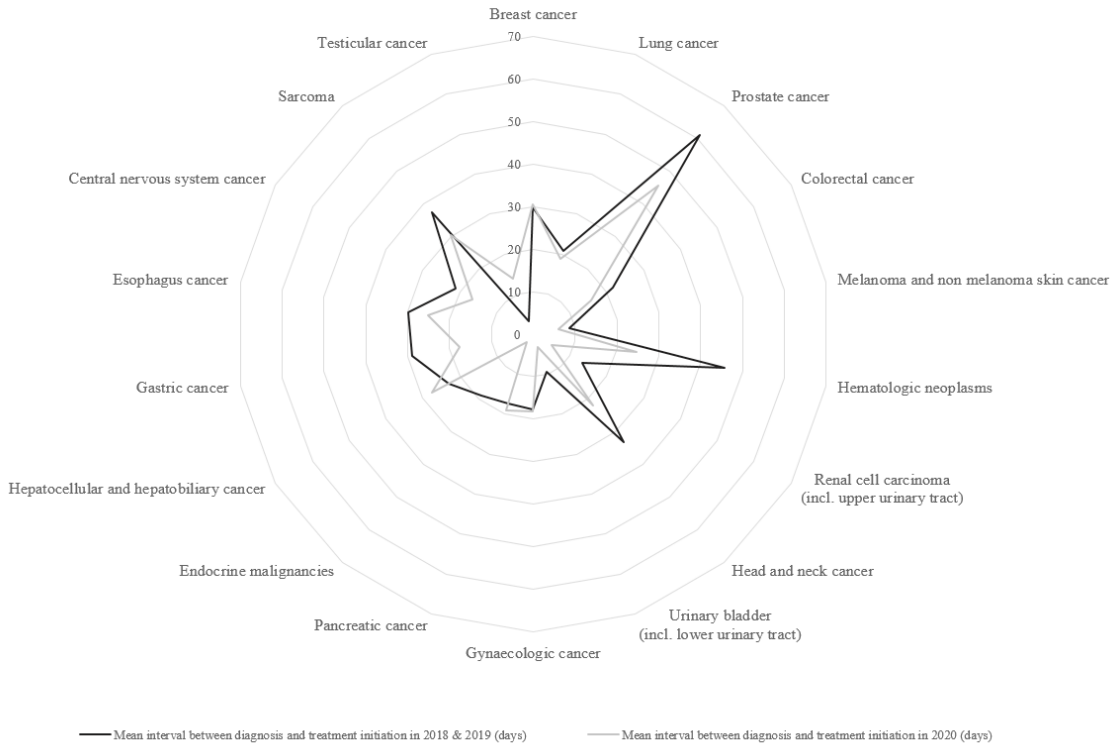

Figure 4: Interval between diagnoses-start of therapies.

The number of diagnoses was not uniformly distributed across 2020. There was a clear shift to the non-lock-down period (p<0·001). Lock-down-I and lock-down-II represented 13·7% and 23·6% of 2020, respectively. Yet, only 11·5% (453/3952) and 22 % (871/3952) of cancers were diagnosed in lock-down-I and lock-down-II respectively. Seasonal variations in diagnoses were also seen in 2018 and 2019 with less (985/7903; 12·5%) and more (1913/7903; 24·2%) new diagnoses compared to the rest of the years in the time frame corresponding to lock-down-I and lock-down-II respectively (p=0·01). Yet, 2020 lock-downs retained a negative impact on the number of new diagnoses (p<0·001).

(II) Outcome

Survival

The one- and two-years OS probabilities for patients diagnosed in 2020 were 87% and 80% respectively compared to 87% and 81% in 2018 and 2019 (p=0·08) (Figure-5a). The trend was towards an inferior survival for diagnoses made in 2020 [mean survival time 31 months (95%CI, 30·6–31·7)] compared to 2018 and 2019 [mean survival time 48 months (95%CI, 47·3–48·6)].

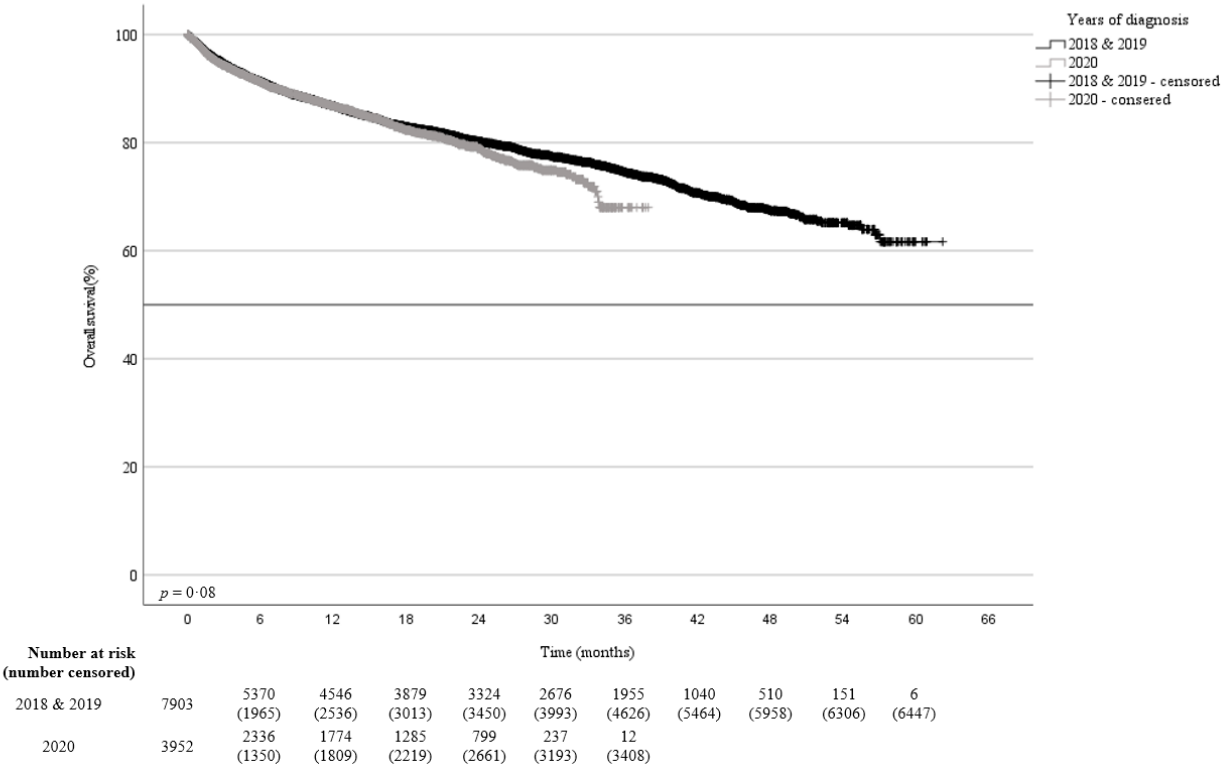

Figure 5a: Overall survival probability for patients diagnosed with cancer in 2020 compared to 2018 and 2019.

Death was documented in 1982 (532 in 2020 and 1450 in 2018 and 2019) out of 7984 (24·8%) patients. No differences in the cause of death (tumor-related versus non-tumor-related) were found for patients diagnosed in the three years where the causes of death were known (Supplement-I).

	2018 cohort	**2019 cohort**	**2020 cohort**	***p* value**
Causes of death	**n = 715**	**n = 735**	**n = 532**	
Tumor-related, n (%)	381 (53·3)	435 (59·2)	247 (33·6)	0·86
Non-tumor-related, n (%)	78 (10·9)	69 (9·4)	43 (5·9)	
Missing, n (%)	256 (35·8)	231 (31·4)	242 (32·9)	

Supplement-I: Causes of death of patients with newly-diagnosed cancer in 2018, 2019, and 2020

Patients diagnosed in 2020 with colorectal (p=0·003), renal cell (p=0·02), and urinary bladder (p=0·02) cancers as well as sarcoma (p=0·04) had a significant inferior survival compared to patients diagnosed in 2018 and 2019 (Table-3).

Tumor entity	**Number of patients 2020 versus 2018 & 2019 (n)**	**OS**	**EFS**	**TTP**
		***p* value univariate**	***p* value univariate**	***p* value univariate**
Breast cancer	439 vs. 1065	0·93	0·17	**0·01**
Lung cancer	300 vs. 768	0·07	0·59	**< 0·001**
Prostate cancer	273 vs. 622	0·08	**0·02**	0·09

Colorectal cancer	237 vs. 686	**0·003**	**0·001**	**0·01**
Melanoma and non-melanoma skin cancer	142 vs. 363	0·72	0·30	0·23
Hematologic neoplasms	193 vs. 437	0·51	0·26	0·26
Renal cell carcinoma (incl. upper urinary tract)	103 vs. 249	**0·02**	0·11	0·88
Head and neck cancer	141 vs. 239	0·36	0·15	0·14
Urinary bladder (incl. lower urinary tract)	108 vs. 261	**0·02**	**0·03**	0·21
Gynecologic cancer	96 vs. 215	0·58	0·27	**0·02**
Pancreatic cancer	77 vs. 183	0·20	0·74	**0·03**
Endocrine malignancies	20 vs. 88	0·06	0·64	0·73
Hepatocellular and hepatobiliary cancer	59 vs. 88	0·09	**0·03**	0·15
Gastric cancer	36 vs. 93	0·79	0·81	0·65
Esophagus cancer	27 vs. 77	0·57	0·85	0·46
Central nervous system cancer	27 vs. 58	0·91	0·07	0·10
Sarcoma	16 vs. 32	**0·04**	**0·01**	**0·01**
Testicular cancer	17 vs. 17	0·24	0·79	0·71
Other*	60 vs. 72	0·12	0·29	0·84
Total cohort	2371 vs. 5613	0·08	**< 0·001**	**< 0·001**
Abbreviation: Event-free survival (EFS), overall survival (OS), time-to-progression (TTP), versus (vs.)				
* Other include: cancer of unknown primary (n = 133), small bowl cancer (n = 45), penile cancer (n = 21), anal cancer (n = 17), cardiac, mediastinal, and pleural cancer (n = 6), cancer of other male genital tract (n = 3)				
Significant *p* values (<0·05) are highlighted (BOLD).				

Table 3: Two-years outcome across tumor entities in 2020 compared to 2018 and 2019.

Event-free Survival

The one- and two-years EFS probabilities for patients diagnosed in 2020 were 77% and 63% respectively compared to 79% an 67% in 2018 and 2019 (p<0·001) (Figure-5b). The mean EFS time of 26 months (95%CI, 25·6–26·8) for 2020 made diagnoses was significantly inferior to the mean EFS time of 39 months (95%CI, 38·6–39·9) for patients diagnosed in 2018 and 2019. Besides colorectal (p=0·001) and urinary bladder (p=0·03) cancers and sarcoma (p=0·01), an inferior EFS for patients diagnosed in 2020 was documented for prostate (p=0·02) and hepatocellular carcinomas (p=0·03) (Table-3).

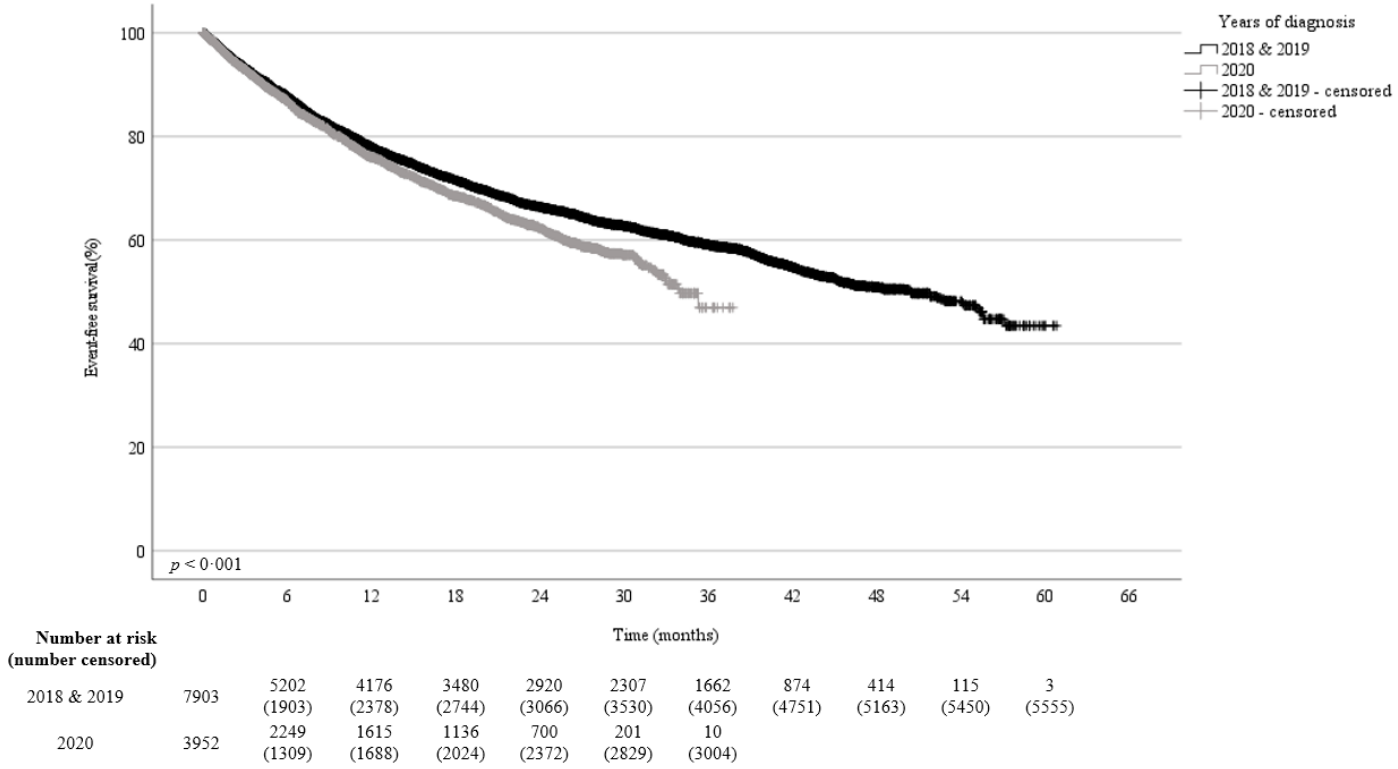

Figure 5b: Event-free survival 2020 compared to 2018 & 2019

Time-to-Progression

The one- and two-years TTP probabilities for patients diagnosed in 2020 were 86% and 74% respectively compared to 89% and 79% in 2018 and 2019 (p<0·001) (Figure-5c). The mean TTP of 30 months (95%CI, 29·4–30·5) in patients diagnosed in 2020 was significantly inferior to the mean TTP of 47 months (95% CI, 46·2–47·5) for patients diagnosed in 2018 and 2019. Patients with colorectal cancer (p=0·01) and sarcoma (p=0·01) had a significant shorter TTP if diagnosed in 2020. Breast, lung, gynecologic, and pancreatic malignancies were also associated with a shorter TTP if diagnosed in 2020 (Table-3).

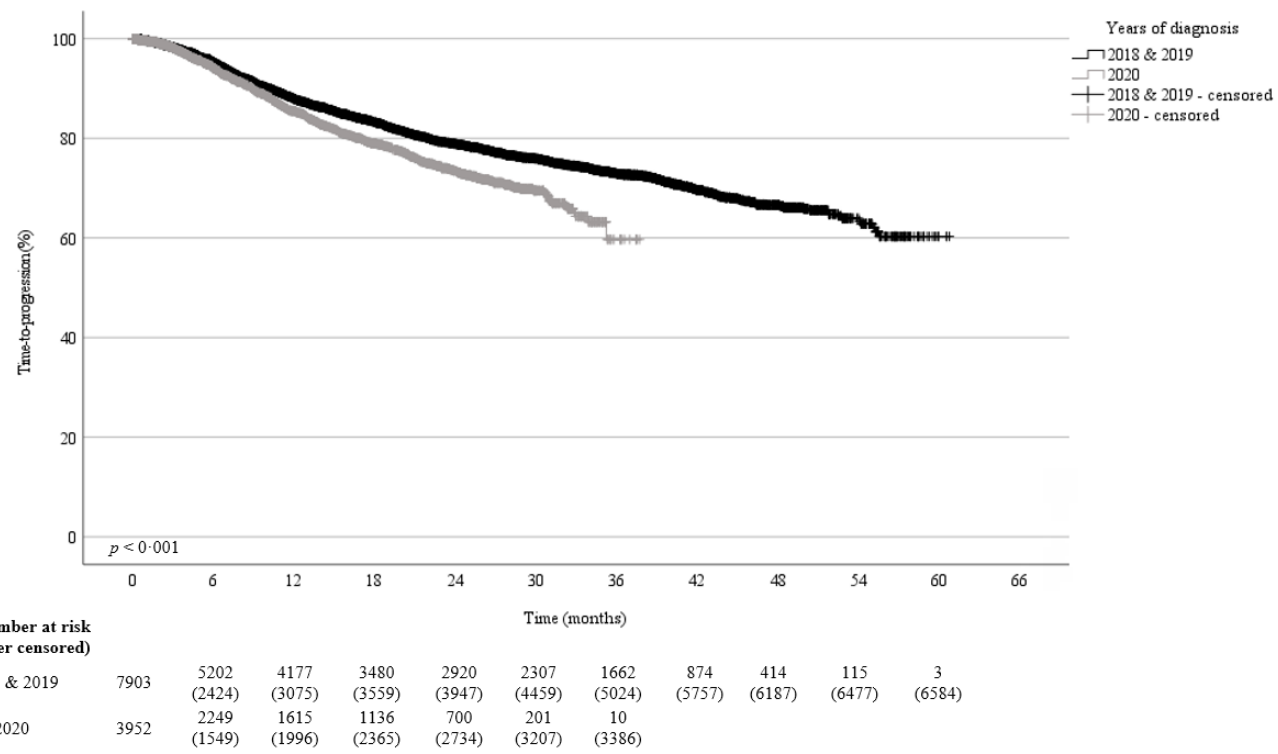

Figure 5c: Time-to-progression probability for patients diagnosed with cancer in 2020 compared to 2018 and 2019.

Predictors of inferior outcome of patients diagnosed in 2020 compared to 2018 and 2019

For entities associated with an inferior outcome if the diagnoses was made in 2020, patient-, cancer-, and treatment- characteristics were compared to patients diagnosed in 2018 and 2019 to identify predictors for the inferior outcome (Table-4 and Supplement-II).

Variables	Breast cancer p value univariate	Lung cancer p value univariate	Prostate cancer p value univariate	Colorectal cancer p value univariate	Renal cell carcinoma (incl. upper urinary tract) p value univariate	Urinary bladder (incl. lower urinary tract) p value univariate	Gynecologic cancer p value univariate	Pancreatic cancer p value univariate	Hepatocellular and hepatobiliary cancer p value univariate	Sarcoma p value univariate
Age at time of diagnosis	0·43	0·95	0·92	0·36	0·27	0·85	0·16	0·35	0·73	0·87
Patients ≥ 70 years	0·10	0·40	0·67	0·24	0·30	0·41	0·27	0·97	0·75	0·17
Gender	0·43	0·66	-	0·90	0·10	0·73	-	0·98	0·55	0·83
Place of residence, n (%)	0·86	0·90	0·65	0·55	0·38	**0·02**	0·08	0·36	0·25	0·48
Patients with former malignancies, n (%)	0·99	0·10	0·75	**0·01**	0·36	**0·01**	0·97	0·85	0·74	0·17
Tumor stage, n (%)	0·22	0·56	0·85	0·47	0·39	0·60	0·63	0·70	0·39	0·65
Treatment intention, n (%)	0·07	0·46	0·88	0·79	0·26	**0·01**	**0·02**	0·56	0·23	0·74
Therapy modalities, n (%)*										
Surgery	0·90	**0·03**	0·07	0·95	**0·03**	0·998	0·74	**0·003**	0·11	0·95
Radiotherapy	0·25	0·78	**0·002**	0·58	0·54	0·38	0·75	-	0·45	0·09
Systemic medical therapy	0·13	0·92	**0·01**	0·06	0·40	**< 0·001**	0·22	0·74	0·32	0·14
Watch & Wait / Active surveillance	-	-	0·23	-	-	-	-	-	-	-
Best supportive care	-	**< 0·001**	**0·01**	0·74	0·87	0·38	0·28	**0·02**	0·49	0·25
Diagnosis time point corresponding to lock-downs of 2020	0·06	0·28	0·09	0·55	0·58	0·69	0·13	0·62	0·34	0·16
Interval between diagnosis and therapy	0·65	0·49	**< 0·001**	**0·01**	**0·002**	**0·02**	0·90	0·74	0·53	0·64
* more than one modality per patient possible										
Significant *p* values (< 0·05) are highlighted (BOLD).										

Table 4: Univariate analysis of patient-, cancer-, and treatment- variables for patients diagnosed in 2020 versus 2018 and 2019 for cancer entities associated with an inferior 2020 outcome.

Supplement-II - Patient, tumor, and treatment characteristics in 2020 compared to 2018 and 2019

Variables	Total cohort n = 1857	Cohort of 2018 n = 618	Cohort of 2019 n = 628	Cohort of 2020 n = 611	*p* value*
Median age at time of diagnosis (IQR), (years)	62·5 (52·3-74·4)	61·9 (52·3-72·3)	62·8 (52·1-74·9)	62·7 (52·5-75·8)	0·43
Patients ≥ 70 years, n (%)	585 (31·5)	176 (28·5)	201 (32·0)	208 (34·0)	0·10
Gender, n (%)					
Male	14 (0·8)	3 (0·5)	5 (0·8)	6 (1·0)	0·43
Female	1843 (99·2)	615 (99·5)	623 (99·2)	605 (99·0)	
Place of residence, n (%)					
Urban	625 (33·7)	224 (36·2)	197 (31·4)	204 (33·4)	0·86
Rural	1229 (66·2)	393 (63·6)	430 (68·5)	406 (66·4)	
Missing	3 (0·2)	1 (0·2)	1 (0·2)	1 (0·002)	
Patients with former malignancies, n (%)					
Yes	176 (9·5)	52 (8·4)	66 (10·5)	58 (9·5)	0·99
No	1677 (90·3)	565 (91·4)	560 (89·2)	552 (90·3)	
Missing	4 (0·2)	1 (0·2)	2 (0·3)	1 (0·002)	
Tumor staging (UICC), n (%)					
Early tumor stages (0, I, and II)	1526 (82·2)	513 (83·0)	526 (83·8)	487 (79·7)	0·22
Advanced tumor stages (III and IV)	260 (14·0)	90 (14·6)	77 (12·3)	93 (15·2)	
Not applicable / missing	71 (3·8)	15 (2·4)	25 (4·0)	31 (5·1)	
Treatment intention, n (%)					
Curative	1695 (91·3)	570 (92·2)	578 (92·0)	547 (89·5)	0·07
Palliative	54 (2·9)	25 (4·0)	18 (2·9)	11 (1·8)	
Missing	108 (5·8)	23 (3·7)	32 (5·1)	53 (8·7)	
Therapy modalities, n (%)**					
Surgery	1582 (85·2)	523 (84·6)	536 (85·4)	523 (85·6)	0·90
Radiotherapy	1145 (61·7)	403 (65·2)	374 (59·6)	368 (60·2)	0·25
Systemic medical therapy	1263 (68·0)	434 (70·2)	397 (63·2)	432 (70·7)	0·13
Missing	48 (2·6)	18 (29·1)	18 (2·9)	12 (2·0)	-
Diagnosis time point corresponding to lock- downs of 2020, n (%)					
Yes	642 (34·6)	239 (38·7)	214 (34·1)	189 (30·9)	0·06
No	1215 (65·4)	379 (61·3)	414 (65·9)	422 (69·1)	
Mean interval between diagnosis and therapy (SD), (days)	30·0 (39·7)	30·9 (47·4)	28·4 (38·3)	30·6 (31·6)	0·65

Abbreviation: Interquartile range (IQR), Standard deviation (SD), Union Internationale Contre le Cancer (UICC). *p values for difference in mean between 2020 versus 2018 and 2019; **more than one modality per patient possible; Significant p values (< 0·05) are highlighted (BOLD).

Supplement-II, Table-I: Breast cancer.

Variables	Total cohort n = 1534	Cohort of 2018 n = 498	Cohort of 2019 n = 535	Cohort of 2020 n = 501	*p* value*
Median age at time of diagnosis (IQR), (years)	67·3 (60·8-75·4)	67·9 (61·2-75·6)	67·7 (60·9-75·5)	66·6 (60·6-74·8)	0·95
Patients ≥ 70 years, n (%)	617 (40·2)	208 (41·8)	215 (40·2)	194 (38·7)	0·40
Gender, n (%)					
Male	1019 (66·4)	342 (68·7)	348 (65·0)	329 (65·7)	0·66
Female	515 (33·6)	156 (31·3)	187 (35·0)	172 (34·3)	
Place of residence, n (%)					
Urban	375 (24·4)	117 (23·5)	134 (25·0)	124 (24·8)	0·90
Rural	1152 (75·1)	377 (75·7)	398 (74·4)	377 (75·2)	
Missing	7 (0·5)	4 (0·8)	3 (0·6)	0 (0)	
Patients with former malignancies, n (%)					
Yes	91 (5·9)	24 (4·8)	30 (5·6)	37 (7·4)	0·10
No	1430 (93·2)	470 (94·4)	499 (93·3)	461 (92·0)	
Missing	13 (0·8)	4 (0·8)	6 (1·1)	3 (0·6)	
Tumor staging (UICC), n (%)					
Early tumor stages (0, I, and II)	451 (29·4)	146 (29·3)	164 (30·7)	141 (28·1)	0·56
Advanced tumor stages (III and IV)	1034 (67·4)	337 (67·7)	358 (66·9)	339 (67·7)	
Not applicable / missing	49 (3·2)	15 (3·0)	13 (2·4)	21 (4·2)	
Treatment intention, n (%)					
Curative	563 (36·7)	188 (37·8)	191 (35·7)	184 (36·7)	0·46
Palliative	574 (37·4)	194 (39·0)	204(38·1)	176 (35·2)	
Missing	397 (25·9)	116 (23·3)	140 (26·2)	141 (28·1)	
Therapy modalities, n (%)**					
Surgery	406 (26·5)	141 (28·3)	151 (28·2)	114 (22·8)	**0·03**
Radiotherapy	411 (26·8)	149 (29·9)	127 (23·7)	135 (26·9)	0·78
Systemic medical therapy	793 (48·2)	263 (52·8)	273 (51·0)	257 (51·3)	0·92
Best supportive care	582 (37·9)	203 (40·8)	221 (41·3)	158 (31·5)	**< 0·001**
Missing	262 (17·1)	62 (12·4)	110 (20·6)	90 (18·0)	-
Diagnosis time point corresponding to lock- downs of 2020, n (%)					
Yes	534 (34·8)	179 (35·9)	192 (35·9)	163 (32·5)	0·28
No	1000 (65·2)	319 (64·1)	343 (64·1)	338 (67·5)	
Mean interval between diagnosis and therapy (SD), (days)	20·1 (47·7)	22·1 (65·8)	19·2 (37·6)	18·9 (30·9)	0·49

Abbreviation: Interquartile range (IQR), Standard deviation (SD), Union Internationale Contre le Cancer (UICC). * *p* values for difference in mean between 2020 versus 2018 and 2019; ** more than one modality per patient possible; Significant *p* values (< 0·05) are highlighted (BOLD).

Supplement-II, Table-II: Lung cancer.

Variables	Total cohort n = 1516	Cohort of 2018 n = 483	Cohort of 2019 n = 534	Cohort of 2020 n = 499	*p* value*
Median age at time of diagnosis (IQR), (years)	68·9 (64·0-75·1)	69·1 (64·5-75·4)	68·6 (63·6-74·5)	68·9 (63·2-75·5)	0·92
Patients ≥ 70 years, n (%)	656 (43·3)	224 (46·4)	220 (41·2)	212 (42·5)	0·67
Place of residence, n (%)					
Urban	613 (40·4)	209 (43·3)	198 (37·1)	206 (41·3)	0·65
Rural	899 (59·3)	273 (56·5)	334 (62·5)	292 (58·5)	
Missing	4 (0·3)	1 (0·2)	2 (0·4)	1 (0·2)	
Patients with former malignancies, n (%)					
Yes	111 (7·3)	33 (6·8)	43 (8·1)	35 (7·0)	0·75
No	1405 (92·7)	450 (93·2)	491 (91·9)	464 (93·0)	
Tumor staging (UICC) n (%)					
Early tumor stages (0, I, and II)	978 (64·5)	309 (64·0)	341 (63·9)	328 (65·7)	0·85
Advanced tumor stages (III and IV)	451 (29·7)	143 (29·6)	159 (29·8)	149 (29·9)	
Not applicable / missing	87 (5·7)	31 (6·4)	34 (6·4)	22 (4·4)	
Treatment intention, n (%)					
Curative	1097 (72·4)	393 (81·4)	400 (74·9)	304 (60·9)	0·88
Palliative	127 (8·4)	45 (9·3)	46 (8·6)	36 (7·2)	
Missing	292 (19·3)	45 (9·3)	88 (16·5)	159 (31·9)	
Therapy modalities, n (%)**					
Surgery	966 (63·7)	293(60·7)	357 (66·9)	316 (63·3)	0·07
Radiotherapy	248 (16·4)	94 (20·5)	97 (16·2)	57 (11·4)	**0·002**
Systemic medical therapy	256 (16·9)	99 (41·8)	95 (17·8)	62 (14·4)	**0·01**
Watch & Wait / Active surveillance	92 (6·1)	35 (7·2)	23 (4·3)	34 (6·8)	0·23
Best supportive care	198 (1·3)	51 (10·6)	69 (12·9)	78 (15·6)	**0·01**
Missing	210 (13·9)	56 (11·6)	64 (12·0)	90 (18·3)	-
Diagnosis time point corresponding to lock- downs of 2020, n (%)					
Yes	583 (38·5)	215 (44·5)	194 (36·3)	174 (34·9)	0·09
No	933 (61·5)	268 (55·5)	340 (63·7)	325 (65·1)	
Mean interval between diagnosis and therapy (SD), (days)	56·3 (75·2)	62·3 (108·3)	60·1 (58·6)	45·6 (41·3)	**< 0·001**

Abbreviation: Interquartile range (IQR), Standard deviation (SD), Union Internationale Contre le Cancer (UICC). * *p* values for difference in mean between 2020 versus 2018 and 2019; ** more than one modality per patient possible. Significant *p* values (< 0·05) are highlighted (BOLD).

Supplement-II, Table-III: Prostate cancer.

Variables	Total cohort n = 1154	Cohort of 2018 n = 360	Cohort of 2019 n = 437	Cohort of 2020 n = 357	*p* value*
Median age at time of diagnosis (IQR), (years)	70·1 (61·5-78·4)	69·5 (60·7-77·2)	69·9 (62·0-78·8)	70·7 (61·6-79·1)	0·36
Patients ≥ 70 years, n (%)	578 (50·1)	172 (47·8)	218 (49·9)	188 (52·7)	0·24
Gender, n (%)					
Male	737 (63·9)	226 (62·8)	284 (65·0)	227 (63·6)	0·90
Female	417 (36·1)	134 (37·2)	153 (35·0)	130 (36·4)	
Place of residence, n (%)					
Urban	401 (34·7)	125 (34·7)	147 (33·6)	129 (36·1)	0·55
Rural	749 (64·9)	233 (64·7)	288 (65·9)	228 (63·9)	
Missing	4 (0·3)	2 (0·6)	2 (0·5)	0 (0)	
Patients with former malignancies, n (%)					
Yes	105 (9·1)	25 (6·9)	35 (8·0)	45 (12·6)	**0·01**
No	1045 (90·6)	332 (92·2)	402 (92·0)	311 (87·1)	
Missing	4 (0·3)	3 (0·8)	0 (0)	1 (0·3)	
Tumor staging (UICC), n (%)					
Early tumor stages (0, I, and II)	535 (46·4)	163 (45·3)	203 (46·5)	169 (47·3)	0·47
Advanced tumor stages (III and IV)	555 (48·1)	182 (50·6)	209 (47·8)	164 (45·9)	
Not applicable / missing	64 (5·5)	15 (4·2)	25 (5·7)	24 (6·7)	
Treatment intention, n (%)					
Curative	942 (81·6)	309 (85·8)	355 (81·2)	278 (77·9)	0·79
Palliative	158 (13·7)	45 (12·5)	68 (15·6)	45 (12·6)	
Missing	54 (4·7)	6 (1·7)	14 (3·2)	34 (9·5)	
Therapy modalities, n (%)**					
Surgery	981 (85·0)	311 (86·4)	370 (84·7)	300 (84·0)	0·95
Radiotherapy	224 (19·4)	59 (16·4)	93 (21·3)	72 (20·2)	0·58
Systemic medical therapy	479 (41·5)	172 (47·8)	175 (40·0)	132 (37·0)	0·06
Best supportive care	449 (38·9)	130 (36·1)	179 (41·0)	140 (39·2)	0·74
Missing	27 (2·3)	5 (1·4)	10 (2·3)	12 (3·4)	-
Diagnosis time point corresponding to lock- downs of 2020, n (%)					
Yes	394 (34·1)	118 (32·8)	160 (36·6)	116 (32·5)	0·55
No	760 (65·9)	242 (67·2)	277 (63·4)	241 (67·5)	
Mean interval between diagnosis and therapy (SD), (days)	19·9 (51·9)	26·9 (76·4)	17·4 (42·9)	15·6 (21·9)	**0·01**

Abbreviation: Interquartile range (IQR), Standard deviation (SD), Union Internationale Contre le Cancer (UICC). * *p* values for difference in mean between 2020 versus 2018 and 2019; ** more than one modality per patient possible. Significant *p* values (< 0·05) are highlighted (BOLD).

Supplement-II, Table-IV: Colorectal cancer.

Variables	Total cohort n = 659	Cohort of 2018 n = 209	Cohort of 2019 n = 208	Cohort of 2020 n = 242	*p* value*
Median age at time of diagnosis (IQR), (years)	68·1 (61·5-76·6)	68·4 (61·4-76·9)	67·8 (59·9-75·9)	68·3 (61·7-77·1)	0·27
Patients ≥ 70 years, n (%)	293 (44·5)	92 (44·0)	87 (41·8)	114 (47·1)	0·30
Gender, n (%)					
Male	442 (67·1)	131 (62·7)	139 (66·8)	172 (71·1)	0·10
Female	217 (32·9)	78 (37·3)	69 (33·2)	70 (28·9)	
Place of residence, n (%)					
Urban	254 (38·5)	81 (38·8)	85 (40·9)	88 (36·4)	0·38
Rural	405 (61·5)	128 (61·2)	123 (59·1)	154 (63·6)	
Patients with former malignancies, n (%)					
Yes	75 (11·4)	23 (11·0)	28 (13·5)	24 (9·9)	0·36
No	583 (88·5)	186 (89·0)	179 (86·1)	218 (90·1)	
Missing	1 (0·2)	0 (0)	1 (0·5)	0 (0)	
Tumor staging (UICC), n (%)					
Early tumor stages (0, I, and II)	412 (62·5)	124 (59·3)	143 (68·8)	145 (59·9)	0·39
Advanced tumor stages (III and IV)	196 (29·7)	62 (29·7)	58 (27·9)	76 (31·4)	
Not applicable / missing	51 (7·7)	23 (11·0)	7 (3·4)	21 (8·7)	
Treatment intention, n (%)					
Curative	583 (88·5)	186 (89·0)	192 (92·3)	205 (84·7)	0·26
Palliative	46 (7·0)	14 (6·7)	12 (5·8)	20 (8·3)	
Missing	30 (4·6)	9 (4·3)	4 (1·9)	17 (7·0)	
Therapy modalities, n (%)**					
Surgery	610 (92·6)	197 (94·3)	196 (94·2)	217 (89·7)	**0·03**
Radiotherapy	20 (3·0)	5 (2·4)	9 (4·3)	6 (2·3)	0·54
Systemic medical therapy	69 (10·5)	18 (8·6)	29 (13·9)	22 (9·1)	0·40
Best supportive care	109 (16·5)	35 (16·7)	35 (16·8)	39 (16·1)	0·87
Missing	20 (3·0)	7 (3·3)	4 (1·9)	9 (3·7)	-
Diagnosis time point corresponding to lock- downs of 2020, n (%)					
Yes	234 (35·5)	71 (34·0)	71 (34·1)	92 (38·0)	0·58
No	425 (64·5)	138 (66·0)	137 (65·9)	150 (62·0)	
Mean interval between diagnosis and therapy (SD), (days)	10·4 (40·9)	14·5 (63·7)	12·3 (28·2)	5·0 (18·3)	**0·002**

Abbreviation: Interquartile range (IQR), Standard deviation (SD), Union Internationale Contre le Cancer (UICC); **p* values for difference in mean between 2020 versus 2018 and 2019; **more than one modality per patient possible. Significant *p* values (< 0·05) are highlighted (BOLD).

Supplement-II, Table-V: Renal cell carcinoma (incl. upper urinary tract).

Variables	Total cohort n = 488	Cohort of 2018 n = 148	Cohort of 2019 n = 177	Cohort of 2020 n = 163	*p* value*
Median age at time of diagnosis (IQR), (years)	73·2 (65·2-79·8)	74·9 (65·2-80·2)	72·2 (64·5-79·1)	72·7 (65·5-81·3)	0·85
Patients ≥ 70 years, n (%)	285 (58·4)	97 (65·5)	97 (54·8)	91 (55·8)	0·41
Gender, n (%)					
Male	355 (72·7)	101 (68·2)	137 (77·4)	117 (71·8)	0·73
Female	133 (27·3)	47 (31·8)	40 (22·6)	46 (28·2)	
Place of residence, n (%)					
Urban	259 (53·1)	89 (60·1)	96 (54·2)	74 (45·4)	**0·02**
Rural	228 (46·7)	58 (39·2)	81 (45·8)	89 (54·6)	
Missing	1 (0·2)	1 (0·7)	0 (0)	0 (0)	
Patients with former malignancies, n (%)					
Yes	34 (7·0)	7 (4·7)	9 (5·1)	18 (11·0)	0·01
No	454 (93·0)	141 (95·3)	168 (94·9)	145 (89·0)	
Tumor staging (UICC), n (%)					
Early tumor stages (0, I, and II)	339 (69·5)	85 (57·4)	135 (76·3)	119 (73·0)	0·60
Advanced tumor stages (III and IV)	100 (20·5)	27 (18·2)	35 (19·8)	38 (23·3)	
Not applicable / missing	49 (10·0)	36 (24·3)	7 (4·0)	6 (3·7)	
Treatment intention, n (%)					
Curative	447 (91·6)	140 (94·6)	167 (94·4)	140 (85·9)	**0·01**
Palliative	23 (4·7)	7 (4·7)	3 (1·7)	13 (8·0)	
Missing	18 (3·7)	1 (0·7)	7 (4·0)	10 (6·1)	
Therapy modalities, n (%)**					
Surgery	475 (97·3)	146 (98·6)	171 (96·6)	158 (96·9)	0·998
Radiotherapy	24 (4·9)	10 (6·8)	8 (4·5)	6 (3·7)	0·38
Systemic medical therapy	159 (32·6)	53 (35·8)	73 (41·2)	33 (20·2)	**< 0·001**
Best supportive care	73 (15·0)	17 (11·5)	35 (19·8)	21 (12·9)	0·38
Missing	10 (2·0)	1 (0·7)	5 (2·8)	4 (2·5)	-
Diagnosis time point corresponding to lock- downs of 2020, n (%)					
Yes	191 (39·1)	56 (37·8)	67 (37·9)	68 (41·7)	0·69
No	297 (60·9)	92 (62·2)	110 (62·1)	98 (58·3)	
Mean interval between diagnosis and therapy (SD), (days)	7·4 (37·0)	4·7 (16·7)	13·5 (58·1)	3·2 (12·5)	**0·02**

Abbreviation: Interquartile range (IQR), Standard deviation (SD), Union Internationale Contre le Cancer (UICC). * *p* values for difference in mean between 2020 versus 2018 and 2019; ** more than one modality per patient possible. Significant *p* values (< 0·05) are highlighted (BOLD).

Supplement-II, Table-VI: Urinary bladder (incl. lower urinary tract).

Variables	Total cohort n = 479	Cohort of 2018 n = 162	Cohort of 2019 n = 160	Cohort of 2020 n = 157	*p* value*
Median age at time of diagnosis (IQR), (years)	63·7 (52·8-75·3)	64·1 (54·8-76·4)	64·9 (50·3-76·2)	62·4 (51·8-72·8)	0·16
Patients ≥ 70 years, n (%)	169 (35·3)	59 (36·4)	60 (37·5)	50 (31·8)	0·27
Place of residence, n (%)					
Urban	211 (44·1)	65 (40·1)	68 (42·5)	78 (49·7)	0·08
Rural	266 (55·5)	97 (59·9)	91 (56·9)	78 (49·7)	
Missing	2 (0·4)	0 (0)	1 (0·6)	1 (0·6)	
Patients with former malignancies, n (%)					
Yes	34 (7·1)	15 (9·3)	8 (5·0)	11 (7·0)	0·97
No	437 (91·2)	146 (90·1)	148 (92·5)	143 (91·1)	
Missing	8 (1·7)	1 (0·6)	4 (2·5)	3 (1·9)	
Tumor staging (FIGO), n (%)					
Early tumor stages (0, I, and II)	213 (44·5)	75 (46·3)	66 (41·3)	72 (45·9)	0·63
Advanced tumor stages (III and IV)	177 (37·0)	52 (32·1)	61 (38·1)	64 (40·8)	
Not applicable / missing	89 (18·6)	35 (21·6)	33 (20·6)	21 (13·4)	
Treatment intention, n (%)					
Curative	333 (69·5)	95 (58·6)	126 (78·8)	112 (71·3)	**0·02**
Palliative	44 (9·2)	12 (7·4)	9 (5·6)	23 (14·6)	
Missing	102 (21·3)	55 (34·0)	25 (15·6)	22 (14·0)	
Therapy modalities, n (%)**					
Surgery	404 (84·3)	140 (86·4)	133 (83·1)	131 (83·4)	0·74
Radiotherapy	117 (24·4)	45 (27·8)	33 (20·6)	39 (24·8)	0·75
Systemic medical therapy	147 (30·7)	42 (25·9)	52 (32·5)	53 (33·8)	0·22
Best supportive care	125 (26·1)	40 (24·7)	40 (25·0)	45 (28·7)	0·28
Missing	22 (4·6)	4 (2·5)	8 (5·0)	10 (6·4)	-
Diagnosis time point corresponding to lock- downs of 2020, n (%)					
Yes	186 (38·8)	57 (35·2)	65 (40·6)	64 (40·8)	0·13
No	293 (61·2)	105(64·8)	95 (59·2)	93 (59·2)	
Mean interval between diagnosis and therapy (SD), (days)	17·8 (51·9)	22·1 (76·3)	13·1 (38·6)	18·25 (26·6)	0·90

Abbreviation: Fédération Internationale de Gynécologie et d'Obstétrique (FIGO), Interquartile range (IQR), Standard deviation (SD). * *p* values for difference in mean between 2020 versus 2018 and 2019; ** more than one modality per patient possible. Significant *p* values (< 0·05) are highlighted (BOLD).

Supplement-II, Table-VII: Gynecologic cancer.

Variables	Total cohort n = 357	Cohort of 2018 n = 101	Cohort of 2019 n = 138	Cohort of 2020 n = 118	*p* value*
Median age at time of diagnosis (IQR), (years)	70·8 (60·6-78·4)	71·1 (59·9-77·5)	71·0 (60·2-78·6)	70·5 (63·9-79·0)	0·35
Patients ≥ 70 years, n (%)	187 (52·4)	53 (52·5)	72 (52·2)	62 (52·5)	0·97
Gender, n (%)					
Male	188 (52·7)	60 (59·4)	66 (47·8)	62 (52·5)	0·98
Female	169 (47·3)	41 (40·6)	72 (52·2)	56 (47·5)	
Place of residence, n (%)					
Urban	151 (42·3)	42 (41·6)	63 (45·7)	46 (39·0)	0·36
Rural	205 (57·4)	58 (57·4)	75 (54·3)	72 (61·0)	
Missing	1 (0·3)	1 (1·0)	0 (0)	0 (0)	
Patients with former malignancies, n (%)					
Yes	14 (3·9)	4 (4·0)	5 (3·6)	5 (4·2)	0·85
No	336 (94·1)	92 (91·1)	132 (95·7)	112 (94·9)	
Missing	7 (2·0)	5 (5·0)	1 (0·7)	1 (0·8)	
Tumor staging (UICC), n (%)					
Early tumor stages (0, I, and II)	93 (26·1)	25 (24·8)	42 (30·4)	26 (22·0)	0·70
Advanced tumor stages (III and IV)	219 (61·3)	72 (71·3)	81 (58·7)	66 (55·9)	
Not applicable / missing	45 (12·6)	4 (4·0)	15 (10·9)	26 (22·0)	
Treatment intention, n (%)					
Curative	155 (43·4)	48 (47·5)	63 (45·7)	44 (37·3)	0·56
Palliative	157 (44·0)	50 (49·5)	67 (48·6)	40 (33·9)	
Missing	45 (12·6)	3 (3·0)	8 (5·8)	34 (28·8)	
Therapy modalities, n (%)**					
Surgery	128 (35·9)	50 (49·5)	62 (44·9)	16 (13·6)	**0·003**
Systemic medical therapy	156 (43·7)	50 (49·5)	73 (52·9)	33 (28·0)	0·74
Best supportive care	157 (44·0)	45 (44·6)	72 (52·2)	40 (33·9)	**0·02**
Missing	73 (20·4)	2 (2·0)	11 (8·0)	60 (50·8)	-
Diagnosis time point corresponding to lock- downs of 2020, n (%)					
Yes	113 (31·7)	36 (35·6)	43 (31·2)	34 (28·8)	0·62
No	244 (68·3)	65 (64·4)	95 (68·8)	84 (71·2)	
Mean interval between diagnosis and therapy (SD), (days)	17·8 (46·2)	18·5 (59·8)	16·3 (37·0)	19·0 (42·1)	0·74

Abbreviation: Interquartile range (IQR), Standard deviation (SD), Union Internationale Contre le Cancer (UICC). * *p* values for difference in mean between 2020 versus 2018 and 2019; ** more than one modality per patient possible. Significant *p* values (< 0·05) are highlighted (BOLD).

Supplement-II, Table-VIII: Pancreatic cancer.

Variables	Total cohort n = 240	Cohort of 2018 n = 50	Cohort of 2019 n = 94	Cohort of 2020 n = 96	*p* value*
Median age at time of diagnosis (IQR), (years)	70·8 (63·8-78·2)	66·7 (60·5-76·0)	71·6 (63·9-78·7)	71·2 (64·4-78·8)	0·73
Patients ≥ 70 years, n (%)	127 (52·9)	20 (40·0)	55 (58·5)	52 (54·2)	0·75
Gender, n (%)					
Male	153 (63·7)	31 (62·0)	63 (67·0)	59 (61·5)	0·55
Female	87 (36·3)	19 (38·0)	31 (33·0)	37 (38·5)	
Place of residence, n (%)					
Urban	88 (36·7)	23 (46·0)	34 (36·2)	31 (32·3)	0·25
Rural	152 (63·3)	27 (54·0)	60 (63·8)	65 (67·7)	
Patients with former malignancies, n (%)					
Yes	14 (5·8)	2 (4·0)	7 (7·4)	5 (5·2)	0·74
No	221 (92·1)	45 (90·0)	87(92·6)	89 (92·7)	
Missing	5 (2·1)	3 (6·0)	0 (0)	2 (2·1)	
Tumor staging (UICC), n (%)					
Early tumor stages (0, I, and II)	47 (19·6)	11 (22·0)	21 (22·3)	15 (15·6)	0·39
Advanced tumor stages (III and IV)	102 (42·5)	21 (42·0)	41 (43·6)	40 (41·7)	
Not applicable / missing	91 (37·9)	18 (36·0)	32 (34·0)	41 (42·7)	
Treatment intention, n (%)					
Curative	102 (42·5)	21 (42·0)	43 (45·7)	38 (39·6)	0·23
Palliative	96 (40·0)	25 (50·0)	43 (45·7)	28 (29·2)	
Missing	42 (17·5)	4 (8·0)	8 (8·5)	30 (31·3)	
Therapy modalities, n (%)**					
Surgery	79 (32·9)	19 (36·0)	41 (43·6)	19 (19·8)	0·11
Radiotherapy	7 (2·9)	2 (4·0)	2 (2·1)	3 (3·1)	0·45
Systemic medical therapy	83 (34·6)	19 (38·0)	36 (38·3)	28 (29·2)	0·32
Watch & Wait / Active surveillance	70 (29·2)	22 (44·0)	29 (30·9)	19 (19·8)	0·49
Best supportive care	64 (26·7)	6 (12·0)	15 (16·0)	43 (44·8)	-
Missing					
Diagnosis time point corresponding to lock- downs of 2020, n (%)					
Yes	91 (37·9)	24 (48·0)	36 (38·3)	31 (32·3)	0.34
No	149 (62·1)	26 (52·0)	58 (61·7)	65 (67·7)	
Mean interval between diagnosis and therapy (SD), (days)	24·8 (47·8)	18·1 (27·3)	25·9 (48·5)	27·5 (55·4)	0·53

Abbreviation: Interquartile range (IQR), Standard deviation (SD), Union Internationale Contre le Cancer (UICC). * *p* values for difference in mean between 2020 versus 2018 and 2019; ** more than one modality per patient possible. Significant *p* values (<0·05) are highlighted (BOLD).

Supplement-II, Table-IX: Hepatocellular and hepatobiliary cancer.

Variables	Total cohort n = 81	Cohort of 2018 n = 19	Cohort of 2019 n = 31	Cohort of 2020 n = 31	*p* value*
Median age at time of diagnosis (IQR), (years)	64·9 (49·4-78·4)	63·4 (51·2-71·9)	63·2 (51·6-79·2)	65·3 (46·6-79·4)	0·87
Patients ≥ 70 years, n (%)	29 (35·8)	5 (26·3)	10 (32·3)	14 (45·2)	0·17
Gender, n (%)					
Male	43 (53·1)	10 (52·6)	17 (54·8)	16 (51·6)	0·83
Female	38 (46·9)	9 (47·4)	14 (45·2)	15 (48·4)	
Place of residence, n (%)					
Urban	25 (30·9)	5 (26·3)	9 (29·0)	11 (35·5)	0·48
Rural	56 (69·1)	14 (73·7)	22 (71·0)	20 (64·5)	
Patients with former malignancies, n (%)					
Yes	3 (3·7)	0 (0)	3 (9·7)	0 (0)	0·17
No	78 (96·3)	19 (100)	28 (90·3)	31 (100)	
Tumor staging (UICC), n (%)					
Early tumor stages (0, I, and II)	13 (16·0)	2 (10·5)	5 (16·1)	6 (19·4)	0·65
Advanced tumor stages (III and IV)	26 (32·1)	8 (42·1)	8 (25·8)	10 (32·3)	
Not applicable / missing	42 (51·9)	9 (47·4)	18 (58·1)	15 (48·4)	
Treatment intention, n (%)					
Curative	67 (82·7)	14 (73·7)	26 (83·9)	27 (87·1)	0·74
Palliative	6 (7·4)	2 (10·5)	2 (6·5)	2 (6·5)	
Missing	8 (9·9)	3 (15·8)	3 (9·7)	2 (6·5)	
Therapy modalities, n (%)**					
Surgery	60 (74·1)	13 (68·4)	24 (77·4)	23 (74·2)	0·95
Radiotherapy	16 (19·8)	4 (21·1)	3 (9·7)	9 (29·0)	0·09
Systemic medical therapy	11 (13·6)	3 (15·8)	6 (19·4)	2 (6·5)	0·14
Best supportive care	23 (28·4)	5 (26·3)	7 (22·6)	11 (35·5)	0·25
Missing	5 (6·2)	1 (5·3)	2 (6·5)	2 (6·5)	-
Diagnosis time point corresponding to lock- downs of 2020, n (%)					
Yes	25 (30·9)	13 (63·2)	7 (22·6)	6 (19·4)	0.16
No	56 69·1)	7 (36·8)	24 (77·4)	25 (80·6)	
Mean interval between diagnosis and therapy (SD), (days)	34·6 (61·0)	43·3 (85·4)	33·5 (64·1)	30·3 (37·0)	0·64

Abbreviation: Interquartile range (IQR), Standard deviation (SD), Union Internationale Contre le Cancer (UICC). * *p* values for difference in mean between 2020 versus 2018 and 2019; ** more than one modality per patient possible. Significant *p* values (< 0·05) are highlighted (BOLD).

Supplement-II, Table-X: Sarcoma.

Discussion

To our knowledge, COMA-19 is the first study where real-world short- and long-term consequences of the COVID-19 pandemic were studied according to pre-specified objectives. With a surface area comparable to that of Israel, Saxony-Anhalt is the eighth largest federal state in Germany with more than two million inhabitants. The state has the highest cancer incidence and the oldest population in Germany [24, 25]. For quality control, only patients diagnosed and treated in the certified cancer centers were included. This represented 27·4% of the estimated 14413 new diagnoses per year in the state [26]. Both 2018 and 2019 were included as comparators to avoid the accommodation of only one-year which can influence the value of the annual percent change and challenge the interpretation of the trend measure and its association with risk factors. The four most common entities included were cancers of the female breast, followed by lung, prostate, and colorectal cancer which represented half of the overall burden of cancer in COMA-19 and is similar to cancer burden in Europe [27]. The number of new cancers by age and gender was comparable to what is known [25, 27].

In contrast to other reports, the number of newly-diagnosed cases in 2020 for most entities was not impacted by the pandemic even though, similar to the literature, a temporarily disrupted oncological care in higher restriction periods (lockdowns) was documented [3-8, 11-16, 18]. Indeed, some tumor sites such as head and neck, hepatocellular, and renal cancers were even more frequently diagnosed in 2020. The pandemic-related drop in melanoma and non-melanoma skin cancers goes along with previous observations [13].

The lack of a pandemic dependent triage of patients according to age, gender, or place of residence and the absence of delayed therapy were encouraging facts. It is well known that even a four weeks delay of cancer treatment is associated with increased mortality in various cancers [28].

Indeed, the interval between diagnosis and therapy for most tumor sites in 2020 was curtailed compared to 2018 and 2019. This likely reflected a foresight of the medical staff to deliver health services as early as possible amid the pandemic ambiguities such as upcoming viral outbreaks and further political and/or public health restrictions. Overall, radiotherapy was offered constantly over the years. Yet, there was a modest decline in surgery and systemic therapies of 4% each in 2020. Comparison with other studies is problematic because of the heterogeneity of data and the different periods of time evaluated.

Finally, literature on follow-up rates are limited. Our 60% quotient in 2020, though less than the rates of the pre-pandemic years, suggests that follow-up was basically maintained.

The largely positive short-term results of cancer management in our study highlight the enormous efforts the oncology community undertook to maintain cancer care under an unprecedented pandemic and gave hope that the long-term consequences would not be too devastating.

Regrettably, this turned out not to be true. Despite a shorter follow-up time for patients diagnosed in 2020, EFS and TTP were significantly inferior compared to patients diagnosed in 2018 and 2019. Although statistically not yet significant, overall survival also tended to be less favorable. Even if this negative outcome was not observed across all tumor sites, the four most common entities (breast, lung, prostate, and colorectal cancers) were amid the ten cancer types associated with at least one inferior outcome measure. The alterations in the 2020 treatment patterns (more palliative intentions, less surgeries, or less systemic therapies) for several tumor sites were identified as a key reason accounting for the negative outcome. These changes in treatment patterns most likely were the result of a mixture of unavoidable but also some unnecessary pandemic- and non-pandemic-related reasons.

An optimal outcome depends both on a timely and evidence-based therapy. Thus, it is not surprising that the 2020 shortened interval between diagnosis and treatment could not compensate the shift in treatment patterns in terms of OS, EFS, or TTP.

Three limitations merit mentioning. First, though a large number of patients were available for follow-up, sample size calculation and power were primarily based on the number of newly-diagnosed patients and not outcome. It must be remembered that unknown confounders can ultimately only be controlled with randomization which is not an option in this field of research. Second, intention, type, and number of active tumor therapies were documented but data regarding application sequence, dosing, delay, and or adaption was not collected. As these are additional relevant aspects in the treatment pathway influencing long-term outcome, granularity is essential to make a final judgment to the impact of the pandemic on treatment patterns and outcome. This is currently being investigated. Third, although no differences in the cause of death (tumor-related versus non-tumor-related) were found between the three study years, COVID-19 infections, both in patients and medical staff (quarantine), and their exact impact on treatment modification and long-term outcome were out of the scope of this study.

Conclusion

This real-world study shows that in addition to safeguarding optimal patient access to oncological care and maintaining constant numbers of newly-diagnosed patients under a pandemic, minor modifications in the delivery of cancer therapy, even in high-quality specialized cancer centers in a high-economic region,

could have negative consequences on the long-term outcome of patients with potentially curable cancers. Disseminating good-quality real-world data, even with upsetting findings, is crucial for the oncology community, public health services, and policymakers to create awareness and draw lessons to weather future pandemics. Prioritization of available medical capacities to only one sector is always on the expense of other vulnerable sectors including oncology. Hasty recommendations modifying evidence-based management guidelines must be critically reflected and priorities for cancer therapy meticulously triaged (e. g. a reasonable delay in the management of low-risk tumors such as some dermatologic cancers is not likely to impact outcome as was the case in our study). Finally, resilience is a responsibility that can't be delegated.

Acknowledgments

The COVID-19 study was funded by the East German Study Group for Hematology and Oncology (OSHO). We would like to thank Andreas Wienke for his expertise in providing biometric and statistical advice on the COMA-19 study. Nadja Jäkel supported us in the preparation of figures. In the cancer centers, Manuela Dawid, Elke Decker, Sandra Ehlert, Janin Ehrenberg, Nadine Ernst, Silke Heller, Sandra Haeupke, Janine Herbarth, Sabina Huseynova, Sarah Kolbitz, Katja Maertins, Katrin Losse, Manuela Oelschlaeger, Kathleen Riedel, Alexander Gabriel Schaefer, Nicole Schmidt-Boenicke, and Sylvana Uhlig were helpful in providing the data. Without their support, data collection would not have progressed so quickly.

Ethical Considerations: The protocol was submitted to and approved by the ethics committees and registered in the German Registry for Clinical Trails (DRKS00027370).

Declaration of interests: All authors declare no conflicts of interests.

Contributors

HKAA is the Chief Investigator of the COMA-19 study and has overall responsibility for the study and was involved in the conceptualisation, data curation, data interpretation, formal analysis, funding acquisition, methodology, supervision, validation, visualisation, writing – original draft, and writing – review and editing. SS was involved in the conceptualisation, data curation, data interpretation, formal analysis, investigation, methodology, project administration, software, supervision, validation, visualisation, writing – original draft, and writing review and editing. She had directly accessed and verified the underlying data reported in the manuscript. PFS was involved in data collection, data interpretation, software, validation, writing – original draft, and writing review and editing. LE was involved in data collection, data interpretation, validation, and writing review and editing. FS, BO, LT, CK were involved in data collection and gave access to the local databases, writing – review and editing. The authors were not precluded from accessing data in the study and they accept responsibility to submit for publication.

Data Sharing:

Application for access to de-identified participant data can be made to the Krukenberg Cancer Center (susann.schulze2@uk-halle.de). All data access applications will be considered on their individual merits and by consensus of the investigators and the OSHO headquarters. If applications are approved there will be no limitations on the length of time that the data are available. Data will be made available after publication of this Article. A data sharing agreement between the researcher or institutions would then be set up before release of the approved data.

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