

ORIGINAL ARTICLE

THE INCIDENCE OF CANCER AT THE TIME OF COVID-19 IN NORTHERN ITALY

L. Mangone¹, F. Marinelli¹, I. Bisceglia¹, C. Pinto²

¹ Epidemiology Unit, Azienda Unità Sanitaria Locale – IRCCS Reggio Emilia, Reggio Emilia, Italy

² Medical Oncology Unit, Comprehensive Cancer Center, Azienda Unità Sanitaria Locale – IRCCS Reggio Emilia, Reggio Emilia, Italy

CORRESPONDING AUTHOR:

Francesco Marinelli
Epidemiology Unit
Azienda Unità Sanitaria Locale – IRCCS Reggio Emilia
via Amendola 2
42122 Reggio Emilia, Italy
E-mail: francesco.marinelli@ausl.re.it
ORCID: 0000-0002-0047-456X

Doi: 10.48286/aro.2022.41

History

Received: Mar 9, 2022

Accepted: Apr 27, 2022

Published: June 8, 2022

ABSTRACT

Recent studies have assessed the impact of the COVID-19 pandemic and related control measures on the number of new cancer diagnoses. The aim of this work was to evaluate the real impact of the lockdown on new cancer diagnoses in 2020. To compare the incidence of tumors in 2020 with that in 2019, we used data collected by the Reggio Emilia Cancer Registry. We reported the variations (number of cases and % values) of all tumors and of the main sites by sex and period of lockdown. We calculated the standardized incidence and mortality rate of the last twenty years (2001-2020) for all tumor sites and the main sites (breast, colorectal, lung and prostate) by sex. In 2020, 4,031 cases of cancer were recorded, 669 fewer than in 2019 (-14.2%). The sites that recorded the largest decline compared to 2019 were: skin (non-melanoma) (-281 cases), prostate (-110 cases), melanoma and bladder (-53 cases)

and colorectal (-38 cases). The incidence trend in males decreased from 491.74 cases per 100,000 p/y in 2001 to 471.58 in 2019 and dropped to 386.59 in 2020. Mortality also decreased over the years from 250.8 cases per 100,000 p/y in 2001 to 164.4 cases in 2019 and 161.9 in 2020. In women, the incidence remained almost constant over the years, whereas there was a decline in mortality. The decrease in cancers recorded, especially during the lockdown, has been widely reported in the literature, but the data usually only cover the months leading up to September 2020. The COVID-19 pandemic has caused delays in the diagnosis of new cancers. However, it is necessary to document with data the real impact the pandemic has had on new diagnoses, taking into account the tumor site, gender, the presence of cancer screening, and in general the organization of healthcare of the territory in question.

KEY WORDS

Cancer; Covid-19; impact; incidence.

INTRODUCTION

The incidence of tumors in Italy is monitored by the constant activity of the Cancer Registries (1). Every year in Italy there are about 376,000 new diagnoses of malignant cancer: breast, colorectal and lung are the most frequent cancers in women; prostate, lung and colorectal are the most frequent sites in men. For the majority of cancers, the rates are progressive. Melanoma (due to greater exposure to ultraviolet rays) and pancreatic tumors are on the increase in both sexes. Among women, the incidence of lung cancer continues to increase (largely linked to smoking), and breast cancer diagnoses have increased, due to more widespread screening throughout the national territory and to an extension of the target population age range (from 50-69 to 45-74).

But the situation changed quickly. The outbreak of the global pandemic dramatically changed our lives, and the impact of this phenomenon on new cancer diagnoses was not long in coming. The first analysis, published by Liang *et al.* (2), highlighted the impact of the SARS-CoV-2 infection on cancer patients in China; in particular, Intensive Care Unit (ICU) admissions and deaths were higher in cancer patients, especially if the cancer had been diagnosed in recent years. Subsequently, several papers were published on the subject and on the impact of infection on new cancer diagnoses. An Italian study (3) showed that during the lockdown (March-May 2020) in Italy there was a 45% reduction in new cancer diagnoses compared with the same months of 2018-19. In particular, the decrease concerned skin cancers and melanomas (-57%), and colorectal (-47%), prostate (-45%) and bladder (-44%) cancer. A subsequent study evaluated the impact that the lockdown (and the suspension of screening) had on new cancer diagnoses (4), highlighting a 35% decrease in new diagnoses compared to the previous year. In particular, there was a 35% reduction in diagnoses of breast cancer, 32% in prostate cancer and 53% in colorectal cancer.

The same attention was also given in Italy to stud-

IMPACT STATEMENT

The pandemic has caused a decline in new cancer diagnoses but there is a strong variability linked to sex, tumor site and health organization.

ying the association between COVID-19 infection and cancer diagnosis. A study in the Veneto region (5) confirmed that cancer patients had a greater chance of being hospitalized and dying from COVID-19 than the general population, in particular for lung, breast and hematological cancers. Similar results were observed in a population study in Reggio Emilia (6), which confirmed the higher risk in patients with cancer compared to the general population (OR 1.45, 95% CI 1.12-1.89). The risk increased in the presence of distant metastases and if the patient had been diagnosed with cancer less than 2 years prior, and was higher for hematological cancers (excluding lymphoma), melanomas and cancers of the female genital organs.

The aim of this work is to describe the impact of Covid-19 on the incidence of tumors in a province of northern Italy, over a long period of time and using population data.

MATERIALS AND METHODS

This is a population-based cohort study using data from the Reggio Emilia Cancer Registry (CR) approved by the provincial Ethics Committee of Reggio Emilia (Protocol no. 2014/0019740 of 04/08/2014). The main information sources of the RE-CR are anatomic pathology reports, hospital discharge records, and mortality data, integrated with laboratory tests, diagnostic reports, and information from general practitioners. The RE-CR covers a population of 532,000 inhabitants and is considered a high-quality CR thanks to the fact that its data are up to date (the incidence data extend to the end of 2020), and it has a high percentage of microscopic confirmation (for example, 98.8% for breast cancer and 93.4% for colon cancer, and the percentage of Death Certificate Only is below 0.1%) (7). The study included cancer data for 2001-2020 obtained from the RE-CR and specifically compares the 2019-2020 data by site, gender and

for breast, colorectal and cervical cancer, also the in-situ forms were reported. The difference between the cases registered in 2020 and 2019 was calculated, also reporting the percentage of variation. Data are presented in both aggregate form and stratified form for males and females.

The standardized incidence and mortality rate of the last twenty years (2001-2020) was calculated divided by males and females for all sites (excluding the skin) and for the main tumor types: breast, prostate, lung and colorectal. We performed the annual percent change (APC) analysis in age-standardized rates with 95% confidence intervals using Joinpoint regression.

Population estimates, which were used to derive rates, are represented by the general population of the Province of Reggio Emilia recorded on January 1st of each year. Incidence rates and incidence-based mortality rates were adjusted to the 2013 European standard population and calculated per 100,000 person-years.

RESULTS

82,564 diagnosed patients in the period 2001-2020 were considered. The distribution of cases by gender, age at diagnosis, tumor site and period of incidence is shown in **table I**.

From the comparison of the cases registered in 2020 compared to 2019, it is clear that in 2020, 4,031 cas-

es of cancer were recorded, 669 fewer than in 2019 (-14.2%). The sites that showed the greatest decline compared to 2019 were: skin (non-melanoma) (-281 cases), prostate (-110 cases), melanoma and bladder (-53 cases) and colorectal (-38 cases) (**table II**).

In males, the largest decline involved non-melanoma skin cancers (-159 cases; -24.3%), prostate (-110 cases; -28.4%), lung (-46 cases; -17.6%), colorectal (-34 cases; -18.7%), and melanoma -24 cases; -22.4%) and bladder (-24 cases; -13.4%) (**table III**). In females, the decline primarily involved non-melanoma skin cancers (-122 cases; -25.4%), followed by *corpus uteri* (-31 cases; -31%), bladder (-29 cases; -26.6%), melanoma (-29 cases; -27.65%), and stomach tumors (-25 cases; -44.6%) (**table III**). There was no decline for breast cancer in situ (+2 cases); on the other hand, for the cervix and colon in situ, fewer cancers were diagnosed than in 2020 (-68 and -22 cases, respectively) (**table IV**).

Considering 20 years of incidence and mortality, it is observed that the incidence trend in males (**figure 1 A**) decreased from 491.74 cases per 100,000 persons/year in 2001 to 471.58 in 2019 and dropped to 386.59 in 2020, with a decline especially in the last year (APC -1.1; 95% CI -1.5 to -0.7). Mortality also decreased over the years, from 250.8 cases per 100,000 p/y in 2001 to 164.4 cases in 2019 and 161.9 in 2020 (APC -2.3; 95% CI -2.8 to -1.8). In females, the incidence remained almost constant over the years (APC 0.1; 95% CI -0.1 to 0.3), while there was a significant decline in mortality rate (APC -1.5; 95% CI -1.9 to -1.0) (**figure 1 B**). The incidence of breast cancer slightly increased in the last year (from 126.35 cases per 100,000 p/y recorded in 2019 to 133.23 cases in 2020) (APC 0.0; 95% CI -0.4 to 0.3), while mortality slightly decreased in the last period (**figure 2 A**) (APC -2.4; 95% CI -3.5 to -1.4). For prostate cancer, there was a sharp increase in incidence until the mid-2000s (APC 2001-2003, 18.4; 95% CI -16.9 to -68.8), due to the excessive use of PSA testing; in the last two years, instead, the incidence showed a significant decline (from 94.98 cases per 100,000 p/y in 2019 to 67.79 cases in 2020) (APC 2003-2020, -1.9; 95% CI -3.0 to -0.8) (**figure 2 B**).

There has been a constant and significant decline in the incidence (APC -2.7; 95% CI -3.3 to -2.1) and mortality (APC 2001-2012, -5.6; 95% CI -7.5 to -3.7) of lung cancer over the years in males: the incidence dropped from 83.67 cases per 100,000 p/y in 2001 to 61.87 in 2019 and 49.16 cases in 2020; mortality declined from 73.9 cases in 2001 to 38.4

VARIABLES	N	%
ALL	82,564	
Sex		
Male	44,182	53.5
Female	38,382	46.5
Age at diagnosis		
< 50	9,785	11.8
50-69	29,388	35.6
70 +	43,391	52.6
Sites		
Breast female	9,271	11.2
Prostate	6,346	7.7
Lung	7,214	8.7
Colorectal	3,214	3.9
Other sites	56,519	68.5
Years of diagnosis		
2001-2005	18,612	22.5
2006-2010	19,959	24.2
2011-2015	21,886	26.5
2016-2020	22,107	26.8

Table I. Number and percentage of cases, period 2001-2020.

SITE	YEAR		DIFFERENCE 2020 VS. 2019	
	2019	2020	N.	%
	N.	N.		
Head-neck*	53	50	- 3	- 5.7
Esophagus	17	16	- 1	- 5.9
Stomach	124	102	- 22	- 17.7
Small intestine	14	16	2	14.3
Colorectal	325	287	- 38	- 11.7
Liver	77	77	0	0.0
Gallbladder and bile ducts	25	30	5	20.0
Pancreas	152	143	- 9	- 5.9
Larynx and nasal cavity	35	40	5	14.3
Lung and other thoracic organs	397	370	- 27	- 6.8
Bone	9	7	- 2	- 22.2
Skin, melanoma	212	159	- 53	- 25.0
Skin, non-melanoma	1133	852	- 281	- 24.8
Mesothelioma	18	27	9	50.0
Soft tissue and Kaposi sarcoma	18	16	- 2	- 11.1
Breast	509	524	15	2.9
<i>Cervix uteri</i>	12	18	6	50.0
<i>Corpus uteri</i>	100	69	- 31	- 31.0
Ovary	49	53	4	8.2
Other female genitals	10	12	2	20.0
Penis	5	4	- 1	- 20.0
Prostate	387	277	- 110	- 28.4
Testicle and other genitals	22	19	- 3	- 13.6
Bladder (including not malignant)	248	195	- 53	- 21.4
Kidney and urinary duct	117	107	- 10	- 8.5
Eye	6	0	- 6	- 100.0
Brain (including not malignant)	132	111	- 21	- 15.9
Thyroid	110	97	- 13	- 11.8
Other endocrine glands	10	5	- 5	- 50.0
Hodgkin Lymphoma	15	22	7	46.7
Non-Hodgkin Lymphoma	146	120	- 26	- 17.8
Myeloma	50	48	- 2	- 4.0
Leukemia	57	67	10	17.5
Other MPD and MDS**	75	46	- 29	- 38.7
Other sites	31	45	14	45.2
TOTAL	4700	4031	- 669	- 14.2

Table II. Number of cases by cancer site and year of diagnosis 2019-2020.

* (C00-C14, C30, C31, C32); **myeloproliferative disorders, myelodysplastic syndromes.

and 38.5 cases in 2019 and 2020, respectively (**figure 2 C**). In females, however, the situation is the opposite, where both incidence (APC 1.8; 95 % CI 0.9 to 2.7) and mortality (APC 0.9; 95% CI -0.4 to 2.2) are slightly but steadily increasing (**figure 2**

D). For colorectal cancer, there was a peak of incidence in both sexes around 2006 due to the more extensive use of screening, and then decreasing in both sexes over the years (APC Males, -3.2; 95 % CI -4.1 to -2.2; APC Females, -2.4; 95% CI -3.5 to -1.3).

SITE	MALES				FEMALES			
	2019	2020	DIFFERENCE 2020 VS. 2019		2019	2020	DIFFERENCE 2020 VS. 2019	
	N.	N.	N.	%	N.	N.	N.	%
Head-neck*	38	38	0	0.0	15	12	- 3	- 20.0
Esophagus	11	9	- 2	- 18.2	6	7	1	16.7
Stomach	68	71	3	4.4	56	31	- 25	- 44.6
Small intestine	8	9	1	12.5	6	7	1	16.7
Colorectal	182	148	- 34	- 18.7	143	139	- 4	- 2.8
Liver	55	59	4	7.3	22	18	- 4	- 18.2
Gallbladder and bile ducts	13	19	6	46.2	12	11	- 1	- 8.3
Pancreas	81	71	- 10	- 12.3	71	72	1	1.4
Larynx and nasal cavity	30	31	1	3.3	5	9	4	80.0
Lung and other thoracic organs	262	216	- 46	- 17.6	135	154	19	14.1
Bone	6	4	- 2	- 33.3	3	3	0	0.0
Skin, melanoma	107	83	- 24	- 22.4	105	76	- 29	- 27.6
Skin, non-melanoma	653	494	- 159	- 24.3	480	358	- 122	- 25.4
Mesothelioma	12	22	10	83.3	6	5	- 1	- 16.7
Soft tissue and Kaposi sarcoma	14	8	- 6	- 42.9	4	8	4	100.0
Breast	7	5	- 2	- 28.6	502	519	17	3.4
<i>Cervix uteri</i>	-	-	-	-	12	18	6	50.0
<i>Corpus uteri</i>	-	-	-	-	100	69	- 31	- 31.0
Ovary	-	-	-	-	49	53	4	8.2
Other female genitals	-	-	-	-	10	12	2	20.0
Penis	5	4	- 1	- 20.0	-	-	-	-
Prostate	387	277	- 110	- 28.4	-	-	-	-
Testicle and other genitals	22	19	- 3	- 13.6	-	-	-	-
Bladder (including not malignant)	179	155	- 24	- 13.4	69	40	- 29	- 26.6
Kidney and urinary duct	78	66	- 12	- 15.4	39	41	2	5.1
Eye	4	0	- 4	- 100.0	2	0	- 2	- 100
Brain (including not malignant)	61	49	- 12	- 19.7	71	62	- 9	- 12.7
Thyroid	33	31	- 2	- 6.1	77	66	- 11	- 14.3
Other endocrine glands	6	2	- 4	- 66.7	4	3	- 1	- 25.0
Hodgkin Lymphoma	12	11	- 1	- 8.3	3	11	8	266.7
Non-Hodgkin Lymphoma	78	57	- 21	- 26.9	68	63	- 5	- 7.4
Myeloma	27	23	- 4	- 14.8	23	25	2	8.7
Leukemia	30	35	5	16.7	27	32	5	18.5
Other MPD and MDS**	38	25	- 13	- 34.2	37	21	- 16	- 43.2
Other sites	16	19	3	18.8	15	26	11	73.3
TOTAL	2523	2060	- 463	- 18.4	2177	1971	- 206	- 9.5

Table III. Number of cases by cancer site and sex, years 2019-2020.

**(C00-C14, C30, C31, C32); **myeloproliferative disorders, myelodysplastic syndromes.*

In 2020 the incidence declined more in males, as a result of lack of diagnosis probably due to the COVID-19 pandemic. Mortality also declined over

the years in both sexes: it decreased by about 50% from 2001 to 2020 (from 24.5 cases per 100,000 p/y in 2001 for males and 13.6 for females to 12.5

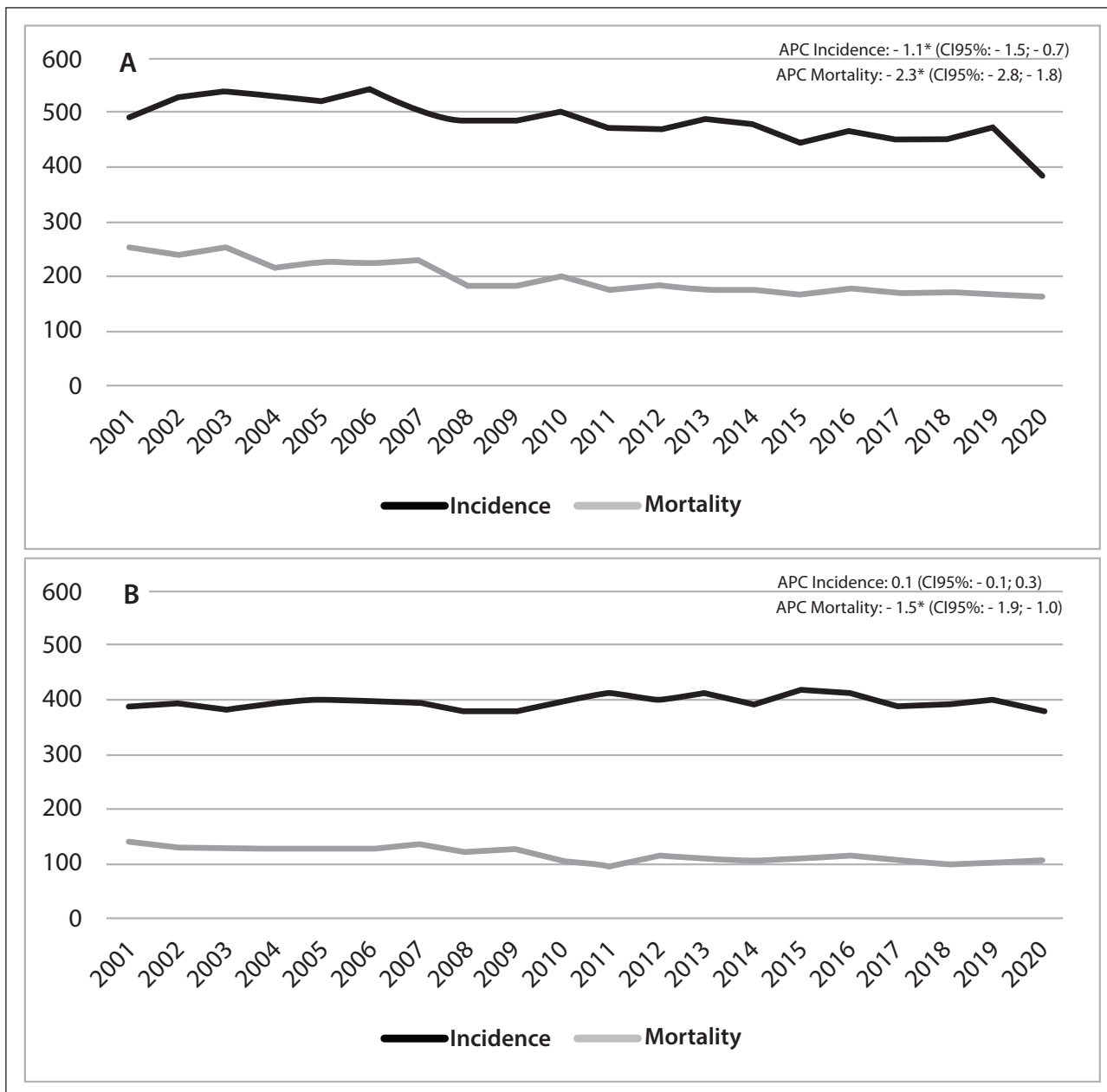


Figure 1. Incidence and mortality trend of all cancer sites (excluding skin) years 2001-2020; A. In males; B. in females.

	2019	2020	DIFFERENCE 2020 VS. 2019
Breast	75	77	2
Cervix	288	220	- 68
Colorectal	28	6	- 22
TOTAL	391	303	- 88

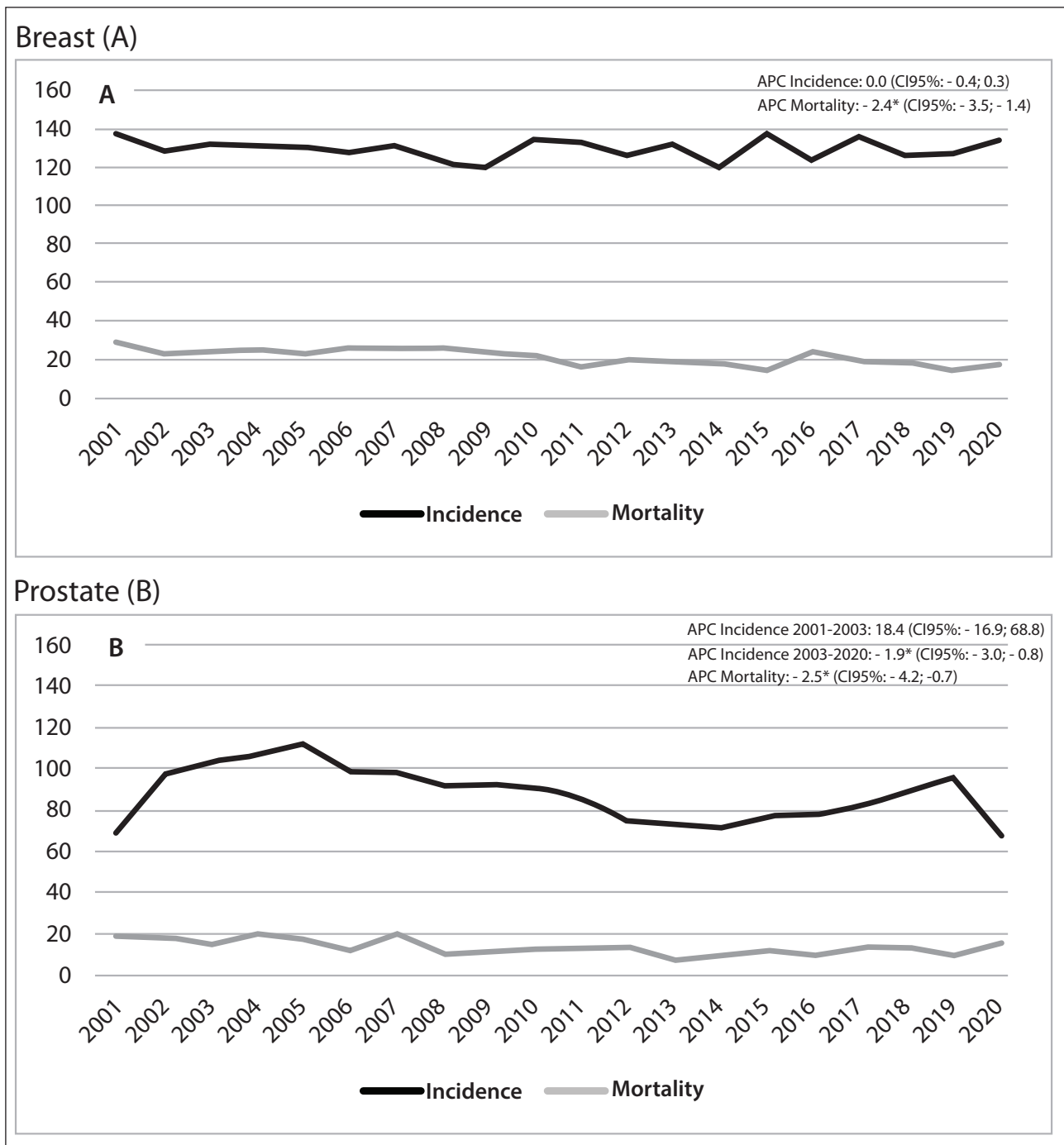
Table IV. Number of in situ cases by cancer site in the three screened cancers, years 2019-2020.

cases in males and 7.6 in females, respectively) (APC Males, -3.0; 95 % CI -4.2 to -1.8; APC Females, -2.4; 95% CI -3.5 to -1.3) (figure 2 E, F).

DISCUSSION

The aim of this work was to compare the tumors incidence in 2020 with those of 2019 and describe the incidence and mortality trends relating to 20 years of registration, to better understand the phenomenon in recent years, for all sites and for the main tumor sites.

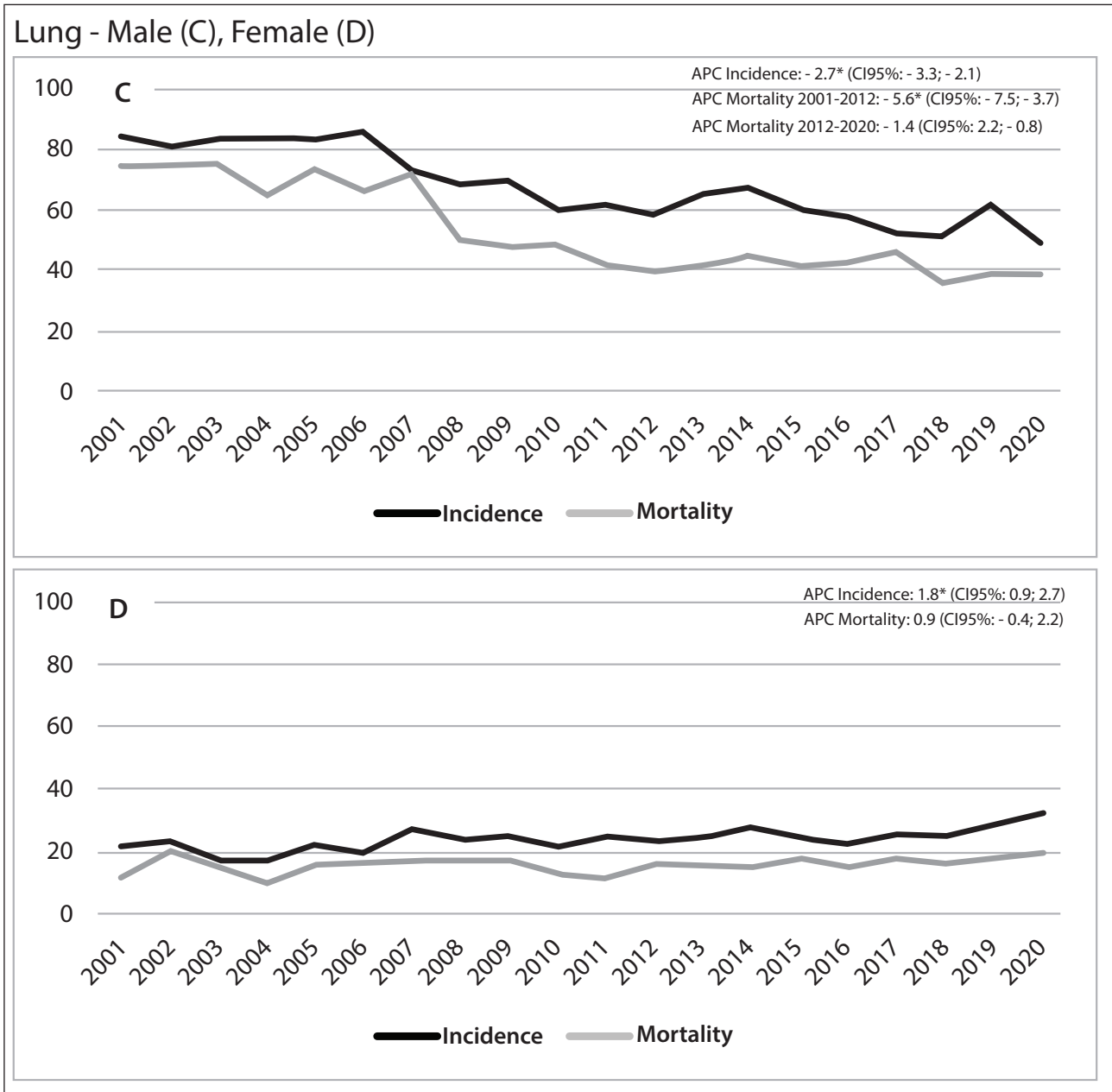
The first interesting data is the decrease in cancers recorded in 2020 compared to 2019: -669 cases, equal to 14.2% less. The decline, especially during the lockdown, has been widely reported in the literature but usually covers the months leading up to September 2020, recording first a decrease and



Figures 2A, B. Incidence and mortality trend for main site of cancer by sex, years 2001-2020.

then a recovery in the incidence (8). In particular, the decline concerned cancers of the skin (-25%), prostate (-28.4%), melanoma (-25%), bladder (-21.4%), colorectal (-11.7%) and the body of the uterus (-31%). A decrease in skin cancers (-74%) and melanoma (-54%), probably due to diagnostic failures, has already been reported in the English literature in a recent study by Venables *et al.* (9) and by Eskander *et al.* (8) as regards melanoma. The decrease in prostate cancer (-28.4%) has been widely reported in other studies: -54.7% in Eskander (8) and -64%

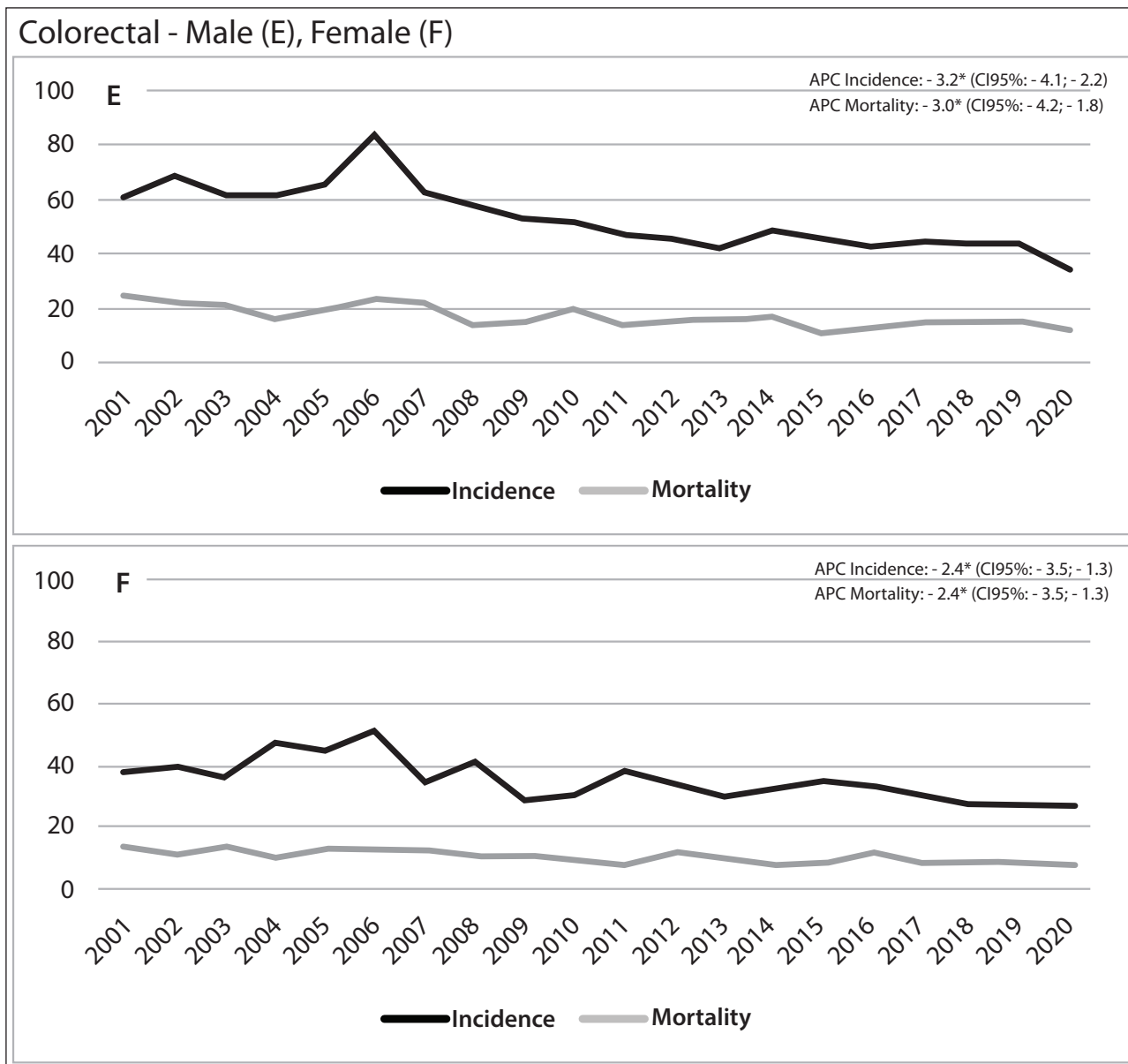
in Venables (9). This decrease was not confirmed, however, in a German study (10). It should be noted that the two studies cited above, Eskander (8) and Venables (9), refer to the incidence up to September 2020, thus not allowing a possible resumption of diagnoses. A decrease in diagnoses was observed in all countries and for almost all tumor sites (3), in particular those subject to screening (11). The recovery of the post-lockdown diagnoses almost never compensates for the decrease observed during the lockdown (12), with a few exceptions (4).



Figures 2 C, D. Incidence and mortality trend for main site of cancer by sex, years 2001-2020.

For the three cancers screened, our study did not show any decrease in breast cancer diagnoses (+15 cases equal to +2.9%) since after the interruption of screening during the lockdown, a rapid resumption of screenings, and therefore of diagnoses, followed in the target population. The interruption of screening already reported in the literature (13) seems to have had a greater impact on the decrease of early forms (tumors in situ and T1 and stage I tumors) but not on the increase of advanced forms. Our study does not report delays in the diagnosis of cervical cancer, though referring to small numbers, from 12 to 18 cases in the two-year period considered, while the literature

shows a decrease in the incidence (8) or a delay in HPV-negative patients (14). Rather, the delay led to problems in the management and treatment of cervical cancers. As regards colorectal cancers, the decline concerned primarily colon cancers and mainly in males (-20 cases), while in females the incidence remained almost stable (-7 cases). A decrease in colorectal cancers had already been reported by the Ferrara study (3). A shift in the diagnosis of these tumors could have a greater impact, given the natural history of this cancer, with an increase in advanced forms from 26% to 29% for a delay of 7-12 months and from 26% to 33% for a delay of 12 months (15).



Figures 2 E, F. Incidence and mortality trend for main site of cancer by sex, years 2001-2020.

The impact this will have on the next few years can only be predicted with estimates. Ward *et. al* (16) report that after a decline in 2020 there will be a recovery in 2021 and that in the future there will be above all an increase in advanced stages. The decline in lung cancers reported in the literature finds a strong difference between genders in our study: it decreased in men and increased in women, in this case attributing the incidence exclusively to the main risk factor, cigarette smoking (10). Finally, little or no impact was seen on hematological cancers, which continued to be diagnosed unaffected by the pandemic.

The absolute numbers are also confirmed by the standardized incidence rates. In males there was a decrease in tumors from 471.6 in 2019 to 386.6

in 2020, while in females the incidence is almost constant, largely linked to the “resistance” of tumors of the breast. In males, in addition to lung cancer, there was a sharp decline in prostate cancer, from 95.0 in 2019 to 67.8 in 2020. Lung cancer continued to record a downward trend in males: 61.9 in 2019 and 49.2 in 2020, while in females it rose from 28.6 to 32.3, respectively. Mesothelioma continues to increase in males, as reported by a recent published paper (17).

Finally, colorectal cancer incidence shows a sharp increase in 2006 after population screening was started in 2004. The trend then steadily declined over the years and in the last year it dropped from 43.4 to 34.5 in males but not in females (26.6 in 2019 and 26.8 in 2020). The mortality trend in re-

cent years has been stable in males and females. Breast cancer incidence showed a slight increase in 2020 (from 14.7 in 2019 to 17.3 in 2020) as did prostate cancer (from 9.5 in 2019 to 15 in 2020).

CONCLUSIONS

The aim of this work was to describe the impact of Covid-19 on the incidence of tumors in a province of northern Italy, over a long period of time and using population data. Our study confirmed that in 2020 there were nearly 700 fewer cancer diagnoses than the previous year: the decline affected almost all sites, especially skin cancers and prostate cancer. Breast cancer did not show a decline in incidence and, unlike what emerged in the literature, no decline in early stage tumors.

ETHICS

Fundings

There were no institutional or private fundings for this article.

Conflicts of interests

The authors have declared no conflict of interests.

Availability of data and materials

The data underlying this article can be shared just before a reasonable request to the corresponding author.

Authors' contribution

LM: conceptualization, investigation, writing - original draft, visualization, supervision; FM: formal analysis, methodology; IB: writing - review and editing, and visualization; CP: conceptualization, writing - original draft, investigation, and supervision.

Ethical approval

Protocol no. 2014/0019740 of 04/08/2014.

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