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 impact of the lockdown on new cancer diagnoses. To compare the incidence of tumors in 2020 with that in 2019, we used the data from the pathology anatomy reports available until the 31st of August 2020 and collected by the Reggio Emilia Cancer Registry. Over 90% of all incident cancer cases have microscopic confirmation. We report the variations (number of cases and % values) of all tumors and of the main sites by sex, age and period. From the 1st of January to the 31st August 2020, we recorded 3,548 new cancer diagnoses, 14% fewer than in the corresponding months of 2019. For all cancers, the pre-lockdown period (January-February) had a similar number compared to the same months in 2019; the lockdown period (March-May) showed a decrease (-35%), but the post-lockdown (June-August) period showed similar numbers to those observed in 2019 (-2%). The difference is more evident in males and in the elderly. Breast cancer shows an increase in the first months (24%), a decrease during the lockdown (-35%), but a rapid recovery of the diagnosis after the lockdown (11%). Lung cancer showed a decrease in incidence in all three periods (-18%, -22%, and 21%, respectively). Colorectal cancers shows similar value during the first two months (-4%), a large decrease during lockdown (-53%), but an immediate return to normality after lockdown (-4%). Prostate cancer declined sharply during lockdown (-32%), as well as haematological cancers (-49%). We observed a sharp decrease in cancers diagnosed during lockdown compared to the same period in 2019 particularly evident for the two cancers of organized screening programs (breast and colorectal cancer) and in the older people.
INTRODUCTION
The SARS-CoV-2 virus first appeared in Italy at the end of January 2020, with an outbreak of infections detected in Codogno, Lombardy, after the first diagnosis of a COVID-19 in Italy case without any link to travel exposure on the 21st February 2020. The initial 16 confirmed cases increased to 60 the following day, with the first deaths reported in those same days (1). The Prime Minister Decree of the 9th of March 2020 (I stay at home) closed all non-essential businesses; this decree was in force until 16 May, when restrictions were gradually lifted; the ban on inter-regional travel was lifted on the 3rd of June. The three-month lockdown saw a slowdown in many diagnostic activities and a stop to the three organized screening programs in Italy, i.e., cervical, colorectal, and breast cancer screening. The aim of this work was to evaluate the impact that the COVID-19 pandemic and the resulting containment measures have had, in quantitative terms, on new cancer diagnoses. The study was conducted in the Province of Reggio Emilia, a province in Northern Italy characterized both by a high incidence of tumors and by a high incidence of SARS-CoV-2 infections (2).

METHODS
The study presents preliminary data from the Reggio Emilia Cancer Registry, whose primary task is to monitor temporal and spatial variations in cancer incidence. The Reggio Emilia Cancer Registry (CR) has been approved by the provincial Ethics Committee of Reggio Emilia (Protocol n. 2014/0019740 of 04/08/2014).

Data source
The Reggio Emilia CR registers all new cancer diagnoses occurring in people residing in the Reggio Emilia province. The main information sources of the CR are the anatomic pathology reports, the hospital discharge records, and mortality data. The CR has been active since 2000 and has registered all incident cases since 1996 (3).

RESULTS
From the 1st of January to the 31st of August 2020, 3,548 new cancer diagnoses in the province of Reggio Emilia were recovered from the pathology records, 14% less than in the corresponding months in 2019, we used data from the most complete among the cancer registry data sources, the only one that was already complete up to end of August 2020, i.e., the anatomic pathology reports from the only Local Histopathology and Cytopathology Network active in the province. Cancer Registry operators conducted the initial case assessment for eligibility for incidence (excluding prevalent cases, non-residents, and non-invasive cancer diagnoses) according to international registration rules (4).

Analyses
We analyzed all tumor sites and the principal sites: breast, prostate, colorectal, lung, and haematologic cancers. For all sites we also report analyses by sex and age group (0-64, 65-79, 80 +). We first compared absolute numbers of new diagnoses per month occurring in 2019 and in 2020 for the period January-August. We also present the percentage change of 2020 compared to 2019 per month. Data are also grouped as follows: pre-lockdown (January-February), full lockdown (March-May), and post-lockdown (June-August). We also report percentage differences between 2020 and 2019 in the three periods, with relative 95% confidence intervals (95%CI) estimated on Poisson distribution assuming equal denominator.

The study has an estimated power to identify a one third reduction in incidence comparing the three month period of the lockdown in 2020 with 2019 of 90% with alpha 5% for breast cancer, and approximately 70% for lung, colorectal and prostate cancer. Therefore we did not explore changes in incidence for cancer sites or subgroups with incidence lower than that of colorectal cancer, i.e., about yearly crude incidence rate of cyto/histologically confirmed cases of about 60/100,000 inhabitants.

KEY WORDS
Covid-19; cancer; new diagnoses; period; age; screening.
of 2019 (table I), more evident in males (-15%) than in females (-13%) (figure 1). Concerning age, the difference is minimal for the age group 0-64 years (-8%), more marked for the age 65-74 (-17%), and 80+ (-17%) (figure 2). Looking at specific cancer sites, 423 diagnoses of breast cancer were made (-1%), 188 of lung cancer (-21%), 167 of colorectal cancer (-24%), 179 of prostate cancers (-19%), and 234 haematologic cancers (-8%) (table I).

Regarding the period trend in 2020 (table II), January and February (pre-lockdown) had a similar number of diagnoses for all cancers compared to the same months in 2019 (0%, 95%CI -8% to +8%), while March, April, and May (full lockdown) showed a decrease in the number of diagnoses (-35%, 95%CI -40% to -30%). However, June, July, and August (post-lockdown) showed numbers of diagnoses that were slightly lower than those observed in 2019 (-14%, 95%CI -20% to -6%). For breast cancer, there were more diagnoses during pre-lockdown than in the same period in 2019 (+24%, 95%CI 0% to +55%). Incidence, however, dropped during lockdown (-35%, 95%CI -50% to -16%) but increased slightly in the post-lockdown period (+11%, 95%CI -13% to +43%). Lung cancer showed a decline in incidence throughout lockdown (-22%, 95%CI -44% to +7%), but a decrease was also observed in pre-lockdown (-18%, 95%CI -44% to +19%) and in post-lockdown (-21%, 95%CI -44% to +11%). The number of colorectal cancer diagnoses during pre-lockdown was similar to that of 2019 (-4%, 95%CI -32% to +35%); the large decrease in numbers seen during lockdown (-53%, 95%CI -68% to -32%) immediately returned in post-lockdown to the numbers observed in 2019 (-4%; 95%CI

<table>
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<tr>
<th>MONTH</th>
<th>ALL SITES</th>
<th>BREAST</th>
<th>LUNG</th>
<th>COLORECTAL</th>
<th>PROSTATE</th>
<th>HAEMATOLOGIC</th>
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<td>185</td>
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<td>3548</td>
<td>427</td>
<td>423</td>
<td>237</td>
<td>188</td>
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</table>

Table I. Number of new cancer diagnoses reported by the Reggio Emilia pathology network for all cancer sites and for the most frequent cancer sites, by month and period, 2019 and 2020, Reggio Emilia, Italy.

Figure 1. Number of cyto/histologically confirmed cases by month in 2020 and in 2019, for all sites by sex. Reggio Emilia, Italy.
DISCUSSION

We observed a sharp decrease in the number of cancers diagnosed in Italy during the March-May 2020 lockdown in contrast to the spread of pan-

- 35% to + 42%). There was a sharp decline in prostate cancer diagnoses during lockdown (- 32%, 95%CI - 51% to - 5%), which persisted through post-lockdown (- 26%, 95%CI - 50% to + 9%). Haematologic cancer diagnoses had higher numbers both in the pre- and post-lockdown periods than in 2019, (+ 29%, 95%CI - 10% to + 84% and + 20%, 95%CI - 11% to + 62%, respectively), but registered a notable decrease during lockdown (- 49%, 95%CI - 64% to - 29%). For all tumor sites and for individual sites, percentage changes are shown in figure 3.

Table II. Percentage change for the three periods, pre-lockdown (January, February), lockdown (March, April, May), post-lockdown (June, July, August) in 2020 compared to the same periods in 2019, for all cancers and by cancer site, Reggio Emilia, Italy.

![Table II](image-url)
Two major studies have evaluated the reduction in the number of new cancer diagnoses during the initial period of the COVID-19 pandemic. The first study (9) reported data from the US and the UK to compare the number of cancer diagnoses in January-April 2020 with the number in the same months of 2019. The number of new cases identified in January and February 2020 was slightly higher than that in January-February 2019 (+11.5% and +4.3%, respectively). Cancer cases in March and April 2020 versus March and April 2019 decreased by -22.3% and -65.2%, respectively. Identified patients with melanoma, prostate cancer, or breast cancer displayed the largest decrease, with -51.8%, -49.1%, and -47.7% cases, respectively. The second major study, conducted in the Netherlands (10), also showed a decline in the incidence of cancer, more marked in the age group 80+ years and for breast cancer.

While new diagnoses of cancer increased after lockdown, the number remained slightly lower than in the previous year. The decrease was stronger in over 65 and in females. This trend is appreciable for all cancer sites analyzed, except for lung cancer, where an anomalous peak in diagnoses in March 2020 partially compensated for the drop observed during the following two months of full lockdown. Instead, the drop was particularly evident for the two cancers that are the target of organized screening programs, i.e., breast and colorectal cancers, and for haematologic cancers. Recent studies indicate how much the COVID-19 pandemic has impacted the management of patients with cancer and how the treatment modality has also changed (5-7). Certainly, balancing the harms and benefits of exposing patients at risk of infection and of a worse prognosis due to diagnostic delay has been a daily challenge in these last months (8). The decrease in diagnoses during lockdown was larger for people over 65 and this is consistent with decision making based on the balance of risk of SARS-CoV-2 infection and the benefit of timely diagnosis. In fact, the role of age as risk factor for SARS-CoV-2 infection and COVID-19 severity was clear since the very beginning of pandemic spread in western countries, thus it is not surprising that older people renounced undergoing testing and assessment during lockdown, by their own decision or advised by their physicians.

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Our study confirms that the situation in our province in January and February 2020 was comparable to that in the same period in 2019. This is consistent with the data from the UK: -1.9% and +4.4% in January and in February 2020, respectively (9). In the three months of lockdown we observed a more marked but also a more homogenous reduction in cancer diagnoses in our province (-32%, -36%, and -38% in March, April, and May, respectively) compared to that in other countries: in the USA the reduction was -10.9% and -65.2% for the months of March and April, respectively, and in the UK it was -10.9% and -64.6% (9).
This greater homogeneity probably reflects the duration and the strictness of the lockdown in Italy, which has been recognized as one of the most restrictive and long lasting among the Western world. An interesting feature of our study is that we were able to also examine what happened after the end of lockdown. As soon as lockdown ended, there was a rapid resumption of new diagnoses of cancer (+7% in June, +1% in July). In August 2020, in addition to the usual decrease in diagnoses during this summer month (also observed in 2019), there was a further decrease of 15%. This may have been due to the backlog of vacation time taken by those health workers who could not take time off during the initial phase of the COVID-19 emergency but also to the fact that the patients themselves may have preferred to postpone surgery for a few weeks.

Our study confirms a decline in diagnoses of prostate, breast, and haematologic cancers and an even more considerable decline in colon cancer diagnosis (-53%), certainly due to the strong impact of the suspension of the organized screening program. It is worth noting that the number of diagnoses of colorectal and breast cancer in the post-lockdown period reached the same numbers observed in 2019, once the screening programs resumed, despite slightly fewer monthly invitations compared to the pre-COVID-19 era. It will be interesting to see whether the temporary suspension of the screening programs had any impact on the stage at diagnosis (11, 12).

A delay in tumor diagnosis is also indirectly documented by the lengthening of waiting times for a biopsy (13) and by the delay in receiving histopathological or clinical reports (14). However, while this decrease in diagnoses was unavoidable in the earlier months of the pandemic, it is very important to resume diagnostic pathways as soon as possible; any further delay could result in a large number of excess deaths and of years of life lost (15, 16). This is especially true for those cancer sites that progress rapidly and for which no screening is available; timely diagnosis at symptom onset may make the difference for cancers such as lung and pancreas cancer.

This study includes only the anatomy pathology reports, the most informative source in terms of the specificity of the diagnosis as well as the one with highest sensitivity, considering that over 95% (3) of all incident cancer cases in the Reggio Emilia CR has a microscopic confirmation. A limitation of our study is that the numbers are small because they refer to a small geographical area. Counterweighting this, however, is the fact that ours are population-based data covering an interval of 8 months, including the 3 months following lockdown, when economic and healthcare activities in Italy resumed.

The complete suspension of some clinical activities during the early months of the COVID-19 emergency was the result of many hospital departments being converted into COVID-19 wards to cope with the high numbers of cases. However, while urgent oncological examinations and therapies were never suspended, there was still a drastic decline in new cancer diagnoses, particularly in older people. Indeed, general practitioners referred to the oncologist only those cases that could not be postponed. It is important now to resume diagnostic pathways to limit as much as possible the impact of diagnostic delay on the prognosis of these patients.

**ETHICS**

**Fundings**

There were no institutional or private fundings for this article.

**Conflict of interests**

The authors have declared no conflict of interests.

**Availability of data and material**

All the data supporting the findings of this study are available within the article and can be shared just before a reasonable request to the corresponding author.

**Authors’ contribution**

LM: conceptualization, investigation, writing-original draft, visualization, supervision; PGR: investigation, methodology; IB: writing - review & editing, supervision; RG: conceptualization, supervision; CP: conceptualization, supervision. All authors have read and agreed to the published version of the manuscript.

**Ethical approval and consent to participate**

N/A
REFERENCES